F. No. 26-03/2026-CIR-I (E-183551)
Government of India
Ministry of Agriculture & Farmers' Welfare
Department of Agriculture & Farmers Welfare
Directorate of Plant Protection, Quarantine and Storage
N. H. IV., Faridabad (Haryana)
Website:www.ppqs.gov.in, E-mail:- cibsecy@nic.in

Dated: February, 2026

PUBLIC NOTICE

Subject: Public Notice of agenda item No. 3.2 of 468 th RC meeting at held on 12.01.2026- reg.

This is to inform all stakeholders/registrations/applicants etc. that, as per decision taken by the Registration Committee (RC) vide Agenda Item No. 3.2 during its 468th meeting held on 12.01.2026, wherein the Registration Committee has decided as under:

3.2	Consideration of proforma/template for scrutiny of application under various categories of the Insecticides Act, 1968 for speeding-up of scrutiny process.
	The RC perused the agenda and deliberated the same in details and appreciated the vision and subsequent efforts put by the Sectt. of CIB&RC for devising the templates, spelling out the technical information extracted from the data in addition to the data submitted by the applicant as per the applicable guidelines to be furnished by the applicants w.r.t Chemistry, Toxicology, Bioassay and Packaging in order to facilitate the Sectt. of CIB&RC for speedy examination of applications under various categories of registration within the stipulated time as provided under the statute. The draft templates are annexed as **Annexure-3.2.1**. RC also directed that the approved draft templates developed by the Sectt. of CIB&RC shall be kept on public domain for inviting suggestions of the stakeholders within a period of 30 days from the date of hosting of the minutes. The Sectt. of CIB&RC is also directed to issue a public notice to this effect. The comments/inputs/suggestion so received shall be analyzed and the same may be placed before the RC for appropriate decision and implementation.

In view of the above, a public notice is hereby issued giving fifteen days' time from the date of publication of the notice to all the stakeholders for submission of their objections/suggestions at cibsecy@nic.in on the above proposed initiatives and if no comments/inputs/suggestions received from stake holders in the prescribed timeline, further necessary action will be taken as per the decision of RC.

This issues with the approval of Secretary, CIB&RC.

Digitally signed by
Sangeeta Meena
Date: 12-02-2026
13:00:54
(Sangeeta Meena)
Section Officer, CIR-I&II

ANNEXURE – 3.2.1

Template (Legal for Submission of applications for registration of insecticide)

Application Number: ----------

Category: 9(3B)/9(3)B/F/FIM/TIM/TI/FI, 9(4) TIM

Product Name: ----------

Company Name: M/s ----------

Sr No.	Characteristics	Details to be Inserted / Filled
1.	Form-I dully filled and signed, stamped and verified giving complete details along with requisite fee as applicable.	**Submitted** Insert name of the authorized person as per BOD/partnership deed/Affidavit in case of proprietorship along with the company ID
2.	Copy of BOD Resolution /Affidavit/Partnership deed (Notarized) as applicable	Submitted / Not Submitted
3.	Relevant Affidavit as required under the applicable guidelines duly photographed and executed in accordance with law (Notarized)	Submitted / Not Submitted
4.	Certificate as per category of Industry/ Manufacturing license (Notarized)	Submitted (Insert Date of Issue & the designation of the issuing competent authority) / Not Submitted
5.	PAN Card	Submitted (PAN Number: ----------)/ Not Submitted
6.	Aadhar Card of authorized Person	Submitted (Adhar Number: -------)/ Not Submitted
7.	Incorporation Certificate/ Proprietorship Affidavit/Partnership deed (Notarized) as applicable duly issued / executed in accordance with law	Submitted (Insert Date of Execution / Issuance etc)
8.	Proof of ownership / of manufacturing premises as mentioned in Form-1 duly executed in accordance with law (Notarized)	Submitted (Insert Date of Execution / Authority etc.)/ Not Submitted
9.	Any Other Relevant Information	Please mention (If any)

Template (Chemistry for Submission of applications for registration of Bio-pesticide)

Application Number: ----------

Category: 9(3b)B/F or 9(3)B/F

Product Name: Verticillium ***chlamydosporium*** **1.5%WP (Example)**

CFU Count: ---------- / gm or ml. Min.

Strain No.----------, Accession No----------

Company Name: M/s ABC Private Limited

Biopesticide Composition (Example): -

Chemical Composition (on per cent basis)	Qantity (%W/V)
Name of active ingredients	Verticillium *chlamydosporium* 1.5% CFU count per ml - 1 x 10^8 /ml
Adjuvant (other ingredients, in case of formulation)	-
Glycerine	15%
Aqueous base	Q.S.
Total	100%

The Data Requirements for Microbial Pest Control Agents (MPCA) Pesticides for Entomo-pathogenic/ Entomo-toxicBacteria/ AntagonisticBacteria/ Entomo-pathogenicFungi/ AntagonisticFungi/ Nuclear Polyhedrosis Virus (NPV) & Granulosis Virus (GV)

A. Chemistry:

Sr No.	Characteristics	Formulated product 9(3B)/ 9(3)B/F	Microbial (Antagonistic bacteria, Entomo-pathogenic/Entomo-toxic bacteria, Entomo-pathogenic fungi, Antagonistic fungi, and Baculovirus
10.	Form-I dully filled and signed giving complete details along with requisite fee as applicable (duly Notarized)	R	Submitted (Insert name and address of Company, Adress of premises, name of the authorized person as per BOD/partnership deed/Affidavit in case of proprietorship) Applicable Guidelines:449 RC Category: 9(3b)B/F or 9(3)B/F Strain of Inventor: --------
11.	Undertaking on bio-pesticides composition as Annexure (With duly photograph of the applicant)		Affidavit Submitted (Insert the designation of the issuing competent authority)
12.	Authorization letter from the inventor of strain OR undertaking by the applicant about the name of inventor/source of strain as per Annexure (With duly photograph of the applicant)		Affidavit Submitted or Authorization letter submitted Affidavit Submitted (Insert the designation of the issuing competent authority)
13.	Copy of depositing microbial bio-pesticides strain sample in National Repository with reference code number		Notarized Submitted (Insert Accession Information:, Issuing Authority & Designation):
14.	Systematic name (Genus and species)	R	Ex: Verticillium *chlamydosporium* 1.0% W.P (CFU count: 2x10^6/ gm min.)
15.	Strain name	R	Ex: IIHR-VC-3

16.	Common name, if any	R	
17.	Source of origin	R	Ex: *Applicant has submitted* Source of origin as Annexure-1.1 mentioned by the approved Affidavit format. They grow in the mesophilic temperature range with the optimal temperature between 25-35°C. submitted in biological and chemistry parameters folder
18.	Specification of the product containing Habitat, Physical appearance and morphological description, pH, particle size, suspensibility, miscibility etc parameters	R	Submitted (Insert Habitat, Physical appearance Morphology, pH, CFU, Percent content of the Biocontrol organism in the formulation & nature of biomass, Percentage of carrier/filler, wetting/ dispending agent, stabilizers/ emulsifiers, contaminants/ impurities Moisture content, suspensibility etc,
19.	Isolation of strain &Manufacturing process	R	**Example:** AIR /Water / Soil CROP ex rhizosphere zone (from where isolated) Process of Mfg: in brief
20.	Methods of analysis including Quantitativeanalysis Form and appearance	R*	**Example:** Submitted (Insert Habitat, Physical appearance Morphology, pH, CFU, Percent content of the Biocontrol organism in the formulation & nature of biomass, Percentage of carrier/filler, wetting/ dispending agent, stabilizers/ emulsifiers, contaminants/ impurities Moisture content, suspensibility etc,)
21.	Contaminants Biological	R	Should be Absent
	Pathogenic Contaminants: such as gram-negative bacteria *Salmonella, Shigella, Vibrio* etc.:		Should be Absent
	Other contaminants Chemical/botanical pesticides contaminants: absent.		Should not exceed $1x10^4$/ml or g
	Method of analysis: CFU counts by serial dilution and examination under regular compound research microscope with bright field optics.		Should be submit (Insert Procedure in brief) of the Biocontrol organism in the formulation &
	Plating for contaminants on specific media		Submitted (Insert percent information)
	Entomopathogenic capability on target insects by bioassay.		Should be submit (if required)
	An undertaking should be submitted that strain is indigenous, naturally occurring, not exotic in origin and not genetically modified as per Annexure-1.1.		Affidavit Submitted or Authorization letter submitted Affidavit Submitted (Insert the designation of the issuing competent authority)
22.	Shelf-life claims	R	Shelf-life -claim ---- years.
23.	Data on storage stability as per	NR/R	Example:

<table>
<tr><td></td><td>shelf life claims</td><td></td><td>Shelf-life:- The applicant has submitted the Shelf-life data for 0, 3, 6, 12, 18, 24, and 30 month and the same is generated from Lab M/s ABC Pvt. Ltd.,

Study Initiated date:
Study Completion date:
Report Date:

Batch No:
Date of manufacturing:
Date of Expiry:

<table><tr><td>Duration</td><td>Locations</td></tr><tr><td>0, 3, 6, 12, 18, 24, and 30 months</td><td>Mumbai ,Delhi, Coimbatore</td></tr></table>
Met Data: -
Mumbai:
Delhi:
Coimbatore:</td></tr>
<tr><td>24.</td><td>Composition of the product</td><td>R</td><td>Ex:<table><tr><td>Chemical Composition (on per cent basis)</td><td>Qantity (%W/V)</td></tr><tr><td>Name of active ingredients</td><td>Verticillium chlamydosporium 1.5%
CFU count per ml - 1 x 10^8 /ml</td></tr><tr><td>Adjuvant (other ingredients, in case of formulation)</td><td></td></tr><tr><td>Glycerine</td><td>15%</td></tr><tr><td>Aqueous base</td><td>Q.S.</td></tr><tr><td>Total</td><td>100%</td></tr></table></td></tr>
<tr><td>25.</td><td>Potency of product by bioassay method
(LC 50 (Beta, Delta ,Cry toxin endotoxin content, classification(delta endotoxin)</td><td>NR#</td><td>Ex: Required in the case of entomotoxic bacteria

(delta endotoxin) should not less than 2 %
Beta, Delta, Cryo toxin required as per the guidelines</td></tr>
<tr><td>26.</td><td>CFU/gm or ml</td><td>R</td><td>Ex: 2x10^6/ gm min.)</td></tr>
<tr><td>27.</td><td>POE/Capsule count per ml/g of the product</td><td>R%</td><td>these parameters are required for Virus.</td></tr>
<tr><td>28.</td><td>Adjuvants</td><td>R</td><td>Ex: Glycerine, Aqueous base etc (as mentioned in CC)</td></tr>
<tr><td>29.</td><td>Human pathogens (culture method)</td><td>R</td><td>Ex: Submitted in MoA (Insert name of pathogen if any)</td></tr>
<tr><td>30.</td><td>Percent content of the Bio-control mass/organism in the formulation & nature of biomass.</td><td>R</td><td>Ex: (Insert as mentioned in CC)</td></tr>
<tr><td>31.</td><td>Percentage of carrier/filler, wetting/ dispending agent, stabilizers/ emulsifiers,</td><td>R</td><td>Ex: if any i.e. Talc Powder (as mentioned in CC)</td></tr>
</table>

	contaminants/ impurities etc.		
32.	Moisture content	R	Should not more than 8% (Not applicable in case of liquid formulation)
33.	Contaminants: Pathogenic contaminants such as Salmonella, Shigella, Vibrio and such other microbial, not to exceed 1 x $1o^4$ count per ml or per g of formulation.	R	not to exceed 1 x $1o^4$ count per ml or per g of formulation.
34.	Undertaking for free from Chemical and botanical pesticide contaminants	R	Affidavit Submitted (Insert the designation of the issuing competent authority)
35.	Natural occurrence of the organism	R	**Example:** Naturally occurring bacteria, Strain IIHR-VC-3 was isolated from the rhizosphere soil of tomato collected from Dhamori Village, Ahmednagar, Maharashtra (GPS location: 19.5866 ° N, 74.8152° E) M/s IIHR It's a local isolate and Non-GMO Strain. The Strain was deposited with NCMR. (ITCC, IARI, New Delhi) as Safe Deposit and Accession Number allotted to the strain is ITCC 6888.
36.	PCR / Immunology assays ELISA Test	NR$	Ex: these parameters are required for Entomo-toxic bacteria.
37.	Separation and purification of crystals	NR	NR
38.	A sample for verification (500® g or *500* @ mL as the case may be)		**Information and document to be submit wrt** Two samples of same batch of 500 gm/ml each along with copy of the Fee receipt shall be submitted to Central Insecticides Laboratory, Faridabad for PRV purpose by the applicant for Entomo-toxic bacteria.
	DNA fingerprinting for the strain verification from NBAIM, Maunath Bhanjan.	R	Acknowledgement slip from NBAIM, Mau, Uttar Pradesh (Insert Sample Submission date)
	PRV at Central Insecticide laboratory (CIL)	R	Acknowledgement slip from CIL, DPPQS, Faridabad (Insert Sample Submission date)

*Test procedure and criteria used for identification - morphology, biochemistry, serology/ Immunology for Entomo-toxic-bacteria.

#and$ these parameters are required for Entomo-toxic bacteria.
% these parameters are required for Virus.
@ Two samples of same batch of 500 gm/ml each along with copy of the Fee receipt shall be submitted to Central Insecticides Laboratory, Faridabad for PRY purpose by the applicant for Entomo-toxic bacteria.
POE/Capsule count per ml/g of the product only forNPV.

Viral unit: NPVs $lx10^9$ POB/ml or gm. minimum, GVs: $5x10^9$ capsules /ml or gm mm1mum.
Dual culture to attain at least 50% reduction in target organism (35% for antagonistic bacteria). Bioassay: based on diseased severity and rootcolonization.
Natural occurrence of the organism, Immunology assays: Elisa and Separation and purification of crystals are required for Entomo-toxicbacteria.

Test procedure and criteria used for identification by DNA test (Restriction enzymes analysis test).

Biological assays for determining the LC50 / LD50 of the formulation for Entomo-pathogenic Viruses. Production of Entomo-pathogenic Viruses at commercial- scale was done exclusively *in-vivo* by culturing large number of larvae of host insect and subsequently feeding them with semi-synthetic diet contaminated with virus inoculums in laboratory. Viruses' production *in-vitro* by culturing insect cells in bioreactors was a substitute for labor intensive maintenance of the massive host-insect colony.

Manufacturing process including type of fermentation and biological end products. The microbial cultures are multiplied by liquid solid fermentation. Information pertaining to use of entire mycelia mats with spores separated must be provided in terms of biomass.

Note:

1. Bt products should be labeled with bio potency and (or) toxin content. In addition, the labels will have to contain a measurement of toxin protein as percent protein, referring to the Lepidopteran-active toxin(s) present in thecrystal.
2. The presently used Bt var. kurstaki standard is HD- l-S-1980 and its potency was calculated at 16,000 IUs per milligram of powder (Beegle et al. 1986. Standardization of HD-1-S-1980: US Standard for Lepidopterous-active *Bacillus thuringiensis.* Bulletin Ent. Soc. America 32: 44-45.). This standard strain is now available with PDBC, Bangalore and DOR,Hyderabad.
3. Defined potency and toxin concentration - Bioassay would require the use of an insect species. Normally manufacturers could select *Trichoplusiani/ Helicovelpaarmigerafor* Lepidopteran specific Bt formulations. *Spodoptera* Units (SPU), *Leptinotarsa* Units (LTUs) or International Toxin Units (ITUs) are to be used for denoting a specificinsect.
4. No test for beta exotoxin is required for *Bacillus sphaericus,* because this species is not known to produceexotoxins.
5. The bio-potency of products based on *B. thuringiensis* subsp. *israelensis(Bti)* is compared against a reference strain IPS82, 1884 using early fourth-instar larvae of *Aedes aegypti* (strain Bora Bora). The toxicity of IPS82 has an arbitrarily assigned toxicity of 15,000 ITU/mgpowder.
6. The biopotency of products based on *B. sphaericus(Bsh)* is determined against a reference standard SPH88, strain 2362 using early fourth-instar larvae of Culex pippins (strain Montpellier). The toxicity of SPH88 has an arbitrarily assigned toxicity of 1,700 ITU/mg of the powder (Guidelines for laboratory and field testing of mosquito larvicides, WHO 2005 pp45).
7. The use of alternative bacterial reference powders and/ or strains must be approached cautiously. Such alternatives must be the subject of careful cross- calibration against the reference powders and should be conducted by recognized laboratories and should be made available to anyone who wishes to use, or check, the test with the altemativepowders/strains.
8. Water content should not exceed 8 %, (12% in *Pseudomonas spp)* to preclude premature degradation of theproduct.

ITU/mgpowder.

Annexure-1.1

UNDERTAKING BY MANUFACTURERS OF MICROBIAL PESTICIDES

I,----------,aged-------years, s/o----------, R/o----------and----------of M/s.----------Registered Office at----------do hereby undertake as follows:

(a) That the product----------based on----------, Strain----------, manufactured by M/s.----------and /or imported by M/s.....does not contains any genetically modified organism (GMO) .

(b) That I/We shall abide by the provisions contained in the International Plant Protection Convention with regard to the import of this product.

(c) That I/We shall abide by the provisions in context of International Standards for Phyto-Sanitary Measures-Code of Conduct for the import and release of exotic biological control agents of the International Plant Protection Convention (IPPC), FAO, Rome.

(d) That I/We shall provide the samples of our----------product as and when desired by the competent authorities of Government of India for verification.

(e) That I/We further undertake that in the event of the above product having proved otherwise by any competent authority and resulting in environmental damage, I/We shall inform the Central Insecticides Board and Registration Committee, the relevant authorities for Manufacturing Licensing, Pollution Control and of appropriate District/State/National Level and shall comply with the directions/decisions from them.

(f) That my/our above undertaking is true, and no portion is false and I have concealed nothing relevant to the above matter.

Signature:

Name----------

Designation----------

Seal of the Company--------

Date_____

Place:----------

Signature:

TEMPLATES

Chemistry:

DATA REQUIREMENTS FOR CHEMICAL PESTICIDES: 9(3B) TI

Sr. No.	Parameters
1	Details of source of supply of Technical
2	Chemical Composition (clearly showing claims of purity of active ingredient, impurities or adjuvants, as the case may be) in Form-I and L/L
3	Physical and Chemical Properties of the active ingredient in Technical and adjuvant in case of a formulation
4	Technical Bulletin
5	Product Specification in BIS format/BIS No. if published
6	Method of Analysis
7	Analytical Test Report (ATR) from GLP/NABL accredited laboratory
8	Characterization (Identity Test) of active ingredient by UV-VIS, IR, MS and NMR spectra)
9	Identification& Quantification of Impurities
10	Shelf-life claim
11	Storage Stability Data (samples stored in three varied agro-climatic conditions) for six months in excess of claimed shelf-life along with meteorological data for corresponding period Accelerated Storage Data can be considered for grant of provisional shelf-life. However, in such cases the Certificate of Registration (CR) shall be issued with a validity of two years. Shelf-life claim of up to 2-years or as the case may be (provisionally) be granted to the insecticides with a condition that applicant is required to submit real time / actual storage stability study data in the proposed construct and container of sale for duration of minimum 30 months, within two and half years of submission of application for granting the registration, failing which Registration Certificate shall stand invalid. (As approved in 424 RC dated 23 & 24 December 2020 vide agenda item no. 10.48)
12	Detailed stepwise manufacturing process (provide chemical reactions explained with structural formulae, all applicable reaction other conditions in case of technical grade insecticides including flow sheet diagram).
13	Information about Raw Materials Used along with their source of supply
14	Effluent Treatment method with complete details
15	Legalized letter of consent that the manufacturer is registered the Technical Grade Pesticide/ Insecticide /Formulation and that the consents supplying the Technical Grade Pesticide/ Insecticide/ Formulation to the applicant.
16	Registration Certificate from Designated National Authority (DNA) of the pesticides from source country.
17	In case the supplies are to be made through a supplier, a duly legalized certificate from the exporting manufacturer that the supplier is his authorized agent and that the invoice would originate from the approved source of import (actual manufacturer).Or Principal company or Subsidiary of registrant of pesticide in India or the supplier authorized by manufacturer and mention the full details of the source of import in the invoice.
18	An In-Process sample to be drawn from the R&D/manufacturing facility of applicant in case of technical indigenous manufacture of the insecticide/sample to be submitted in case of technical import$; along with certified reference material (CRM) and standard impurities along with purity certificate in case of technical grade insecticides for preregistration verification in the Central Insecticides Laboratory, Faridabad (CIL). In case of FIM and FI category sample and CRM to be submitted in CIL Faridabad.
19	Methodology for residue estimation in BIS format.

DATA REQUIREMENTS FOR CHEMICAL PESTICIDES: 9(3) TI

Sr. No.	Parameters
1	Details of source of supply of Technical
2	Chemical Composition (clearly showing claims of purity of active ingredient, impurities or adjuvants, as the case may be) in Form-I and L/L
3	Physical and Chemical Properties of the active ingredient in Technical and adjuvant in case of a formulation
4	Technical Bulletin
5	Product Specification in BIS format/BIS No. if published
6	Method of Analysis
7	Analytical Test Report (ATR) from GLP/NABL accredited laboratory
8	Characterization (Identity Test) of active ingredient by UV-VIS, IR, MS and NMR spectra)
9	Identification& Quantification of Impurities
10	Shelf-life claim
11	Storage Stability Data (samples stored in three varied agro-climatic conditions) for six months in excess of claimed shelf-life along with meteorological data for corresponding period Accelerated Storage Data can be considered for grant of provisional shelf-life. However, in such cases the Certificate of Registration (CR) shall be issued with a validity of two years. Shelf-life claim of up to 2-years or as the case may be (provisionally) be granted to the insecticides with a condition that applicant is required to submit real time / actual storage stability study data in the proposed construct and container of sale for duration of minimum 30 months, within two and half years of submission of application for granting the registration, failing which Registration Certificate shall stand invalid. (As approved in 424 RC dated 23 & 24 December 2020 vide agenda item no. 10.48)
12	Detailed stepwise manufacturing process (provide chemical reactions explained with structural formulae, all applicable reaction other conditions in case of technical grade insecticides including flow sheet diagram).
13	Information about Raw Materials Used along with their source of supply
14	Effluent Treatment method with complete details
15	Legalized letter of consent that the manufacturer is registered the Technical Grade Pesticide/ Insecticide /Formulation and that the consents supplying the Technical Grade Pesticide/ Insecticide/ Formulation to the applicant
16	Registration Certificate from Designated National Authority (DNA) of the pesticides from source country.
17	In case the supplies are to be made through a supplier, a duly legalized certificate from the exporting manufacturer that the supplier is his authorized agent and that the invoice would originate from the approved source of import (actual manufacturer). Or Principal company or Subsidiary of registrant of pesticide in India or the supplier authorized by manufacturer and mention the full details of the source of import in the invoice.
18	An In-Process sample to be drawn from the R&D/manufacturing facility of applicant in case of technical indigenous manufacture of the insecticide/sample to be submitted in case of technical import$; along with certified reference material (CRM) and standard impurities along with purity certificate in case of technical grade insecticides for preregistration verification in the Central Insecticides Laboratory, Faridabad (CIL). In case of FIM and FI category sample and CRM to be submitted in CIL Faridabad.
19	Methodology for residue estimation in BIS format.

DATA REQUIREMENT FOR REGISTRATION OF PESTICIDES FOR TECHNICAL IMPORT FROM NEW SOURCE (TI-NEW SOURCE) V/S AGAINST THE MOLECULE REGISTERED UNDER FIM-WRT, FI-WRT AND TI UNDER SECTION 9(3) APPROVED IN 467TH RC.

Sr. No.	Parameters
1	**Source of Supply of Technical**
a	Office address of the Source of Manufacturer with documentary evidence
b	Manufacturing/factory address of the Manufacturer with documentary evidence
c	Copy of registration certificate in the exporting country (Where technical is not granted regn. Proof of registered chemical composition is required)
d	Documentary evidence of manufacturing address to prove that the manufacturing address belongs to the manufacturer
e	Copy of manufacturing license of the manufacturer, (In case license of manufacturing of technical is not issued in the exporting country then a notification from the exporting country that the manufacturing license is not issued to the manufacturer in the country as per law). Other documents to be provided to prove manufacturing.
2	**Chemical Composition**
a	Chemical Identity of technical & Physico- Chemical Properties
b	Physico-Chemical Properties of adjuvants
c	IUPAC name, CAS name & CAS no of Raw materials/adjuvants
d	Technical Bulletin of the product
3	Specification of the product in BIS format
a	Method of Analysis of active ingredients, impurities and adjuvants
b	Analytical Test Report (5 Batch)
c	Identification& Quantification of identifiable Impurities from GLP lab (5 Batch)
4	Shelf-life claim
5	Shelf-life Data from GLP lab (As per OECD requirement) Storage Stability Data (samples stored in three varied agro-climatic conditions) for six months in excess of claimed shelf-life along with meteorological data for corresponding period Accelerated Storage Data can be considered for grant of provisional shelf-life. However, in such cases the Certificate of Registration (CR) shall be issued with a validity of two years. Shelf-life claim of up to 2-years or as the case may be (provisionally) be granted to the insecticides with a condition that applicant is required to submit real time / actual storage stability study data in the proposed construct and container of sale for duration of minimum 30 months, within two and half years of submission of application for granting the registration, failing which Registration Certificate shall stand invalid. (As approved in 424 RC dated 23 & 24 December 2020 vide agenda item no. 10.48)
6	Process of Manufacture
6.1	Information about Raw Materials Used & their Source of Supply
6.2	Step-wise Manufacturing Process, conditions etc.
6.3	Route of formation of impurities, chemical reaction and flow chart diagram
6.4	IUPAC/CAS no. of known/detected Impurities
6.5	Chemical structure of known impurities, Molecular weight of Impurities etc.
6.6	Manufacturing Chemical Equation
6.7	Formula of all raw material, stepwise products etc.
6.8	Flow sheet diagram of process of manufacture

6.9	Effluent Treatment method
7	Documents such as registration certificate / Certificate of DNA giving detailed CC, Manufacturing license or any other approval under any Govt. regulation will be acceptable to support that manufacturer is actual producer
8	Certificate from manufacturer that the supplier is an authorized supplier of the manufacturer, wherever applicable.
9	A test report about the quality of the product from a laboratory as per GLP scheme or from a company of ISO-9000. This requirement will be provided along with first consignment. Thereafter, each consignment should have proper analytical test report of the manufacturer
10	The applicant should provide sample along- with standards sample from the principals/ authorized supplier for chemical verification. In case of technical grade pesticides u/s 9(3), samples of std. impurities are also to be provided for chemical verification. An undertaking is also to be submitted by the importer for readiness for drawl of in-process sample from the manufacturer.
11	Methodology for residue estimation as per BIS format.

DATA REQUIREMENTS FOR CHEMICAL PESTICIDES: 9(3) FI

Sr. No.	Parameters
1	Details of source of supply of Technical
2	Chemical Composition (clearly showing claims of purity of active ingredient, impurities or adjuvants, as the case may be) in Form-I and L/L
3	Physical and Chemical Properties of the active ingredient in Technical and adjuvant in case of a formulation
4	Technical Bulletin
5	Product Specification in BIS format/BIS No. if published
6	Method of Analysis
7	Analytical Test Report (ATR) from GLP/NABL accredited laboratory
8	Shelf-life claim
9	Storage Stability Data (samples stored in three varied agro-climatic conditions) for six months in excess of claimed shelf-life along with meteorological data for corresponding period Accelerated Storage Data can be considered for grant of provisional shelf-life. However, in such cases the Certificate of Registration (CR) shall be issued with a validity of two years. Shelf-life claim of up to 2-years or as the case may be (provisionally) be granted to the insecticides with a condition that applicant is required to submit real time / actual storage stability study data in the proposed construct and container of sale for duration of minimum 30 months, within two and half years of submission of application for granting the registration, failing which Registration Certificate shall stand invalid. (As approved in 424 RC dated 23 & 24 December 2020 vide agenda item no. 10.48)
10	Establishment of Chemical Equivalence
11	Detailed stepwise manufacturing process (provide chemical reactions explained with structural formulae, all applicable reaction other conditions in case of technical grade insecticides including flow sheet diagram).
12	Information about Raw Materials Used along with their source of supply

13	Effluent Treatment method with complete details
14	Legalized letter of consent that the manufacturer is registered the Technical Grade Pesticide/ Insecticide /Formulation and that the consents supplying the Technical Grade Pesticide/ Insecticide/ Formulation to the applicant
15	Registration Certificate from Designated National Authority (DNA) of the pesticides from source country.
16	In case the supplies are to be made through a supplier, a duly legalized certificate from the exporting manufacturer that the supplier is his authorized agent and that the invoice would originate from the approved source of import (actual manufacturer).Or Principal company or Subsidiary of registrant of pesticide in India or the supplier authorized by manufacturer and mention the full details of the source of import in the invoice.
17	An In-Process sample to be drawn from the R&D/manufacturing facility of applicant in case of technical indigenous manufacture of the insecticide/sample to be submitted in case of technical import$; along with certified reference material (CRM) and standard impurities along with purity certificate in case of technical grade insecticides for preregistration verification in the Central Insecticides Laboratory, Faridabad (CIL). In case of FIM and FI category sample and CRM to be submitted in CIL Faridabad.
18	Methodology for residue estimation in BIS format.

S. No. 10. Not required (NR)- For first Registration, Required (R)- for subsequent registration after the first registration.

TEMPLATE FOR SCRUTINY AND VERIFICATION OF FILES U/s 9(3) TIM

- **Category of application:-**
- **Name of the insecticide which applicant proposes to manufacture:-**
- **Status of insecticide in schedule:-**
- **Address of manufacturing site:-**
- **Applicable Gulideline :-**
- **Chemical Name (IUPAC Name, if available):-**
- **Common name:-**
- **CAS Number:-**
- **Establishment of Chemical Equivalence with undertaking (if claimed):-**
- **Chemical composition:-**
- **Characterization (Identity Test) of active ingredient by UV-VIS, IR, MS and NMR spectra):-**
- **Manner of labelling:-**
- **Label and leaflets:-**
- **Physical and Chemical Properties of the active ingredient in Technical and adjuvant in case of a formulation:-**
- **Product Specification in BIS format/BIS No. if published:-**
- **Method of Analysis:-**
- **Chemical Equation:-**
- **Methodology for residue estimation in BIS format:-**
- **Identification & Quantification of identifiable Impurities (In case of registration of Technical product):- D**ata has been generated from NABL/GLP accredited lab as per existing guideline of RC, the following details need to be submit:-

S.no.	Parmeter	Details
1.	Product name	
2.	Testing facility/Name of the Laboratory	
3.	NABL/GLP accreditation status of testing facility	
4.	Study No	
5.	Project no.	
6.	Study initiated date	
7.	Study completion date	
8.	Report submission date	
9.	Test substance details	
10.	Reference item details	
11.	List of chemical and	

	reagents	
12.	Test Methods	
13.	Formula of calculation	
14.	Chromatographic conditions	
15.	Chromatograms with Calculations	
16.	Reference standard COA	

- **Shelf-life claim (Provide shelf-life undertaking):-**
- ***Shelf-life Data/ Storage Stability Data (samples stored in three varied agro-climatic conditions) for six months in excess of claimed shelf-life along with meteorological data for corresponding period:-** If complete data has been submitted from NABL/GLP accredited lab along with the meteorological data as per existing guideline of RC or ASS data along with the Affidavit for the acceptance of ASS data as per decision 424th RC vide agenda item no. 10.48. The following details need to be submit:-

S.no.	Parmeter	Details
1.	Product name	
2.	Testing facility/Name of the Laboratory	
3.	NABL/GLP accreditation status of testing facility	
4.	Study No	
5.	Project no.	
6.	Study initiated date	
7.	Study completion date	
8.	Report submission date	
9.	Batch no.	
10.	Test substance details	
11.	Experimental details	
12.	Test methodology	
13.	Apparatus and materials	
14.	Temperature conditions inside the test chamber	
15.	Summary report of different agroclimatic conditions	
16.	Result of 0^{th} day and 14^{th} day analysis and calculation details (In case of ASS data has been	

	submitted) (for provisional shelf life)	
17.	Physico-chemical properties	
18.	Formula of calculation	
19.	Chromatograms with Calculations	

- **Process of Manufacture:-**

S.no.	Parmeter	Details
1.	Information about Raw Materials Used	
2.	Their Source of Supply	
3.	Step-wise Manufacturing Process	
4.	Effluent Treatment method with complete details	
5.	Flow sheet diagram of process of manufacture	
6.	chemical reactions explained with structural formulae, all applicable reaction other conditions	

- **Analytical test report:- D**ata has been submitted from NABL/GLP accredited lab as per existing guideline of RC the following details need to be submit:-

S.no.	Parmeter	Details
1.	Product name	
2.	Testing facility/Name of the Laboratory	
3.	NABL/GLP	

	accreditation status of testing facility	
4.	Study No	
5.	Project no.	
6.	Study initiated date	
7.	Study completion date	
8.	Report submission date	
9.	Batch no.	
10.	Test substance details	
11.	Reference item details	
12.	List of chemical and reagents	
13.	Test Methods	
14.	Formula of calculation	
15.	Chromatographic conditions	
16.	Chromatograms with Calculations	
17.	Reference standard COA	

- **The applicant should provide the sample of standards technical from principal/authorized dealers for chemical verification, In case of technical grade pesticide u/s 9(3), reference standard of impurities are also to be provided for chemical verification.**
- **An In-Process sample to be drawn from the R&D/manufacturing facility of applicant in case of technical indigenous manufacture of the insecticide/sample to be submitted in case of technical import; along with certified reference material (CRM) and standard impurities along with purity certificate in case of technical grade insecticides for preregistration verification in the Central Insecticides Laboratory, Faridabad (CIL).**

TEMPLATE FOR SCRUTINY AND VERIFICATION OF FILES U/s 9(3) FIM

- **Category of application:-**
- **Name of the insecticide which applicant proposes to manufacture:-**
- **Status of insecticide in schedule:-**
- **Address of manufacturing site:-**
- **Applicable Gulideline :-**
- **Chemical Name (IUPAC Name, if available):-**
- **Common name:-**
- **CAS Number:-**
- **Establishment of Chemical Equivalence with undertaking (if claimed):-**
- **In case of formulation, the source of supply of technical grade material and status of registration in India:-**
- **Chemical composition:-**
- **Manner of labelling:-**
- **Label and leaflets:-**
- **Physical and Chemical Properties of the active ingredient in Technical and adjuvant in case of a formulation {Adjuvant(s) shall be mentioned by their common names(s) and not by code names or numbers and their complete chemical identity shall be provided}:-**
- **Product Specification in BIS format/BIS No. if published:-**
- **Method of Analysis (In case of formulation of pre-mix combination product having three active ingredients, preferably a single method of analysis must be used, otherwise applicant should be submitted technical justification for using more than one method of analysis) :-**
- **Methodology for residue estimation in BIS format:-**
- **Shelf-life claim (Provide shelf-life undertaking):-**
- ***Shelf-life Data/ Storage Stability Data (samples stored in three varied agro-climatic conditions) for six months in excess of claimed shelf-life along with meteorological data for corresponding period:-** If complete data has been submitted from NABL/GLP accredited lab along with the meteorological data as per existing guideline of RC or ASS data along with the Affidavit for the acceptance of ASS data as per decision 424th RC vide agenda item no. 10.48. The following details need to be submit:-

S.no.	Parmeter	Details
20.	Product name	
21.	Testing facility/Name of the Laboratory	

22.	NABL/GLP accreditation status of testing facility	
23.	Study No	
24.	Project no.	
25.	Study initiated date	
26.	Study completion date	
27.	Report submission date	
28.	Batch no.	
29.	Test substance details	
30.	Experimental details	
31.	Test methodology	
32.	Apparatus and materials	
33.	Temperature conditions inside the test chamber	
34.	Summary report of different agroclimatic conditions	
35.	Result of 0^{th} day and 14^{th} day analysis and calculation details (if ASS data has been submitted)	
36.	Physico-chemical properties	
37.	Formula of calculation	
38.	Chromatograms with Calculations	

- **Process of Manufacture:-**

S.no.	Parmeter	Details
7.	Information about Raw Materials Used	
8.	Their Source of Supply	
9.	Step-wise Manufacturing Process	
10.	Effluent Treatment method with complete details	
11.	Flow sheet diagram of process of manufacture	
12.	chemical reactions explained with structural formulae, all applicable reaction other conditions	

- **Analytical test report:- D**ata has been submitted from NABL/GLP accredited lab as per existing guideline of RC the following details need to be submit:-

S.no.	Parmeter	Details
18.	Product name	
19.	Testing facility/Name of the Laboratory	
20.	NABL/GLP accreditation status of testing facility	
21.	Study No	
22.	Project no.	
23.	Study initiated date	
24.	Study completion date	
25.	Report submission date	
26.	Batch no.	
27.	Test substance details	
28.	Reference item details	
29.	List of chemical and reagents	
30.	Test Methods	
31.	Formula of calculation	
32.	Chromatographic conditions	
33.	Chromatograms with Calculations	
34.	Reference standard COA	

- **Acknowledgement copy of submission of sample and CRM in CIL Faridabad:-**

PROFORMA FOR 9(3) FORMULATION IMPORT(FI)/ FORMULATION INDIGENOUS MANUFACTURE (FIM)/Label Expansion,TI,TIM.

General Information

1.	Application category	:	
2.	Chemical Name	:	
3.	Crop	:	
4.	Disease with scientific name	:	
5.	Applicant details	:	
6.	Label claim	:	

	Crop	Common name of the pests	Dosage per hectare		Dilution in water	Waiting period
			A.i. (g)	Formulation (ml)		

Treatment details

T. No	Treatments	Dose / ha		Dilution in water L/ha
		Technical (g a.i.)	Formulation (ml or gm)	
T1.				
T2.				
T3.				
T4.				
T5.				
T6.				
T7.				
T8.				
T9.	Untreated Control	-	-	-

Experimental Details

Details	Location 1	Location 2	Location 3
Year and Season			
Variety / Hybrid			
Plot size			
Date of transplanting			
Number & date of treatment imposition			
Number of treatments			
Number of replications			
Design of experiments			

Observations recorded			

1. BIO-EFFICACY DATA AGAINST DISEASE

Table 1. Data requirement for Bioefficacy of (Chemical Name) against (Pest species) in (Crop Name)

T. No	Location 1						Location 2						Location 3					
	Season 1			Season 2			Season 1			Season 2			Season 1			Season 2		
	PDI (BS)	PDI (DAA)	% ROC	PDI (BS)	PDI (DAA)	% ROC	PDI (BS)	PDI (DAA)	% ROC	PDI (BS)	PDI (DAA)	% ROC	PDI (BS)	PDI (DAA)	% ROC	PDI (BS)	PDI (DAA)	% ROC
T1																		
T2																		
T3																		
T4																		
T5																		
T6																		
T7																		
T8																		
S.E.m ±																		
C.D. at 5%																		

BS: Before Spray; PDI- Percent Disease Index/Incidence/Intensity *DAA: Days after Application (Fill the data pertinent to the last observation); % ROC: % cent reduction over control

2. YIELD DATA

Table 2. Data requirement for Yield (Kg/ha or Q/ha or T/ha) from various locations:

T. No	Location 1		Location 2		Location 3	
	Season 1	Season 2	Season 1	Season 2	Season 1	Season 2
T1						
T2						
T3						
T4						
T5						
T6						
T7						
T8						
S.E.m ±						
C.D. at 5%						

2. PHYTOTOXICITY

Table 3. Data requirement for phytotoxicity of (Chemical Name) against (Pest species) in (Crop Name)

T. No	Location 1												Location 2												Location 3											
	Season 1						Season 2						Season 1						Season 2						Season 1						Season2					
	Phytotoxicity grade (0-10 Scale)												Phytotoxicity grade (0-10 Scale)												Phytotoxicity grade (0-10 Scale)											
	DAA						DAA						DAA						DAA						DAA						DAA					
	0	1	3	5	7	10	0	1	3	5	7	10	0	1	3	5	7	10	0	1	3	5	7	10	0	1	3	5	7	10	0	1	3	5	7	10
T1																																				
T2																																				
T3																																				
T4																																				
T5																																				
T6																																				
T7																																				
T8																																				
S.E.m ±																																				
C.D. at 5%																																				

DAA: Days After Application; Observations should be recorded on 0,1,3,5,7, and 10 days after treatment against necrosis, chlorosis, epinasty, hyponasty, leaf tip injury, leaf surface injury, wilting and vein clearing.

4. PERSISTENCE IN SOIL(Not required in Label Expansion)

Institute where the residue analysis carried out	:	
Treatment details (i.e. T0, T1 & T2)	:	
Types of soil samples collected	:	
Instruments used for the analysis	:	
Limit of Detection (LOD)	:	
Limit of Quantification	:	

Soil type	Half – life (DT_{50} In Days)	
	T1	T2
Sandy loam		
Clay		
Loam		
Silt Clay		

Sampling occasion days	Average Residue (µg/g)											
	Sandy Loam			Clay			Loam			Silt Clay		
	T0	T1	T2	T0	T1	T2	T0	T1	T2	T0	T1	T2
0												
1												
3												
5												

10												
15												

5. PERSISTENCE IN WATER(Not required in Label Expansion)

Institute where the residue analysis carried out	:	
Treatment details (i.e. T0, T1 & T2)	:	
Types of water samples collected	:	
Instruments used for the analysis	:	
Limit of Detection (LOD)	:	
Limit of Quantification	:	

Water type	Half – life (DT_{50} In Days)	
	T1	T2
Acidic Water		
Neutral Water		
Basic Water		

Sampling occasion days	Average Residue (µg/g)								
	Acidic (pH = 4.0)			Neutral (pH = 7.0)			Basic (pH = 9.0)		
	T0	T1	T2	T0	T1	T2	T0	T1	T2
0									
1									
3									
5									

10									
15									

6. PERSISTENCE IN PLANT

Institute where the residue analysis carried out	:	
Crop (i.e. name of the crop) and Samples (i.e. parts of plant)		
Variety		
Date of Transplanting	:	
Date of Application	:	
Treatment details (i.e. T0, T1 & T2)	:	
Instruments used for the analysis	:	
Limit of Detection (LOD)	:	
Limit of Quantification (LOQ)	:	

Half – life (DT_{50} In Days)	
T1	**T2**

Sampling occasion days	**Average Residue (µg/g)**		
	T0	**T1**	**T2**
0			
1			
3			
5			

10			
15			

6. RESIDUES IN PLANT AND SOIL

	Location 1	Location 2	Location 3	Location 4
Institute name & address				
Variety				
Transplanting date				
Date of Application				
Sampling date				
Treatment details				
Plant part used for analysis				
Instruments used for analysis				
Limit of Determination				
Limit of Quantification				

Sampling occasion days	id			Residue (µg/g)								
	Location 1			Location 2			Location 3			Location 4		
	T0	T1	T2	T0	T1	T2	T0	T1	T2	T0	T1	T2
Soil												

Other informations required for scrutiny

Compatibility with other chemicals if claimed	:	
Residue tolerance limit fixed by foreign countries	:	
Registration status in foreign countries	:	
Germination % and Effect on Beneficial Soil micro flora and fauna (In case of seed treatment)	:	
Form – I	:	
Copy of RTT Permit	:	Only applicable in FI &TI
MRL Proforma in duplicate with CD/pendrive	:	
Label & Leaflets (7 copies) in Hindi & Language	:	
Copy of 9(3) registration certificate		Required only for Label Expansion
Translocation in Plants		Only applicable in TIM &TI
Metabolism(Soil, Plant , Water)		Only applicable in TIM &TI

For 9(4) TIM; only Maximum Residue Limit values.

For 9(4) Endorsement: RC reference in which 9(3) application was approved and MRL fixation.

Template for Packaging Discipline for Applications U/s 9(3)-TI

S. No.	Parameters	Reply/Response of applicant
1.	Form I	
2.	Labels and Leaflets per IR-1971, all fields (as applicable) and as amended from time to time	
3.	Manner of labeling and Leaflet	
4.	Type of packaging (Ultra small, small or Big whichever is applicable)	
5.	Manner of packaging Manner of Import packaging with details UN IMDG Code, packaging group, Hazard class, (a)Primary Packing (b) Secondary Packing (c) Transport Packing	
6.	Specification for primary, Secondary and Transport packages (whichever is applicable) Specification shall include: 1) capacity, 2) thickness, 3) shape, 4) size (LxWxH), 5) brimful capacity, 6) sealing system, 7) Material of construction, Grade, 8) Closure system, 9) Gross/net weight of primary, secondary and transport packing,	
7.	Details of packaging material and its compatibility with content: Container Content Compatibility (CCC) test from NABL accrediated labs as per standard test protocols/BIS specifications. a) Name of the Laboratory : b) NABL Status (Validity of NABL Certificate): c) Period of the Study : From ____ to _____ d) BIS specification/protocol followed : e) Number of Samplesset taken for Test : f) Temperature maintained during the test : g) Primary Packing taken for test : h) Test result of AI before the test : i) Test result of AI after the test : j) Test result of Packaging material before test : k) Test result of Packaging material after test :	
7	Details of packaging material and its compatibility with content: l) Final Conclusion of the Study :	

8.	Performance of container with content during storage stability test(Shelf life Study) at three different agro climate conditions for 30 months/ ASS Data for a.i. content and physico chemical properties of the product and test parameter on container:-- 1) Name of the Laboratory : 2) NABL/GLP Status (Validity of NABL/GLP Certificate): 3) Name of the Study - Shelf life Study / ASS: _____ 4) Period of the Study : From ____ to _____ 5) Number of Months/Days : 6) Three Agro-climatic locations selected for Shelf life Study: Location 01 :_____ Location 02 :_____ Location 03:_____ 7) BIS specification followed : 8) Primary Packing taken for test : 9) Test result of AI before the test : 10) Test result of AI after the test (for ASS) : 11) Zero Month Test result of AI after the test : Location 12) 06 Months Test result of AI after the test : 13) 12 Months Test result of AI after the test : 14) 18 Months Test result of AI after the test : 15) 24 Months Test result of AI after the test : 16) 30 Months Test result of AI after the test : Final Conclusion of Test results of AI after 30 Months : 17) Test result of Packaging Material before the test : 18) Test result of Packaging Material after the test(for ASS) : 19) Zero Month Test result of Packaging Material after the test : 20) 06 Months Test result of Packaging Material after the test : 21) 12 Months Test result of Packaging Materialafter the test : 22) 18 Months Test result of Packaging Material after the test : 23) 24 Months Test result of Packaging Material after the test : 24) 30 Months Test result of Packaging Material after the test : Final Conclusion of Test results of Packaging Material after 30 Months : 25) Metrological data of 3 locations: Name of the Institute/Organization of Metrological data: a) Location 01 :_____ b) Location 02 :_____ c) Location 03:_____ 26) Average Temperature range during the entire Shelf Life Study:	

	(i) Location 01 :_____ Zero Month : _____ to _____ ℃ 06 Months : _____ to _____ ℃ 12 Months : _____ to _____ ℃ 18 Months: _____ to _____ ℃ 24 Months : _____ to _____ ℃ 30 Months : _____ to _____ ℃ (ii) Location 02 :_____ Zero Month : _____ to _____ ℃ 06 Months : _____ to _____ ℃ 12 Months : _____ to _____ ℃ 18 Months: _____ to _____ ℃ 24 Months : _____ to _____ ℃ 30 Months : _____ to _____ ℃ (iii) Location 03 :_____ Zero Month : _____ to _____ ℃ 06 Months : _____ to _____ ℃ 12 Months : _____ to _____ ℃ 18 Months: _____ to _____ ℃ 24 Months : _____ to _____ ℃ 30 Months : _____ to _____ ℃	
9.	Transport worthiness test (TWT) for proposed transport packing from NABL accrediated lab. 1) Name of the Laboratory : 2) NABL/GLP Status (Validity of NABL/GLP Certificate): 3) Name of the Study - _____ 4) Period of the Study : From ____ to _____ 5) Number of Months/Days : 6) BIS specification followed : 7) Primary Packing taken for test : 8) Secondary Packaging Taken for Test : 9) Transport Packing Taken for test : 10) Whether the primary,secondary and transport packing taken for tests are same as proposed in Manner of Packing : Yes/No 11) Number of Samples taken for Test : !2) Details of the Tests Conducted :(to cover all type of proposed packing combinations -(Primary+Secondary+Transport) **A) Vertical Drop Test** a) BIS No. : b) Scheme for Dropping Test : c) Test results :	

	B) Stack Load Test : a) BIS No. : b)Scheme for Stack Load Test : c) Test results : C) **Vibration Leak Test :** a) BIS No. : b) Scheme for Vibration Test : c) Test results : D) **Rolling Test:** a) BIS No. : b) Scheme for Rolling Test : c) Test results : **E) Inclined Impact Test :** a) BIS No. : b) Scheme for Rolling Test : c) Test results : F) Any other Packaging Test under TWT as per IMDG / BIS /RC requirements : a) BIS No. : b) Scheme for Vibration Test : b) Test results :	

Template for Packaging Discipline for Applications U/s 9(3)-FI

S. No.	Parameters	Reply/Response of applicant
1.	Form I	
2.	Labels and Leaflets per IR-1971, all fields (as applicable) and as amended from time to time	
3.	Manner of labelling and Leaflet	
4.	Type of packaging (Ultra small, small or Big whichever is applicable)	
5.	Manner of packaging: Manner of Import packaging with details UN IMDG Code, packaging group, Hazard class, (a)Primary Packing (b) Secondary Packing (c) Transport Packing Manner of Re-packing: (a)Primary Packing (b) Secondary Packing (c) Transport Packing	
6.	Specification for primary, Secondary and Transport packages (whichever is applicable) Specification shall include: 1) capacity, 2) thickness, 3) shape, 4) size (LxWxH), 5) brimful capacity, 6) sealing system, 7) Material of construction, Grade, 8) Closure system, 9) Gross/net weight of primary, secondary and transport packing,	
7.	Details of packaging material and its compatibility with content: Container Content Compatibility (CCC) test from NABL accrediated labs as per standard test protocols/BIS specifications. a) Name of the Laboratory : b) NABL Status (Validity of NABL Certificate): c) Period of the Study : From ____ to _____ d) BIS specification/protocol followed : e) Number of Samplesset taken for Test : f) Temperature maintained during the test : g) Primary Packing taken for test : h) Test result of AI before the test :	

	i) Test result of AI after the test : j) Test result of Packaging material before test : k) Test result of Packaging material after test : l) Final Conclusion of the Study :	
8.	Performance of container with content during storage stability test(Shelf life Study) at three different agro climate conditions for 30 months/ ASS Data for a.i. content and physico chemical properties of the product and test parameter on container:-- 1) Name of the Laboratory : 2) NABL/GLP Status (Validity of NABL/GLP Certificate): 3) Name of the Study - Shelf life Study / ASS: _____ 4) Period of the Study : From ____ to _____ 5) Number of Months/Days : 6) Three Agro-climatic locations selected for Shelf life Study: 7) Location 01 :_____ 8) Location 02 :_____ 9) Location 03:_____ 10) BIS specification followed : 11) Primary Packing taken for test : 12) Test result of AI before the test : 13) Test result of AI after the test (for ASS) : 14) Zero Month Test result of AI after the test : 15) Location 16) 06 Months Test result of AI after the test : 17) 12 Months Test result of AI after the test : 18) 18 Months Test result of AI after the test : 19) 24 Months Test result of AI after the test : 20) 30 Months Test result of AI after the test : 21) Final Conclusion of Test results of AI after 30 Months : 22) Test result of Packaging Material before the test : 23) Test result of Packaging Material after the test(for ASS) : 24) Zero Month Test result of Packaging Material after the test : 25) 06 Months Test result of Packaging Material after the test : 26) 12 Months Test result of Packaging Materialafter the test : 27) 18 Months Test result of Packaging Material after the test : 28) 24 Months Test result of Packaging Material after the test :	

Template for Packaging Discipline for Applications U/s 9(3)-TIM

S. No.	Parameters	Reply/Response of applicant
1.	Form I	
2.	Labels and Leaflets per IR-1971, all fields (as applicable) and as amended from time to time	
3.	Manner of labeling and Leaflet	
4.	Type of packaging (Ultra small, small or Big whichever is applicable)	
5.	Manner of packaging: (a)Primary Packing (b) Secondary Packing (c) Transport Packing	
6.	Specification for primary, Secondary and Transport packages (whichever is applicable) Specification shall include: a) capacity, b) thickness, c) shape, d) size (LxWxH), e) brimful capacity, f) sealing system, g) Material of construction, Grade, h) Closure system, i) Gross/net weight of primary, secondary and transport packing,	
7.	Details of packaging material and its compatibility with content: Container Content Compatibility (CCC) test from NABL accrediated labs as per standard test protocols/BIS specifications. 1) Name of the Laboratory : 2) NABL Status (Validity of NABL Certificate): 3) Period of the Study : From ____ to _____ 4) BIS specification/protocol followed : 5) Number of Samplesset taken for Test : 6) Temperature maintained during the test : 7) Primary Packing taken for test : 8) Test result of AI before the test : 9) Test result of AI after the test : 10) Test result of Packaging material before test : 11) Test result of Packaging material after test : 12) Final Conclusion of the Study :	

	29) 30 Months Test result of Packaging Material after the test : 30) Final Conclusion of Test results of Packaging Material after 30 Months : 31) Metrological data of 3 locations: Name of the Institute/Organization of Metrological data: Location 01 :_____ Location 02 :_____ Location 03:_____ 32) Average Temperature range during the entire Shelf Life Study: (iv) Location 01 :_____ Zero Month : _____ to _____ ℃ 06 Months : _____ to _____ ℃ 12 Months : _____ to _____ ℃ 18 Months: _____ to _____ ℃ 24 Months : _____ to _____ ℃ 30 Months : _____ to _____ ℃ (v) Location 02 :_____ Zero Month : _____ to _____ ℃ 06 Months : _____ to _____ ℃ 12 Months : _____ to _____ ℃ 18 Months: _____ to _____ ℃ 24 Months : _____ to _____ ℃ 30 Months : _____ to _____ ℃ (vi) Location 03 :_____ Zero Month : _____ to _____ ℃ 06 Months : _____ to _____ ℃ 12 Months : _____ to _____ ℃ 18 Months: _____ to _____ ℃ 24 Months : _____ to _____ ℃ 30 Months : _____ to _____ ℃	
9.	Transport worthiness test (TWT) for proposed transport packing from NABL accrediated lab. 1) Name of the Laboratory : 2) NABL/GLP Status (Validity of NABL/GLP Certificate): 3) Name of the Study - _____ 4) Period of the Study : From ____ to _____	

	5) Number of Months/Days : 6) BIS specification followed : 7) Primary Packing taken for test : 8) Secondary Packaging Taken for Test : 9) Transport Packing Taken for test : 10) Whether the primary,secondary and transport packing taken for tests are same as proposed in Manner of Packing : Yes/No 11) Number of Samples taken for Test : 12) Details of the Tests Conducted :(to cover all type of proposed packing combinations -(Primary+Secondary+Transport) **A. Vertical Drop Test** BIS No. : Scheme for Dropping Test : Test results : **B. Stack Load Test :** a) BIS No. : b)Scheme for Stack Load Test : c) Test results : C. **Vibration Leak Test :** a) BIS No. : b) Scheme for Vibration Test : c) Test results : D. **Rolling Test:** a) BIS No. : b) Scheme for Rolling Test : c) Test results : **E. Inclined Impact Test :** a) BIS No. : b) Scheme for Rolling Test : c) Test results : F. Any other Packaging Test under TWT as per IMDG / BIS /RC requirements : a) BIS No. : b) Test results :	

8.	Performance of container with content during storage stability test(Shelf life Study) at three different agro climate conditions for 30 months/ ASS Data for a.i. content and physico chemical properties of the product and test parameter on container:-- 1. Name of the Laboratory : 2. NABL/GLP Status (Validity of NABL/GLP Certificate): 3. Name of the Study - Shelf life Study / ASS: _____ 4. Period of the Study : From ____ to _____ 5. Number of Months/Days : 6. Three Agro-climatic locations selected for Shelf life Study: 7. Location 01 :_____ 8. Location 02 :_____ 9. Location 03:_____ 10. BIS specification followed : 11. Primary Packing taken for test : 12. Test result of AI before the test : 13. Test result of AI after the test (for ASS) : 14. Zero Month Test result of AI after the test : 15. Location 16. 06 Months Test result of AI after the test : 17. 12 Months Test result of AI after the test : 18. 18 Months Test result of AI after the test : 19. 24 Months Test result of AI after the test : 20. 30 Months Test result of AI after the test : 21. Final Conclusion of Test results of AI after 30 Months : 22. Test result of Packaging Material before the test : 23. Test result of Packaging Material after the test(for ASS) : 24. Zero Month Test result of Packaging Material after the test : 25. 06 Months Test result of Packaging Material after the test : 26. 12 Months Test result of Packaging Materialafter the test : 27. 18 Months Test result of Packaging Material after the test : 28. 24 Months Test result of Packaging Material after the test : 29. 30 Months Test result of Packaging Material after the test : 30. Final Conclusion of Test results of Packaging Material after 30 Months :	

	31. Metrological data of 3 locations: Name of the Institute/Organization of Metrological data: Location 01 :_____ Location 02 :_____ Location 03:_____ 32. Average Temperature range during the entire Shelf Life Study: Location 01 :_____ Zero Month : _____ to _____℃ 06 Months : _____ to _____℃ 12 Months : _____ to _____℃ 18 Months: _____ to _____℃ 24 Months : _____ to _____℃ 30 Months : _____ to _____℃ Location 02 :_____ Zero Month : _____ to _____℃ 06 Months : _____ to _____℃ 12 Months : _____ to _____℃ 18 Months: _____ to _____℃ 24 Months : _____ to _____℃ 30 Months : _____ to _____℃ Location 03 :_____ Zero Month : _____ to _____℃ 06 Months : _____ to _____℃ 12 Months : _____ to _____℃ 18 Months: _____ to _____℃ 24 Months : _____ to _____℃ 30 Months : _____ to _____℃	
9.	Transport worthiness test (TWT) for proposed transport packing from NABL accrediated lab. 1) Name of the Laboratory : 2) NABL/GLP Status (Validity of NABL/GLP Certificate): 3) Name of the Study - _____ 4) Period of the Study : From ____ to _____ 5) Number of Months/Days : 6) BIS specification followed : 7) Primary Packing taken for test : 8) Secondary Packaging Taken for Test : 9) Transport Packing Taken for test : 10) Whether the primary,secondary and transport	

	packing taken for tests are same as proposed in Manner of Packing : Yes/No 11) Number of Samples taken for Test : 12) Details of the Tests Conducted :(to cover all type of proposed packing combinations -(Primary+Secondary+Transport) **A. Vertical Drop Test** BIS No. : Scheme for Dropping Test : Test results : **B.Stack Load Test :** a) BIS No. : b)Scheme for Stack Load Test : c) Test results : **C.Vibration Leak Test :** a) BIS No. : b) Scheme for Vibration Test : c) Test results : **D.Rolling Test:** a) BIS No. : b) Scheme for Rolling Test : c) Test results : **E.Inclined Impact Test :** a) BIS No. : b) Scheme for Rolling Test : c) Test results : F.Any other Packaging Test under TWT as per IMDG / BIS /RC requirements : a) BIS No. : b) Test results :	

Template for Packaging Discipline for Applications U/s 9(3)-FIM

S. No.	Parameters	Reply/Response of applicant
1.	Form I	
2.	Labels and Leaflets per IR-1971, all fields (as applicable) and as amended from time to time	
3.	Manner of labeling and Leaflet	
4.	Type of packaging (Ultra small, small or Big whichever is applicable)	
5.	Manner of packaging: (a)Primary Packing (b) Secondary Packing (c) Transport Packing	
6.	Specification for primary, Secondary and Transport packages (whichever is applicable) Specification shall include:	applicant
	a) capacity, b) thickness, c) shape, d) size (LxWxH), e) brimful capacity, f) sealing system, g) Material of construction, Grade, h) Closure system, i) Gross/net weight of primary, secondary and transport packing,	
7.	Details of packaging material and its compatibility with content: Container Content Compatibility (CCC) test from NABL accrediated labs as per standard test protocols/BIS specifications. 1) Name of the Laboratory : 2) NABL Status (Validity of NABL Certificate): 3) Period of the Study : From ____ to _____ 4) BIS specification/protocol followed : 5) Number of Samplesset taken for Test : 6) Temperature maintained during the test : 7) Primary Packing taken for test : 8) Test result of AI before the test : 9) Test result of AI after the test : 10) Test result of Packaging material before test : 11) Test result of Packaging material after test :	

	12) Final Conclusion of the Study :	
8.	Performance of container with content during storage stability test(Shelf life Study) at three different agro climate conditions for 30 months/ ASS Data for a.i. content and physico chemical properties of the product and test parameter on container:-- 1. Name of the Laboratory : 2. NABL/GLP Status (Validity of NABL/GLP Certificate): 3. Name of the Study - Shelf life Study / ASS: _____ 4. Period of the Study : From ____ to _____ 5. Number of Months/Days : 6. Three Agro-climatic locations selected for Shelf life Study: 7. Location 01 :_____ 8. Location 02 :_____ 9. Location 03:_____ 10. BIS specification followed : 11. Primary Packing taken for test : 12. Test result of AI before the test : 13. Test result of AI after the test (for ASS) : 14. Zero Month Test result of AI after the test : 15. Location 16. 06 Months Test result of AI after the test : 17. 12 Months Test result of AI after the test : 18. 18 Months Test result of AI after the test : 19. 24 Months Test result of AI after the test : 20. 30 Months Test result of AI after the test : 21. Final Conclusion of Test results of AI after 30 Months : 22. Test result of Packaging Material before the test : 23. Test result of Packaging Material after the test(for ASS) : 24. Zero Month Test result of Packaging Material after the test : 25. 06 Months Test result of Packaging Material after the test : 26. 12 Months Test result of Packaging Material after the test : 27. 18 Months Test result of Packaging Material after the test : 28. 24 Months Test result of Packaging Material after the test : 29. 30 Months Test result of Packaging Material after the test :	

	30. Final Conclusion of Test results of Packaging Material after 30 Months : 31. Metrological data of 3 locations: Name of the Institute/Organization of Metrological data: Location 01 :_____ Location 02 :_____ Location 03:_____ 32. Average Temperature range during the entire Shelf Life Study: Location 01 :_____ Zero Month : _____ to _____℃ 06 Months : _____ to _____℃ 12 Months : _____ to _____℃ 18 Months: _____ to _____℃ 24 Months : _____ to _____℃ 30 Months : _____ to _____℃ Location 02 :_____ Zero Month : _____ to _____℃ 06 Months : _____ to _____℃ 12 Months : _____ to _____℃ 18 Months: _____ to _____℃ 24 Months : _____ to _____℃ 30 Months : _____ to _____℃ Location 03 :_____ Zero Month : _____ to _____℃ 06 Months : _____ to _____℃ 12 Months : _____ to _____℃ 18 Months: _____ to _____℃ 24 Months : _____ to _____℃ 30 Months : _____ to _____℃	
9.	Transport worthiness test (TWT) for proposed transport packing from NABL accrediated lab. 1) Name of the Laboratory : 2) NABL/GLP Status (Validity of NABL/GLP Certificate): 3) Name of the Study - _____ 4) Period of the Study : From ____ to _____ 5) Number of Months/Days : 6) BIS specification followed : 7) Primary Packing taken for test :	

Template for Packaging Discipline for Applications U/s 9(3)-Bio-Pesticides: Primary culture/mother culture & Formulated product

S. No.	Parameters	Reply/Response of applicant
1.	Form I	
2.	Labels and Leaflets per IR-1971, all fields (as applicable) and as amended from time to time	
3.	Manner of labeling and Leaflet	
4.	Type of packaging (Ultra small, small or Big whichever is applicable)	
5.	Manner of packaging: (a)Primary Packing (b) Secondary Packing (c) Transport Packing	
6.	Specification for primary, Secondary and Transport packages (whichever is applicable) Specification shall include: 1) capacity, 2) thickness, 3) shape, 4) size (LxWxH), 5) brimful capacity, 6) sealing system, 7) Material of construction, Grade, 8) Closure system, 9) Gross/net weight of primary, secondary and transport packing,	
7.	Details of packaging material and its compatibility with content: Container Content Compatibility (CCC) test from NABL accrediated labs as per standard test protocols/BIS specifications. a) Name of the Laboratory : b) NABL Status (Validity of NABL Certificate): c) Period of the Study : From ____ to _____ d) BIS specification/protocol followed : e) Number of Samplesset taken for Test : f) Temperature maintained during the test : g) Primary Packing taken for test : h) Test result of AI before the test : i) Test result of AI after the test :	

	8) Secondary Packaging Taken for Test : 9) Transport Packing Taken for test : 10) Whether the primary,secondary and transport packing taken for tests are same as proposed in Manner of Packing : Yes/No 11) Number of Samples taken for Test : 12) Details of the Tests Conducted :(to cover all type of proposed packing combinations -(Primary+Secondary+Transport) **A.Vertical Drop Test** BIS No. : Scheme for Dropping Test : Test results : **B.Stack Load Test :** a) BIS No. : b)Scheme for Stack Load Test : c) Test results : **C.Vibration Leak Test :** a) BIS No. : b) Scheme for Vibration Test : c) Test results : **D.Rolling Test:** a) BIS No. : b) Scheme for Rolling Test : c) Test results : **E.Inclined Impact Test :** a) BIS No. : b) Scheme for Rolling Test : c) Test results : F.Any other Packaging Test under TWT as per IMDG / BIS /RC requirements : a) BIS No. : b) Test results :	

	j) Test result of Packaging material before test : k) Test result of Packaging material after test : l) Final Conclusion of the Study :	
8.	Performance of container with content during storage stability test(Shelf life Study) at three different agro climate conditions for 30 months/ ASS Data for a.i. content and physico chemical properties of the product and test parameter on container:-- 1. Name of the Laboratory : 2. NABL/GLP Status (Validity of NABL/GLP Certificate): 3. Name of the Study - Shelf life Study / ASS: _____ 4. Period of the Study : From ____ to _____ 5. Number of Months/Days : 6. Three Agro-climatic locations selected for Shelf life Study: 7. Location 01 :_____ 8. Location 02 :_____ 9. Location 03:_____ 10. BIS specification followed : 11. Primary Packing taken for test : 12. Test result of AI before the test : 13. Test result of AI after the test (for ASS) : 14. Zero Month Test result of AI after the test : 15. Location 16. 06 Months Test result of AI after the test : 17. 12 Months Test result of AI after the test : 18. 18 Months Test result of AI after the test : 19. 24 Months Test result of AI after the test : 20. 30 Months Test result of AI after the test : 21. Final Conclusion of Test results of AI after 30 Months : 22. Test result of Packaging Material before the test : 23. Test result of Packaging Material after the test(for ASS) : 24. Zero Month Test result of Packaging Material after the test : 25. 06 Months Test result of Packaging Material after the test : 26. 12 Months Test result of Packaging Materialafter the test : 27. 18 Months Test result of Packaging Material after the test : 28. 24 Months Test result of Packaging Material after the test :	

22. Test result of Packaging Material before the test :

	29. 30 Months Test result of Packaging Material after the test : 30. Final Conclusion of Test results of Packaging Material after 30 Months : 31. Metrological data of 3 locations: Name of the Institute/Organization of Metrological data: Location 01 :_____ Location 02 :_____ Location 03:_____ 32. Average Temperature range during the entire Shelf Life Study: Location 01 :_____ Zero Month : _____ to _____ ℃ 06 Months : _____ to _____ ℃ 12 Months : _____ to _____ ℃ 18 Months: _____ to _____ ℃ 24 Months : _____ to _____ ℃ 30 Months : _____ to _____ ℃ Location 02 :_____ Zero Month : _____ to _____ ℃ 06 Months : _____ to _____ ℃ 12 Months : _____ to _____ ℃ 18 Months: _____ to _____ ℃ 24 Months : _____ to _____ ℃ 30 Months : _____ to _____ ℃ Zero Month : to ℃ Location 03 :_____ Zero Month : _____ to _____ ℃ 06 Months : _____ to _____ ℃ 12 Months : _____ to _____ ℃ 18 Months: _____ to _____ ℃ 24 Months : _____ to _____ ℃ 30 Months : _____ to _____ ℃	
9.	Transport worthiness test (TWT) for proposed transport packing from NABL accrediated lab. 1) Name of the Laboratory : 2) NABL/GLP Status (Validity of NABL/GLP Certificate): 3) Name of the Study - _____ 4) Period of the Study : From ____ to _____ 5) Number of Months/Days :	

	6) BIS specification followed : 7) Primary Packing taken for test : 8) Secondary Packaging Taken for Test : 9) Transport Packing Taken for test : 10) Whether the primary,secondary and transport packing taken for tests are same as proposed in Manner of Packing : Yes/No 11) Number of Samples taken for Test : 12) Details of the Tests Conducted :(to cover all type of proposed packing combinations -(Primary+Secondary+Transport) **A.Vertical Drop Test** BIS No. : Scheme for Dropping Test : Test results : **B.Stack Load Test :** a) BIS No. : b)Scheme for Stack Load Test : c) Test results : **C.Vibration Leak Test :** a) BIS No. : b) Scheme for Vibration Test : c) Test results : **D.Rolling Test:** a) BIS No. : b) Scheme for Rolling Test : c) Test results : **E.Inclined Impact Test :** a) BIS No. : b) Scheme for Rolling Test : c) Test results : F.Any other Packaging Test under TWT as per IMDG / BIS /RC requirements : a) BIS No. : b) Test results :	

Template for Packaging Discipline for Applications U/s 9(4)-TIM

S. No.	Parameters	Reply/Response of applicant
1.	Form I	
2.	Manner of labeling and Leaflet	
3.	Type of packaging (Ultra small, small or Big whichever is applicable)	
4.	Manner of packaging: (a)Primary Packing (b) Secondary Packing (c) Transport Packing	
5.	Specification for primary, Secondary and Transport packages (whichever is applicable) Specification shall include: a) capacity, b) thickness, c) shape, d) size (LxWxH), e) brimful capacity, f) sealing system, g) Material of construction, Grade, h) Closure system, i) Gross/net weight of primary, secondary and transport packing,	
6.	Details of packaging material and its compatibility with content: Container Content Compatibility (CCC) test from NABL accrediated labs as per standard test protocols/BIS specifications. 1) Name of the Laboratory : 2) NABL Status (Validity of NABL Certificate): 3) Period of the Study : From ____ to _____ 4) BIS specification/protocol followed : 5) Number of Samplesset taken for Test : 6) Temperature maintained during the test : 7) Primary Packing taken for test : 8) Test result of AI before the test : 9) Test result of AI after the test : 10) Test result of Packaging material before test : 11) Test result of Packaging material after test :	

	12) Final Conclusion of the Study :	

Template for Endorsement Applications of New Packaging Material U/s 9(3)/ 9(4):

S. No.	Parameters	Reply/Response of applicant
1.	Duly signed Endorsement application	
2.	Notarized copy of Certificate of Registration	
3.	Type of packaging (Ultra small, small or Big whichever is applicable)	
4.	Manner of packaging: (a)Primary Packing (b) Secondary Packing (c) Transport Packing	
5.	Specification for primary, Secondary and Transport packages (whichever is applicable) Specification shall include: 1) capacity, 2) thickness, 3) shape, 4) size (LxWxH), 5) brimful capacity, 6) sealing system, 7) Material of construction, Grade, 8) Closure system, 9) Gross/net weight of primary, secondary and transport packing,	
6.	Details of packaging material and its compatibility with content: Container Content Compatibility (CCC) test from NABL accrediated labs as per standard test protocols/BIS specifications. a) Name of the Laboratory : b) NABL Status (Validity of NABL Certificate): c) Period of the Study : From ____ to _____ d) BIS specification/protocol followed : e) Number of Samplesset taken for Test : f) Temperature maintained during the test : g) Primary Packing taken for test : h) Test result of AI before the test : i) Test result of AI after the test : j) Test result of Packaging material before test : k) Test result of Packaging material after test : l) Final Conclusion of the Study :	

7.	Performance of container with content during storage stability test(Shelf life Study) at three different agro climate conditions for 30 months/ ASS Data for a.i. content and physico chemical properties of the product and test parameter on container:-- 1) Name of the Laboratory : 2) NABL/GLP Status (Validity of NABL/GLP Certificate): 3) Name of the Study - Shelf life Study / ASS: _____ 4) Period of the Study : From ____ to _____ 5) Number of Months/Days : 6) Three Agro-climatic locations selected for Shelf life Study: 7) Location 01 :_____ 8) Location 02 :_____ 9) Location 03:_____ 10) BIS specification followed : 11) Primary Packing taken for test : 12) Test result of AI before the test : 13) Test result of AI after the test (for ASS) : 14) Zero Month Test result of AI after the test : 15) Location 16) 06 Months Test result of AI after the test : 17) 12 Months Test result of AI after the test : 18) 18 Months Test result of AI after the test : 19) 24 Months Test result of AI after the test : 20) 30 Months Test result of AI after the test : 21) Final Conclusion of Test results of AI after 30 Months : 22) Test result of Packaging Material before the test : 23) Test result of Packaging Material after the test(for ASS) : 24) Zero Month Test result of Packaging Material after the test : 25) 06 Months Test result of Packaging Material after the test : 26) 12 Months Test result of Packaging Materialafter the test : 27) 18 Months Test result of Packaging Material after the test : 28) 24 Months Test result of Packaging Material after the test : 29) 30 Months Test result of Packaging Material after the test : 30) Final Conclusion of Test results of Packaging Material after 30 Months :	

	31) Metrological data of 3 locations: Name of the Institute/Organization of Metrological data: Location 01 :_____ Location 02 :_____ Location 03:_____ 32) Average Temperature range during the entire Shelf Life Study: Location 01 :_____ Zero Month : _____ to _____℃ 06 Months : _____ to _____℃ 12 Months : _____ to _____℃ 18 Months: _____ to _____℃	
	24 Months : _____ to _____℃ 30 Months : _____ to _____℃ Location 02 :_____ Zero Month : _____ to _____℃ 06 Months : _____ to _____℃ 12 Months : _____ to _____℃ 18 Months: _____ to _____℃ 24 Months : _____ to _____℃ 30 Months : _____ to _____℃ Location 03 :_____ Zero Month : _____ to _____℃ 06 Months : _____ to _____℃ 12 Months : _____ to _____℃ 18 Months: _____ to _____℃ 24 Months : _____ to _____℃ 30 Months : _____ to _____℃	
8.	Transport worthiness test (TWT) for proposed transport packing from NABL accrediated lab. 1. Name of the Laboratory : 2. NABL/GLP Status (Validity of NABL/GLP Certificate): 3. Name of the Study - _____ 4. Period of the Study : From ____ to _____ 5. Number of Months/Days : 6. BIS specification followed : 7. Primary Packing taken for test : 8. Secondary Packaging Taken for Test : 9. Transport Packing Taken for test : 10. Whether the primary,secondary and transport packing taken for tests are same as proposed in	

	Manner of Packing : Yes/No 11. Number of Samples taken for Test : 12. Details of the Tests Conducted :(to cover all type of proposed packing combinations -(Primary+Secondary+Transport) **A.Vertical Drop Test** BIS No. : Scheme for Dropping Test : Test results : **B.Stack Load Test :** a) BIS No. : b)Scheme for Stack Load Test : c) Test results : **C.Vibration Leak Test :** a) BIS No. : b) Scheme for Vibration Test : c) Test results : **D.Rolling Test:** a) BIS No. : b) Scheme for Rolling Test : c) Test results : **E.Inclined Impact Test :** a) BIS No. : b) Scheme for Rolling Test : c) Test results : F.Any other Packaging Test under TWT as per IMDG / BIS /RC requirements : a) BIS No. : b) Test results :	
9.	Justification for change	
10.	Affidavit duly notarized regarding endorsement made earlier in respect of registration certificate	
11.	Label for New pack size (if applicable)	

Template for Endorsement Applications of New Pack Size with already approved packing material U/s 9(3)/ 9(4)

S. No.	Parameters	Reply/Response of applicant
1.	Duly signed Endorsement application	
2.	Notarized copy of Certificate of Registration	
3.	Type of packaging (Ultra small, small or Big whichever is applicable)	
4.	Manner of packaging: (a)Primary Packing (b) Secondary Packing (c) Transport Packing	
5.	Specification for primary, Secondary and Transport packages (whichever is applicable) Specification shall include: a) capacity, b) thickness, c) shape, d) size (LxWxH), e) brimful capacity, f) sealing system, g) Material of construction, Grade, h) Closure system, i) Gross/net weight of primary, secondary and transport packing,	
6.	Transport worthiness test (TWT) for proposed transport packing from NABL accrediated lab. 1) Name of the Laboratory : 2) NABL/GLP Status (Validity of NABL/GLP Certificate): 3) Name of the Study - _____ 4) Period of the Study : From ____ to _____ 5) Number of Months/Days : 6) BIS specification followed : 7) Primary Packing taken for test : 8) Secondary Packaging Taken for Test : 9) Transport Packing Taken for test : 10) Whether the primary,secondary and transport packing taken for tests are same as proposed in Manner of Packing : Yes/No 11) Number of Samples taken for Test : 12) Details of the Tests Conducted :(to cover all type of	

	proposed packing combinations -(Primary+Secondary+Transport) **A.Vertical Drop Test** BIS No. : Scheme for Dropping Test : Test results : **B.Stack Load Test :** a) BIS No. : b)Scheme for Stack Load Test : c) Test results : **C.Vibration Leak Test :** a) BIS No. : b) Scheme for Vibration Test : c) Test results : **D.Rolling Test:** a) BIS No. : b) Scheme for Rolling Test : c) Test results : **E.Inclined Impact Test :** a) BIS No. : b) Scheme for Rolling Test : c) Test results : F.Any other Packaging Test under TWT as per IMDG / BIS /RC requirements : a) BIS No. : b) Test results :	
7.	Justification for change	
8.	Affidavit duly notarized regarding endorsement made earlier in respect of registration certificate	
9.	Label for New pack size (if applicable)	

****

PROFORMA FOR 9(4) TIM

General Information:

1.	**Application Number**	:	
2.	**Application category**	:	
3.	**Name and address of the firm**	:	
4.	**Name of the Authorised person with designation**	:	
5.	**Name of the Product**	:	

Technical Information:

Sr.No.	**Description**	:	
1.	Common of the Pesticide	:	
2.	IUPAC Name		
3.	CAS No.		
4.	Molecular Weight		
5.	Molecular Formula		
6.	Structure		
7.	Chemical Composition		
8.	Establishment of Chemical; equivalence along with RC Number:		
9.	**Physical and Chemical properties of active ingredient. (*)**		

Sr.No	**Name of the test**	**Result**	**Acceptable Limit**	**Reference**
1.	Moisture content			
2.	pH			
3.	Acidity/ alkalinity			

	4.	Relative Density			

10. **Method of Analysis (*) BIS specification number / Registered production specification has to submit as per draft BIS specification.**

Sr.No.	Description of methods	Acceptable Limit
1.	Method of analysis for a.i content	
2.	Method of analysis for impurity profile	
3.	Method of anlysis chemical identity test	

11. Analytical Test Report (ATR)

i. Name of the Laboratory where data generated:
ii) Complete details of NABL/ GLP certification. Of the laboratory:
ii) Complete details of study with date:

12. Shelf life of the product

13. **Detailed stepwise manufacturing process**
[Insert comprehensive description, including starting materials (with % purity) and their sources, stages and conditions, raw material used stagewise, solvents, intermediates, catalysts, extraction and purification steps, quantity recovery in the step of the TC/TK/Formulation.].
Include a flow diagram of the process.
Include the formation of impurities in each step with chemical reaction.
Indicate the location(s) of the manufacturing plant(s).

co	14.	Effluent Treatment method with complete details.		
	15.	In-Process sample: i) Sample (To be drawn from the manufacturing sites) ii) CRM (invoice and original certificate) iii) Impurities (along with invoice and certificates)		

- additional required test may be added depend on the molecule.

PROFORMA FOR 9(4) FI

General Information:

1.	**Application Number**	:	
2.	**Application category**	:	
3.	**Name and address of the firm**	:	
4.	**Name of the Authorised person with designation**	:	
5.	**Name of the Product**	:	

Technical Information:

Sr.No.	Description		
6.	**Details of source of supply of Formulation**		
7.	**Chemical Composition**		
8.	**Shelf-life claim**		
9.	**Establishment of chemical equivalence & RC number**		
10.	**Legalized/apostille letter of consent from the source of manufacturer**		
11.	**Registration Certificate of the molecule from source country.**		
12.	**In case the supplies are to be made through a supplier** **i) Details of legalized certificate from the exporting manufacturer**		
	ii) Detail of supplier in consent letter		
	iii) Complete details of the supplier of import		

PROFORMA FOR 9(4) TI

General Information:

1.	**Application Number**		
2.	**Application category**		
3.	**Name and address of the firm**		
4.	**Name of the Authorised person with designation**		
5.	**Name of the Product**		

Technical Information:

	Description		
1.	**Details of source of supply of Technical**		
2.	**Chemical Composition**		
3.	**Shelf-life claim**		
4.	**Establishment of chemical equivalence & RC number**		
5.	**Legalized/apostille letter of consent from the source of manufacturer**		
6.	**Registration Certificate of the molecule from source country.**		

7.	**In case the supplies are to be made through a supplier** **i) Details of legalized certificate from the exporting manufacturer**		
	ii) Detail of supplier in consent letter		
	iii) Complete details of the supplier of import		

PROFORMA FOR 9(4) FIM

General Information:

1.	**Application Number**		
2.	**Application category**		
3.	**Name and address of the firm**		
4.	**Name of the Authorised person with designation**		
5.	**Name of the Product**		

Technical Information:

Sr.No.	Description	:	
6.	**Details of source of supply of Technical**	:	
7.	**Chemical Composition**	:	
8.	**Shelf-life claim**	:	
9.	**Establishment of chemical equivalence**	:	

PROFORMA FOR 9(3) Export

General Information:

1.	**Application Number**	:	
2.	**Application category**	:	
3.	**Name and address of the firm**	:	
4.	**Name of the Authorised person with designation**	:	
5.	**Name of the Product**	:	

Technical Information:

Sr.No.	Description	:	
1.	**Common of the Pesticide**	:	
2.	**IUPAC Name**		
3.	**CAS No.**		
4.	**Molecular Weight**		
5.	**Molecular Formula**		
6.	**Structure**		
7.	**Chemical Composition**		
8.	**Validity of Chemixil certificate.**		
9.	**Valid Star export certificate. (For Star Export only)**		
10.	**Firm Order/purchase order from importer. (For fast track export only)**		
11.	**Registration status of the importing country. (For fast track export only)**		

12.	**Source of import / Process of manufacture/ Quantity importer along with calculation. (For fast track export only)**		
13.	**Affidivit duly notarized**		
14.	**Source of import / Complete Process of manufacture**		
15.	**Affidavit as per as RC**		
16.	**Shelf life of the product**		
17.	**Physical and Chemical Properties**		
18.	**BIS no. / Specification and method of analysis**		

TOXICOLOGY SCRTINY TEMPLATE

[9(3)TI, TIM,FIWRT-New Molecules]

GENERAL INFORMATIONS:

1.	Application Details (Category etc.)		
2.	Test Substance/Chemical Details (Common Name, IUPAC Name, CAS N. Batch N.)		
3.	Assay Purity/Active Ingredient Content %		
4.	Type of Pesticides (Insecticide/ Fungicide/ Herbicide etc.)		
5.	Decoding Certificates details		
6.	Product Schedule Inclusion Details		
7.	Source of Technical Material In case of TI-New source: information on registered source and its chemical composition. (Including RC decision or CR etc.)		
8.	In case of formulation, status of technical registration (including RC decision or CR)		
9.	Source of manufacturer and supplier		

2. RTT PERMIT

RTT PERMIT DETAILS						
Permit Number	Name of The Insecticide/Chemical	Quantity Approved	Name of The Importer	Name of The Manufacturer	Source of Procurement	Purpose of Import

3. LABEL AND LEAFLET

LABEL AND LEAFLET							
Chemical Composition	Precautions	Symptoms of Poisoning	Cautionary Statement	First Aid	Antidote	Toxicity Triangle	Pictogram Details

4. TEST SUBSTANCE & FORMULATION

1.	Physicochemical property		
2.	Adjuvants details		
3.	Compatibility		

1. STUDY DETAILS (Applicable for all Studies)

S. No.	Parameters							
1.	Study Report No. & Type							
2.	Sponsor (Name and Address)							
3.	Test Facility (Name and Address)							
4.	Test Guideline (OECD/EPA etc.)							
5.	Study Initiation Date							
6.	Study Completion Date							
7.	CoA Attached (Yes/No)							
8.	IAEC No.							
9.	NGCMA GLP Certificate (Validity up to)							

2. **STUDY DESIGN/METHODOLOGY (Applicable for all Studies)**

S. No.	Parameters						
1.	Species/Strain						
2.	No. and sex of animals per dose						
3.	Age and Body weight range at dosing						
4.	Doses/concentrations						
5.	Vehicle & positive control						
6.	Route of administration						
7.	Fasting Details (Duration) pre-dose						
8.	Housing conditions (Temperature, Relative Humidity, Light cycle)						
9.	Diet and water report (source)						
10.	Feed analysis certificate						
11.	Acclimatization period and grouping						
12.	Dosing Schedule/ Single or repeated						
13.	Rationale for dose selection						

14.	**Homogeneity/ Stability Analysis/ Concentration Analysis**						
15.	**Any deviation from protocol or amendments**						

1. ACUTE ORAL TOXICITY RAT

Executive Summary:

In an acute oral toxicity study groups (#/sex) of strain, species (source), (age, weight) were given a single oral dose of (formulation/technical, note a.i. and %) in (vehicle or undiluted test article) at doses of??? or??mg/kg bw. Animals were then observed for (#) days.

Study Endpoints:

Oral LD_{50} = mg/kg bw

Toxicity based on the LD_{50} in males or females whichever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV.

Dose (mg/kg b.w)	Mortality/Number Tested	Morbidity/Number Tested	Survived/ Number Tested
	Males/ Females	Males/ Females	Males/ Females

Statistics/If any: The oral LD_{50} was calculated using the

Observations:

Morality: as noted in table.

Clinical observations including signs & symptoms:

Gross Necropsy/ pathological findings:

Weight changes:

Conclusions:

2. ACUTE DERMAL TOXICITY RAT

Executive Summary:

In an acute dermal toxicity study, groups (#/sex) of strain, species (source), (age, weight) were dermally exposed to (formulation/technical, note a.i. and %) in (vehicle or undiluted test article) to (% or amount of body surface area) at doses of, or mg/kg bw. Test sites were covered with a(n) occlusive/semi-occlusive dressing for (#) hours. Animals were then observed for (#) days.

Study Endpoints:

Dermal LD50 = mg/kg bw

Toxicity based on the LD50 in males or females whichever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV.

Dose (mg/kg b.w)	Mortality/Number Tested Males/ Females	Morbidity/Number Tested Males/ Females	Survived/ Number Tested Males/ Females

Statistics/If any: The Dermal LD_{50} was calculated using the

Observations:

A. **Morality: as noted in table.**

B. **Clinical observations including signs & symptoms:**

C. **Gross Necropsy/ pathological findings:**

D. **Weight changes:**

Conclusions:

3. ACUTE INHALATIONAL TOXICITY RAT

Executive Summary:

In an acute inhalation toxicity study, groups (#/sex) of strain, species (source), (age, weight) were exposed (nose only, head only or whole body) via the inhalation route to (formulation/technical, note a.i. and %) in (name of vehicle or undiluted test article) for [#] hours at concentrations of mg/L. Animals were then observed for [#] days.

Study Endpoints:

LC50 = mg/L

Toxicity: based on (males or females whichever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV.

Nominal Conc. (mg/L)	Actual Conc. (Gravimetric/ Analytical) (mg/L)	MMAD	GSD	Mortality/Number Tested	Morbidity/Number Tested	Survived/ Number Tested
				Males/ Females	Males/ Females	Males/ Females

TEST ATMOSPHERE /CHAMBER DESCRIPTION:

Chamber Volume:	
Airflow:	
Temperature:	
Relative Humidity:	
Time to Equilibrium:	

Test the atmosphere concentration:

Particle size determination:

Statistics/if any: The LC_{50} was calculated using the

Observations:

A. **Morality: as noted in table.**
B. **Clinical observations including signs & symptoms:**
C. **Gross Necropsy/ pathological findings:**
D. **Weight changes:**

Conclusions:

4. ACUTE EYE IRRITATION RABBIT

Executive Summary:

In an acute eye irritation study, (volume or weight of test material applied) of (formulation/technical, note a.i. and %) in (name of vehicle if appropriate, or undiluted test material) was instilled into the conjunctival sac of (which eye) of (#/sex), (strain), (species - rabbits) (source, age, weight) for [#] hours. (Note if eyes were washed) Animals were then observed for *[#]* days. Irritation was scored by the method as per guideline.

In this study, formulation/technical is not an eye irritant OR is minimally, mildly, moderately, severely, or extremely irritating to the eye based on GHS/EPA Toxicity Category I, II, III, IV.

Parameters	**Number "positive"/number tested**							
	Hours				**Days**			
Observations	**1**	**24**	**48**	**72**	**4**	**7**	**14**	**21**
Corneal Opacity								
Iritis								
Redness								
Chemosis								
Discharge								
Conjunctivae:								

Clinical observations including ocular signs & symptoms/ reactions:

Conclusion:

5. ACUTE DERMAL IRRITATION/PRIMARY SKIN IRRITATION RABBIT

Executive Summary:
In a primary skin irritation study, (#/sex) strain, species (source), (age, weight) were dermally exposed to (volume or weight of test material applied) of (formulation/technical, note a.i. and %) in (name of vehicle or undiluted test material) to (% or amount of body surface area - state location of test site). Test sites were covered with a(n) occlusive/semi-occlusive dressing for (#) hours. Animals were then observed for [#] days. Irritation was scored by the method of (cite method).
In this study, formulation/technical is not a dermal irritating OR is corrosive to the skin based on. GHS/EPA Toxicity Category I, II, III, IV.

	Number "positive"/number tested			
	Hours			
Observations	**1**	**24**	**48**	**72**
Erythema and Eschar Formation				
Oedema				

Observations:

Results:

Conclusions:

6. SKIN SENSITIZATION GUINEA PIG/LLNA

Executive Summary:
In a dermal sensitization study with (formulation/technical, note a.i. and %) in (name of vehicle if appropriate or undiluted test article), strain, species (source)(age, weight) were tested using the method of (cite study type). Identify positive control material. List clinical signs (systemic and local for LLNA) and mortality. Necropsy results for LLNA if significant.
Results and discussion:

A. Reactions and duration:

B. Positive control:

C. Conclusions:

OBSERVATIONS FOR MAXIMIZATION TEST (GPMT) AND BUEHLER TEST:

a. Justification for positive control other than mentioned in guideline:

b. Dose Range Finding Study (DRFS) result:

c. Treatment and control skin reaction observation

Group		Skin reaction observation (dermal scoring)		
		21 hours of patch removal	Approx. 48 hours post challenge application	Approx. 72 hours post challenge application
Treatment group	Male			
Naïve control				
Treatment group	Female			
Naïve control				

0 = no visible change 1 = discrete or patchy erythema 2 = moderate and confluent erythema 3 = intense erythema and swelling

d. Result of positive control for reliability check:

e. Clinical observations if any,

histopathological examination	
skin fold thickness	

Observations for Local Lymph Node Assay (LLNA) Test:

Observations	**Results**
Dose Range Finding Study (DRFS) result:	
Clinical Observations	
Body weights changes	
Ear erythema measurements	
Ear thickness measurements	
Statistical tool used	
DPM of positive control (mean and associated error term)	
Stimulation index of positive control (concurrent/ historical)	
DPM of treatment group (mean and associated error term)	
Stimulation index of treatment group	
DPM of vehicle control group (mean and associated error term)	
Stimulation index of Vehicle control group (if any)	

DPM: Disintegration Per Mint

REPEATED DOSE 28-DAY ORAL TOXICITY-RODENT

A. Executive Summary:

In a 28-day oral toxicity study test substance (technical/formulation was administered to *[(# of animals) species, strain]*/sex/dose in *[diet, water, by gavage]* at dose levels of 0, x, x, or x ppm (equivalent to 0, x, x, x mg/kg bw/day).

[Describe toxicity briefly following instructions for exec summary paragraph 2. If there is no toxicity, state that there were no compound related effects on mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology.

***Note:** if there was a NOAEL for clinical findings and when they occurred (for acute reference dose consideration during subsequent risk assessment.)]*.

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

B. STUDY DESIGN:

Animal assignment: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design *[change heading and units as appropriate for method of administration]*

Test Group	Conc. in Diet *(units)*	Dose to Animal *(units)*	# Male	# Female
Control				
Low				
Mid				
High				

Dose selection rationale:

The dose levels were selected based on the results from *[state study type(s)]* where *[route]* - administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available.]*

Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. RESULT & DISCUSSION (Observations):

1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*

2. Mortality:

3. Neurological Evaluations - The following evaluations (measurements) were performed on day *[insert treatment day*: *[list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*

4. Body weight and weight gain: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment-related effect]*

5. Food consumption and compound intake *[if feeding study]*:

a. Food consumption:

b. Compound consumption: *[time-weighted average] [include compound intake in table 1]* -

c. Food efficiency: *[if relevant]* - *[relate to any changes in body weight]*

6. Ophthalmoscopic examination:

7. Blood analyses: [Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]:

a. Hematology: [relate to any histological findings]

Hematology:

Hematocrit (HCT)*		Leukocyte differential count*
Hemoglobin (HGB)*		Mean corpuscular HGB (MCH)*
Leukocyte count (WBC)*		Mean corpusc. HGB conc.(MCHC)*
Erythrocyte count (RBC)*		Mean corpusc. volume (MCV)*
Platelet count*		Reticulocyte count
Blood clotting measurements*		
(Thromboplastin time)		
(Clotting time)		
(Prothrombin time)		

b. Clinical Chemistry: [relate to any histological findings]
Blood was collected *[were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.

ELECTROLYTES		**OTHER**
Calcium		Albumin*
Chloride		Creatinine*
Magnesium		Urea nitrogen*
Phosphorus		Total Cholesterol*
Potassium*		Globulins
Sodium*		Glucose*
ENZYMES		Total bilirubin
Alkaline phosphatase (ALK)*		Total protein (TP)*
Cholinesterase (ChE)		Triglycerides
Creatine phosphokinase		Serum protein electrophoresis
Lactic acid dehydrogenase (LDH)		
Alanine aminotransferase (ALT/also SGPT)*		
Aspartate aminotransferase (AST/also SGOT)*		
Sorbitol dehydrogenase*		
Gamma glutamyl transferase (GGT)*		
Glutamate dehydrogenase		

Clinical Chemistry:

8. Urinalysis:
Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

Appearance*		Glucose
Volume*		Ketones
Specific gravity/osmolality*		Bilirubin
pH*		Blood/blood cells*
Sediment (microscopic)		Nitrate
Protein*		Urobilinogen

* Recommended for 90-day oral rodent studies

9. **Gross and histopathology**: [Tables are recommended for treatment-related findings; limit text to integration of findings, highlights]

1. Organ weight - [absolute and relative as appropriate, relate to any histological changes]
2. Gross pathology -
3. Microscopic pathology - [relate with other findings, as appropriate]

D. CONCLUSION:

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.]

REPEATED DOSE 90-DAY ORAL TOXICITY-RODENT

A. Executive Summary:

In a 90-day oral toxicity study test substance (technical/formulation was administered to *[(# of animals) species, strain]*/sex/dose in *[diet, water, by gavage]* at dose levels of 0, x, x, or x ppm (equivalent to 0, x, x, x mg/kg bw/day).

[Describe toxicity briefly following instructions for exec summary paragraph 2. If there is no toxicity, state that there were no compound related effects on mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology.

***Note:** if there was a NOAEL for clinical findings and when they occurred (for acute reference dose consideration during subsequent risk assessment.)]*.

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

B. STUDY DESIGN:

1. Animal assignment: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design *[change heading and units as appropriate for method of administration]*

Test Group	Conc. in Diet *(units)*	Dose to Animal *(units)*	# Male	# Female
Control				
Low				
Mid				
High				

2. Dose selection rationale:

The dose levels were selected based on the results from *[state study type(s)]* where *[route]* - administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available.]*

3. Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. RESULT & DISCUSSION (Observations):

1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*

2. Mortality:

3. Neurological Evaluations - The following evaluations (measurements) were performed on day *[insert treatment day*: *[list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*

4. Body weight and weight gain: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment-related effect]*

5. Food consumption and compound intake *[if feeding study]*:

a. Food consumption:

b. Compound consumption: *[time-weighted average] [include compound intake in table 1]* -

c. Food efficiency: *[if relevant] - [relate to any changes in body weight]*

6. **Ophthalmoscopic examination:**
7. **Blood analyses:** [Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]:

a. Hematology: [relate to any histological findings]

Hematology:

Hematocrit (HCT)*		Leukocyte differential count*
Hemoglobin (HGB)*		Mean corpuscular HGB (MCH)*
Leukocyte count (WBC)*		Mean corpusc. HGB conc.(MCHC)*
Erythrocyte count (RBC)*		Mean corpusc. volume (MCV)*
Platelet count*		Reticulocyte count
Blood clotting measurements*		
(Thromboplastin time)		
(Clotting time)		
(Prothrombin time)		

b. Clinical Chemistry: [relate to any histological findings]

Blood was collected *[were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.

Clinical Chemistry:

ELECTROLYTES		**OTHER**
Calcium		Albumin*
Chloride		Creatinine*
Magnesium		Urea nitrogen*
Phosphorus		Total Cholesterol*
Potassium*		Globulins
Sodium*		Glucose*
ENZYMES		Total bilirubin
Alkaline phosphatase (ALK)*		Total protein (TP)*
Cholinesterase (ChE)		Triglycerides
Creatine phosphokinase		Serum protein electrophoresis
Lactic acid dehydrogenase (LDH)		
Alanine aminotransferase (ALT/also SGPT)*		
Aspartate aminotransferase (AST/also SGOT)*		
Sorbitol dehydrogenase*		
Gamma glutamyl transferase (GGT)*		
Glutamate dehydrogenase		

8. Urinalysis:

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

Appearance*		Glucose
Volume*		Ketones
Specific gravity/osmolality*		Bilirubin
pH*		Blood/blood cells*
Sediment (microscopic)		Nitrate
Protein*		Urobilinogen

* Recommended for 90-day oral rodent studies

9. **Gross and histopathology**: [Tables are recommended for treatment-related findings; limit text to integration of findings, highlights]

1. Organ weight - [absolute and relative as appropriate, relate to any histological changes]
2. Gross pathology -
3. Microscopic pathology - [relate with other findings, as appropriate]

D. CONCLUSION:

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.]

REPEATED DOSE DERMAL TOXICITY (28-DAY)-RAT/RABBIT

Executive Summary:

In a 28-day dermal toxicity study test substance was applied to the shaved skin of *[(# of animals) species, strain]*/sex/dose at dose levels of 0, x, x, x mg/kg bw/day, 6 hours/day for 5 days/week during a 28-day period.

[Describe toxicity briefly. If there is no toxicity, state that there were no compound related effects in mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology. Note if there was a LOAEL/NOAEL for clinical findings (for acute reference dose consideration during subsequent risk assessment)].

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

B. STUDY DESIGN:

1. Animal assignment: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design *[change heading and units as appropriate for method of administration]*

Test Group	Conc. in Diet *(units)*	Dose to Animal *(units)*	# Male	# Female
Control				
Low				
Mid				
High				

2. Dose selection rationale:

The dose levels were selected based on the results from *[state study type(s)]* where *[route]* - administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available.]*

3. Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. RESULT & DISCUSSION (Observations):

1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*

2. Mortality:

3. Neurological Evaluations - The following evaluations (measurements) were performed on day *[insert treatment day*: *[list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*

4. Dermal irritation:

5. Body weight and weight gain: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment-related effect]*

6. FOOD CONSUMPTION AND COMPOUND INTAKE *[if feeding study]*:

a. Food consumption:

b. Compound consumption: *[time-weighted average] [include compound intake in table 1]* -

c. Food efficiency: *[if relevant]* - *[relate to any changes in body weight]*

7. Ophthalmoscopic examination:

8. Blood analyses: [Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]:

a. Hematology: [relate to any histological findings]

Hematology:

Hematocrit (HCT)*		Leukocyte differential count*
Hemoglobin (HGB)*		Mean corpuscular HGB (MCH)*
Leukocyte count (WBC)*		Mean corpusc. HGB conc.(MCHC)*
Erythrocyte count (RBC)*		Mean corpusc. volume (MCV)*
Platelet count*		Reticulocyte count
Blood clotting measurements*		
(Thromboplastin time)		
(Clotting time)		
(Prothrombin time)		

b. Clinical Chemistry: [relate to any histological findings]

Blood was collected *[were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.

Clinical Chemistry:

ELECTROLYTES		**OTHER**
Calcium		Albumin*
Chloride		Creatinine*
Magnesium		Urea nitrogen*
Phosphorus		Total Cholesterol*
Potassium*		Globulins
Sodium*		Glucose*
ENZYMES		Total bilirubin
Alkaline phosphatase (ALK)*		Total protein (TP)*
Cholinesterase (ChE)		Triglycerides
Creatine phosphokinase		Serum protein electrophoresis
Lactic acid dehydrogenase (LDH)		
Alanine aminotransferase (ALT/also SGPT)*		
Aspartate aminotransferase (AST/also SGOT)*		
Sorbitol dehydrogenase*		
Gamma glutamyl transferase (GGT)*		
Glutamate dehydrogenase		

7. Urinalysis:

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

Appearance*		Glucose
Volume*		Ketones
Specific gravity/osmolality*		Bilirubin
pH*		Blood/blood cells*
Sediment (microscopic)		Nitrate
Protein*		Urobilinogen

* Recommended for 90-day oral rodent studies

8. Gross and histopathology: [Tables are recommended for treatment-related findings; limit text to integration of findings, highlights]

1. Organ weight - [absolute and relative as appropriate, relate to any histological changes]
2. Gross pathology -
3. Microscopic pathology - [relate with other findings, as appropriate]

All animals that died and those sacrificed on schedule were subjected to gross pathological examination and the CHECKED (X) tissues were collected for histological examination *[note if not all collected tissues were examined]*. The (XX) organs, in addition, were weighed.

DIGESTIVE SYSTEM		**CARDIOVASCULAR/ HEMATOLOGY**	**NEUROLOGIC**
Tongue		Aorta*	Brain*+
Salivary glands*		Heart*+	Peripheral nerve*
Esophagus*		Bone marrow*	Spinal cord (3 levels)*
Stomach*		Lymph nodes*	Pituitary*
Duodenum*		Spleen*+	Eyes (optic nerve)*
Jejunum*		Thymus*+	**GLANDULAR**
Ileum*			Adrenal gland*+
Cecum*		**UROGENITAL**	Lacrimal gland
Colon*		Kidneys*+	Parathyroid*
Rectum*		Urinary bladder*	Thyroid*
Liver*+		Testes*+	**OTHER**
Gall bladder (not rat)*		Epididymides*+	Bone (sternum and/or femur)
Bile duct (rat)		Prostate*	Skeletal muscle
Pancreas*		Seminal vesicles*	Skin*
RESPIRATORY		Ovaries*+	All gross lesions and masses*
Trachea*		Uterus*+	
Lung*		Mammary gland*	
Nose*			
Pharynx*			
Larynx*			

+ Organ weights required for rodent studies.

D. CONCLUSION:

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

10. REPEATED DOSE DERMAL TOXICITY (90-DAY) RAT/RABBIT

A. Executive Summary:

In a 90-day dermal toxicity study the test substance was applied to the shaved skin of *[(# of animals) species, strain]*/sex/dose at dose levels of 0, x, x, x mg/kg bw/day, 6 hours/day for 5 days/week during a 90-day period.

[Describe toxicity briefly. If there is no toxicity, state that there were no compound related effects in mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology. Note if there was a LOAEL/NOAEL for clinical findings (for acute reference dose consideration during subsequent risk assessment)].

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

B. STUDY DESIGN:

1. Animal assignment: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design *[change heading and units as appropriate for method of administration]*

Test Group	Conc. in Diet *(units)*	Dose to Animal *(units)*	# Male	# Female
Control				
Low				
Mid				
High				

2. Dose selection rationale:

The dose levels were selected based on the results from *[state study type(s)]* where *[route]* - administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available.]*

3. Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. RESULT & DISCUSSION (Observations):

1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*

2. Mortality:

3. Neurological Evaluations - The following evaluations (measurements) were performed on day *[insert treatment day: [list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*

4. Dermal irritation:

5. Body weight and weight gain: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment-related effect]*

6. FOOD CONSUMPTION AND COMPOUND INTAKE *[if feeding study]*:

a. Food consumption:

b. Compound consumption: *[time-weighted average] [include compound intake in table 1]* -

c. Food efficiency: *[if relevant] - [relate to any changes in body weight]*

7. Ophthalmoscopic examination:

8. Blood analyses: [Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]:

a. Hematology: [relate to any histological findings]

Hematology:

	Hematocrit (HCT)*		Leukocyte differential count*
	Hemoglobin (HGB)*		Mean corpuscular HGB (MCH)*
	Leukocyte count (WBC)*		Mean corpusc. HGB conc.(MCHC)*
	Erythrocyte count (RBC)*		Mean corpusc. volume (MCV)*
	Platelet count*		Reticulocyte count
	Blood clotting measurements*		

	(Thromboplastin time)		
	(Clotting time)		
	(Prothrombin time)		

b. Clinical Chemistry: [relate to any histological findings]

Blood was collected *[were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.

Clinical Chemistry:

	ELECTROLYTES		**OTHER**
	Calcium		Albumin*
	Chloride		Creatinine*
	Magnesium		Urea nitrogen*
	Phosphorus		Total Cholesterol*
	Potassium*		Globulins
	Sodium*		Glucose*
	ENZYMES		Total bilirubin
	Alkaline phosphatase (ALK)*		Total protein (TP)*
	Cholinesterase (ChE)		Triglycerides
	Creatine phosphokinase		Serum protein electrophoresis
	Lactic acid dehydrogenase (LDH)		
	Alanine aminotransferase (ALT/also SGPT)*		
	Aspartate aminotransferase (AST/also SGOT)*		
	Sorbitol dehydrogenase*		
	Gamma glutamyl transferase (GGT)*		
	Glutamate dehydrogenase		

9. Urinalysis:

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

	Appearance*		Glucose
	Volume*		Ketones
	Specific gravity/osmolality*		Bilirubin
	pH*		Blood/blood cells*
	Sediment (microscopic)		Nitrate
	Protein*		Urobilinogen

* Recommended for 90-day oral rodent studies

10. Gross and histopathology: [Tables are recommended for treatment-related findings; limit text to integration of findings, highlights]

1. Organ weight - [absolute and relative as appropriate, relate to any histological changes]
2. Gross pathology -
3. Microscopic pathology - [relate with other findings, as appropriate]

All animals that died and those sacrificed on schedule were subjected to gross pathological examination and the CHECKED (X) tissues were collected for histological examination *[note if not all collected tissues were examined]*. The (XX) organs, in addition, were weighed.

	DIGESTIVE SYSTEM		**CARDIOVASCULAR / HEMATOLOGY**		**NEUROLOGIC**
	Tongue		Aorta*		Brain*+
	Salivary glands*		Heart*+		Peripheral nerve*
	Esophagus*		Bone marrow*		Spinal cord (3 levels)*
	Stomach*		Lymph nodes*		Pituitary*
	Duodenum*		Spleen*+		Eyes (optic nerve)*
	Jejunum*		Thymus*+		**GLANDULAR**
	Ileum*				Adrenal gland*+
	Cecum*		**UROGENITAL**		Lacrimal gland
	Colon*		Kidneys*+		Parathyroid*
	Rectum*		Urinary bladder*		Thyroid*
	Liver*+		Testes*+		**OTHER**
	Gall bladder (not rat)*		Epididymides*+		Bone (sternum and/or femur)
	Bile duct (rat)		Prostate*		Skeletal muscle
	Pancreas*		Seminal vesicles*		Skin*
	RESPIRATORY		Ovaries*+		All gross lesions and masses*
	Trachea*		Uterus*+		
	Lung*		Mammary gland*		
	Nose*				
	Pharynx*				
	Larynx*				

+ Organ weights required for rodent studies.

D. CONCLUSION:

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

REPEATED DOSE INHALATION TOXICITY (28-DAY)-RAT

A. Executive Summary:

In a sub-chronic inhalation toxicity study test substance was administered to *[(# of animals) species, strain]*/sex/concentration by dynamic *[nose only, head only or whole body]* exposure at concentrations of 0, x, x, x mg/L for x hours per day, x days/week for a total of x days *(include concentrations in units reported in the study as well as mg/L conversion).*

[Describe toxicity briefly. If there is no toxicity, state that there were no compound related effects in mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology. Note if there was a LOAEL/NOAEL for clinical findings (for acute reference dose consideration during subsequent risk assessment)].

The LOAEL is mg/L/day, based on the NOAEL is mg/L/day.

B. STUDY DESIGN:

1. Animal assignment

Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design

Test group	Nominal Conc. (mg/L)	Analytical Conc. (mg/L)	MMAD	GSD	Rats/sex
Control					
Low (LCT)					
Mid (MCT)					
High (HCT)					

2. Dose selection rationale

The dose levels were selected based on the results from *[state study type(s)]* where *[route-*administration of up to *[dose]* resulted in *[state effects]. [Use data from range-finding study if available.]*

3. Generation of the test atmosphere / chamber description:

Time to equilibrium was.

Analytical Chemistry.

Test atmosphere concentration *[give method and results]*. Results are in table 1 above.

Particle size determination [*give method and results]*. Results are in table 1 above.

2. **Statistics** - *[list parameters that were analyzed and the statistical methods used]*

C. RESULT & DISCUSSION (Observations):

1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*

2. Mortality:

3. Neurological Evaluations - The following evaluations (measurements) were performed on day *[insert treatment day: [list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*

4. Body weight and weight gain: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment-related effect]*

5. FOOD CONSUMPTION AND COMPOUND INTAKE *[if feeding study]*:

a. Food consumption:

b. Compound consumption: *[time-weighted average] [include compound intake in table 1]* -

c. Food efficiency: *[if relevant] - [relate to any changes in body weight]*

6. Ophthalmoscopic examination:

7. Blood analyses: [Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]:

a. Hematology: [relate to any histological findings]

Hematology:

	Hematocrit (HCT)*		Leukocyte differential count*
	Hemoglobin (HGB)*		Mean corpuscular HGB (MCH)*
	Leukocyte count (WBC)*		Mean corpusc. HGB conc.(MCHC)*
	Erythrocyte count (RBC)*		Mean corpusc. volume (MCV)*
	Platelet count*		Reticulocyte count
	Blood clotting measurements*		
	(Thromboplastin time)		
	(Clotting time)		
	(Prothrombin time)		

b. Clinical Chemistry: [relate to any histological findings]

Blood was collected *[were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.

Clinical Chemistry:

	ELECTROLYTES		**OTHER**
	Calcium		Albumin*
	Chloride		Creatinine*
	Magnesium		Urea nitrogen*
	Phosphorus		Total Cholesterol*
	Potassium*		Globulins
	Sodium*		Glucose*
	ENZYMES		Total bilirubin
	Alkaline phosphatase (ALK)*		Total protein (TP)*
	Cholinesterase (ChE)		Triglycerides
	Creatine phosphokinase		Serum protein electrophoresis
	Lactic acid dehydrogenase (LDH)		
	Alanine aminotransferase (ALT/also SGPT)*		
	Aspartate aminotransferase (AST/also SGOT)*		
	Sorbitol dehydrogenase*		
	Gamma glutamyl transferase (GGT)*		
	Glutamate dehydrogenase		

8. Urinalysis:

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

	Appearance*		Glucose
	Volume*		Ketones
	Specific gravity/osmolality*		Bilirubin
	pH*		Blood/blood cells*
	Sediment (microscopic)		Nitrate
	Protein*		Urobilinogen

* Recommended for 90-day oral rodent studies

9. Gross and histopathology: [Tables are recommended for treatment-related findings; limit text to integration of findings, highlights]

1. Organ weight - [absolute and relative as appropriate, relate to any histological changes]
2. Gross pathology -
3. Microscopic pathology - [relate with other findings, as appropriate]

All animals that died and those sacrificed on schedule were subjected to gross pathological examination and the CHECKED (X) tissues were collected for histological examination *[note if not all collected tissues were examined]*. The (XX) organs, in addition, were weighed.

DIGESTIVE SYSTEM	**CARDIOVASCULAR/ HEMATOLOGY**	**NEUROLOGIC**
Tongue	Aorta*	Brain*+
Salivary glands*	Heart*+	Peripheral nerve*
Esophagus*	Bone marrow*	Spinal cord (3 levels)*
Stomach*	Lymph nodes*	Pituitary*
Duodenum*	Spleen*+	Eyes (optic nerve)*
Jejunum*	Thymus*+	**GLANDULAR**
Ileum*		Adrenal gland*+
Cecum*	**UROGENITAL**	Lacrimal gland
Colon*	Kidneys*+	Parathyroid*
Rectum*	Urinary bladder*	Thyroid*
Liver*+	Testes*+	**OTHER**
Gall bladder (not rat)*	Epididymides*+	Bone (sternum and/or femur)
Bile duct (rat)	Prostate*	Skeletal muscle
Pancreas*	Seminal vesicles*	Skin*
RESPIRATORY	Ovaries*+	All gross lesions and masses*
Trachea*	Uterus*+	
Lung*	Mammary gland*	
Nose*		
Pharynx*		
Larynx*		

+ Organ weights required for rodent studies.

D. CONCLUSION:

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

REPEATED DOSE 90-DAY ORAL TOXICITY-NON-RODENT/ DOG

A. Executive Summary:

In a 90-day oral toxicity study test substance (technical/formulation was administered to *[(# of animals) species, strain]*/sex/dose in *[diet, water, by gavage]* at dose levels of 0, x, x, or x ppm (equivalent to 0, x, x, x mg/kg bw/day).

[Describe toxicity briefly following instructions for exec summary paragraph 2. If there is no toxicity, state that there were no compound related effects on mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology.

***Note:** if there was a NOAEL for clinical findings and when they occurred (for acute reference dose consideration during subsequent risk assessment.)]*.

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

B. STUDY DESIGN:

1. Animal assignment: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design *[change heading and units as appropriate for method of administration]*

Test Group	Conc. in Diet *(units)*	Dose to Animal *(units)*	# Male	# Female
Control				
Low				
Mid				
High				

2. Dose selection rationale:

The dose levels were selected based on the results from *[state study type(s)]* where *[route]* - administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available.]*

3. Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. RESULT & DISCUSSION (Observations):

1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*

2. Mortality:

3. Neurological Evaluations - The following evaluations (measurements) were performed on day *[insert treatment day*: *[list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*

4. Body weight and weight gain: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment-related effect]*

5. FOOD CONSUMPTION AND COMPOUND INTAKE *[if feeding study]*:

a. Food consumption:

b. Compound consumption: *[time-weighted average] [include compound intake in table 1]* -

c. Food efficiency: *[if relevant]* - *[relate to any changes in body weight]*

6. Ophthalmoscopic examination:

7. **Blood analyses:** [Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]:

a. Hematology: [relate to any histological findings]

Hematology:

	Hematocrit (HCT)*		Leukocyte differential count*
	Hemoglobin (HGB)*		Mean corpuscular HGB (MCH)*
	Leukocyte count (WBC)*		Mean corpusc. HGB conc.(MCHC)*
	Erythrocyte count (RBC)*		Mean corpusc. volume (MCV)*
	Platelet count*		Reticulocyte count
	Blood clotting measurements*		
	(Thromboplastin time)		
	(Clotting time)		
	(Prothrombin time)		

b. Clinical Chemistry: [relate to any histological findings]

Blood was collected *[were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.

Clinical Chemistry:

	ELECTROLYTES		**OTHER**
	Calcium		Albumin*
	Chloride		Creatinine*
	Magnesium		Urea nitrogen*
	Phosphorus		Total Cholesterol*
	Potassium*		Globulins
	Sodium*		Glucose*
	ENZYMES		Total bilirubin
	Alkaline phosphatase (ALK)*		Total protein (TP)*
	Cholinesterase (ChE)		Triglycerides
	Creatine phosphokinase		Serum protein electrophoresis
	Lactic acid dehydrogenase (LDH)		
	Alanine aminotransferase (ALT/also SGPT)*		
	Aspartate aminotransferase (AST/also SGOT)*		
	Sorbitol dehydrogenase*		
	Gamma glutamyl transferase (GGT)*		
	Glutamate dehydrogenase		

8. Urinalysis:

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

	Appearance*		Glucose
	Volume*		Ketones

	Specific gravity/osmolality*		Bilirubin
	pH*		Blood/blood cells*
	Sediment (microscopic)		Nitrate
	Protein*		Urobilinogen

* Recommended for 90-day oral rodent studies

9. Gross and histopathology: [Tables are recommended for treatment-related findings; limit text to integration of findings, highlights]

1. Organ weight - [absolute and relative as appropriate, relate to any histological changes]
2. Gross pathology -
3. Microscopic pathology - [relate with other findings, as appropriate]

All animals that died and those sacrificed on schedule were subjected to gross pathological examination and the CHECKED (X) tissues were collected for histological examination *[note if not all collected tissues were examined]*. The (XX) organs, in addition, were weighed.

	DIGESTIVE SYSTEM		**CARDIOVASCULAR / HEMATOLOGY**		**NEUROLOGIC**
	Tongue		Aorta*		Brain*+
	Salivary glands*		Heart*+		Peripheral nerve*
	Esophagus*		Bone marrow*		Spinal cord (3 levels)*
	Stomach*		Lymph nodes*		Pituitary*
	Duodenum*		Spleen*+		Eyes (optic nerve)*
	Jejunum*		Thymus*+		**GLANDULAR**
	Ileum*				Adrenal gland*+
	Cecum*		**UROGENITAL**		Lacrimal gland
	Colon*		Kidneys*+		Parathyroid*
	Rectum*		Urinary bladder*		Thyroid*
	Liver*+		Testes*+		**OTHER**
	Gall bladder (not rat)*		Epididymides*+		Bone (sternum and/or femur)
	Bile duct (rat)		Prostate*		Skeletal muscle
	Pancreas*		Seminal vesicles*		Skin*
	RESPIRATORY		Ovaries*+		All gross lesions and masses*
	Trachea*		Uterus*+		
	Lung*		Mammary gland*		
	Nose*				
	Pharynx*				
	Larynx*				

+ Organ weights required for rodent studies.

D. CONCLUSION:

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

ACUTE NEUROTOXICITY RODENT

A. Executive Summary:

In an acute neurotoxicity study, groups of *(fasted)*, *(age)* *(strain)* *(species)* *(#/sex)* were given a single oral dose of *(chemical name (% a.i., batch/lot #)* in *(name of vehicle)* at doses of x, x, or x mg/kg bw and observed for *(#)* days. Neurobehavioral assessment (functional observational battery and motor activity testing) was performed in *[number]* animals/sex/group *[at what time points]*. *[If applicable]* Cholinesterase activity was determined by the *[?]* method in *X* rats/sex/dose in plasma and erythrocytes *[at what time points]*, and in *[# of regions or whole]* brain *[at what time points]*. At study termination, *[how many?]* animals/sex/group were euthanized and perfused [*in situ*] for neuropathological examination. Of the perfused animals, *[how many from which groups?]* were subjected to histopathological evaluation of brain and peripheral nervous system tissues.

[Any additional measures should be included in procedures section above.]

Discuss findings at low, mid- and high doses. Include only major treatment related clinical signs, FOB findings, motor activity changes, body weight or brain weight changes or gross and histopathology or neuropathology, including onset and/or duration if any, or the following statement: There were no treatment related effects on mortality, clinical signs, body weight, brain weight or gross and histologic pathology or neuropathology. FOB and motor activity testing revealed no treatment-related effects. Note if there was a NOAEL for acute neurotoxicity (for acute reference dose consideration during subsequent risk assessment.)

Based on the effects seen in this study, the LOAEL was xxx mg/kg bw/day (based on xxx), with a NOAEL of xxx mg/kg bw/day.

[If applicable]

The LOAEL for plasma cholinesterase inhibition was xxx mg/kg bw/day, with a NOAEL of xxx mg/kg bw/day.

The LOAEL for erythrocyte cholinesterase inhibition was xxx mg/kg bw/day, with a NOAEL of xxx mg/kg bw/day.

The LOAEL for brain cholinesterase inhibition was xxx mg/kg, bw/day with a NOAEL of xxx mg/kg bw/day.

B. STUDY DESIGN:

1. Animal assignment and treatment: Animals were assigned to the test groups noted in Table 1 *[e.g., by a computerized random sort program to the test groups so that body weight means for each group were comparable. Following an overnight fast]*, rats were given a single dose *[how, in what vehicle/volume]* then observed *[frequency]* and weighed *[frequency]* for 14 days. Dose levels were chosen based on *[what]*. *[Dose selection rationale should be discussed; rationale for selection of time of peak effect should also be discussed. Use data from range-finding study if available.]* Survivors were sacrificed and a necropsy *[was/was not]* performed.

[Include additional description of study design, e.g. use of replicates, as needed, to supplement the information in the table.]

Table 1. Study Design *[change headings and units as appropriate, add or delete rows as needed]*

	Dose Group (mg/kg bw)			
Experimental Parameter	**Control**	**Low Dose**	**Mid Dose**	**High Dose**

Total number of Animals/sex/group				
Behavioral Testing (FOB, Motor Activity)				
Neuropathology				
Blood cholinesterase determination				
Brain cholinesterase determination				

2. Test Substance Preparation and Analysis: *[Indicate how test substance was prepared for administration, how it was stored, and how stability, concentration, and homogeneity were verified.]*

3. Statistics - *[list parameters that were analyzed and the statistical methods used]*

RESULTS & DISCUSSION (Observations):

Mortality and Clinical Observations:

Table 2. Clinical observations

Parameters	**Dose Level (mg/kg bw/day)**			
Observation	**Control**	**Low Dose**	**Mid Dose**	**High Dose**
Males				
[observation type]				
Females				
[observation type]				

Data were extracted from *[cite report page nos.]*

Numbers represent the total number of observations/number of animals with at least one instance of the observation

n=*[give number of animals in each group]*

2. Body weight:

3. Food consumption:

	Dose Level (Mg/kg Bw)			
Brain Region	**Control**	**Low Dose**	**Mid Dose**	**High Dose**
Tissue 1				
Male				
Day 0				
Day 7				
Day 14				
Female				
Day 0				
Day 7				
Day 14				
Tissue 2				
Male				
Day 0				
Day 7				
Day 14				
Female				
Day 0				
Day 7				
Day 14				

4. Cholinesterase Determination:

Table 2. Blood cholinesterase activity

Data were extracted from *[cite study report page nos.]*

Values represent mean ± s.d. *[% difference from control mean]*

**=p<.01, *=p<.05, when compared to control mean.

n=*[give number of animals in each group]*

[Include all data for whole brain (if brain regions were evaluated, also include all data from cortex and hippocampus; for other regions include data from all time points if statistically significant changes were found for a particular region or if changes from baseline of 20% or greater were seen) - add extra lines to table as needed].

Table 3. Brain cholinesterase activity (U/g)

Data were extracted from *[cite study report page nos.]*

Values represent mean ± s.d. *[% difference from control mean]*

**=p<.01, *=p<.05, when compared to control mean, n=*[give number of animals in each group]*

5. Neurobehavioral Assessment:

a. Functional Observational Battery (FOB): *[*The CHECKED (X) parameters were examined. *[Add and delete parameters from the following table, as needed.]*

HOME CAGE OBSERVATIONS	HANDLING OBSERVATIONS	OPEN FIELD OBSERVATIONS
Posture*	Reactivity*	Mobility
Biting	Lacrimation* / chromodacryorrhea	Rearing+
Convulsions*	Salivation*	Arousal/ gereral activity level*
Tremors and twitches*	Piloerection*	Convulsions*
Abnormal Movements*	Fur appearance	Tremors*
Palpebral closure*	Palpebral closure*	Abnormal movements*
Faeces consistency	Respiratory rate+	Urination/ defecation/ Urinary staining*
	Red/crusty deposits*	Grooming
SENSORY OBSERVATIONS	Mucous membranes /eye /skin colour	Gait abnormalities/ posture*
Approach response+	Eye prominence*	Gait score*
Touch response+	Muscle tone*	Bizarre/ stereotypic behaviour*
Startle response*		Backing
Pain response*		Time to first step
Pupil response*		
Eyeblink response	**PHYSIOLOGICAL OBSERVATIONS**	**NEUROMUSCULAR OBSERVATIONS**
Forelimb extension	Body weight*	Hindlimb extensor strength
Hindlimb extension	Body temperature+	Forelimb grip strength*
Air righting reflex+		Hindlimb grip strength*
Olfactory orientation		Landing foot splay*
Reflexes (Sensory and motor)	**OTHER OBSERVATIONS**	Rotarod performance

	Dose Level (mg/kg bw)			
Observation	**Control**	**Low dose**	**Mid dose**	**High dose**
Males				
Type of Observation -1 -Pretest -Day 0 -Day 7 -Day 14				
Type of Observation -2 -Pretest -Day 0 -Day 7 -Day 14				
Females				
Type of Observation -1 -Pretest -Day 0 -Day 7 -Day 14				
Type of Observation -2 -Pretest -Day 0 -Day 7 -Day 14				

*Required parameters; +Recommended parameters

a. FOB Findings:

Table 4. Functional observation battery results

Data were extracted from *[cite study report page nos.] [include units for measurements, as needed]*

Values represent incidence (or other appropriate measure)

n=*[include number of animals for all groups]*

*=p<.05,** p<.01 compared with controls

b. Locomotors Activity:

Table 5. Motor activity (total activity counts for session)

	Dose Level (mg/kg bw)			
Test Day	**Control**	**Low Dose**	**Mid Dose**	**High Dose**
Males				
Pre-test				
Day 0				
Day 7				
Day 14				
Females				
Pre-test				
Day 0				
Day 7				
Day 14				

Data were extracted from *[cite study report page nos.] [Include units for measurements, as needed]*

Values represent mean ±s.d.

n=*[give number of animals for all groups]*

*=p<.05,** p<.01 compared with controls

6. Sacrifice and Pathology:

The CHECKED (X) tissues were evaluated. *[add or delete tissues as needed].*

CENTRAL NERVOUS SYSTEM	**PERIPHERAL NERVOUS SYSTEM**
BRAIN	**SCIATIC NERVE**
Forebrain	Mid-thigh
Center of cerebrum	Sciatic Notch
Midbrain	
Cerebellum	**OTHER**
Pons	Sural Nerve
Medulla oblongata	Tibial Nerve
SPINAL CORD	Peroneal Nerve
Cervical swelling	Lumbar dorsal root ganglion
Lumbar swelling	Lumbar dorsal root fibers
Thoracic swelling	Lumbar ventral root fibers
OTHER	Cervical dorsal root ganglion
Gasserian Ganglion	Cervical dorsal root fibers
Trigeminal nerves	Cervical ventral root fibers
Optic nerve	
Eyes	
Gastrocnemius muscle	

a. Gross pathology: *[describe results, including whether there were any changes in brain weights (if measured - provide table)]*

b. Brain weight - *[absolute and relative as appropriate, relate to any histological changes]*

Table 6: Absolute and relative brain weights

Weights (mg)	Dose Level (mg/kg bw)			
	Control	Low Dose	Mid Dose	High Dose
Males				
Bodywt				
Brain wt				
Brain/body wt				
Female				
Body wt				
Brain wt				
Brain/body wt				

Data were extracted from *[cite study report page nos.]*

* Statistically different ($p < 0.05$) from the control

c. Neuropathology:

Include information as to what types of lesions were found. If neuropathological alterations were observed in the high dose group, were lower dose groups sequentially examined? If evidence of neuropathological alterations was seen, was a subjective diagnosis (dose-blind coded re-reading) conducted? If treatment-related lesions were found, include information in a table, including information regarding lesion severity; if no treatment-related lesions were found, include some information in text regarding reported incidence of lesions unrelated to treatment and in control groups. A sample table (with sample data) is included below.

Table 7. Incidence of neuropathological findings *[Tissues listed are examples, change as needed.]*

Parameters	Treatment Group			
	Male		Female	
Lesion	**Control**	**High Dose**	**Control**	**High Dose**
Sciatic Nerve -mid-thigh -notch (mid-thigh or notch)				
Sural Nerve				
Tibial Nerve				
Lumbar Roots -dorsal -ventral -(dorsal or ventral)				
Axonal degeneration -some peripheral nerve				

All lesions were graded minimal except for sciatic nerve degeneration in one control female (graded mild) MF=multifocal; all other lesions were focal.
Numbers in parentheses represent combined incidence.
Data were extracted from individual animal pathology data tables, *[cite study report page nos.]*

D. CONCLUSIONS:
Based on the effects seen in this study, the LOAEL was *xxx mg/kg bw/day (based on xxx)*, with a NOAEL *of xxx mg/kg bw/day.* *[If applicable]*
The LOAEL for plasma cholinesterase inhibition was *xxx mg/kg bw/day*, with a NOAEL of *xxx mg/kg bw/day*.
The LOAEL for erythrocyte cholinesterase inhibition was *xxx mg/kg bw/day*, with a NOAEL of *xxx mg/kg bw/day*.
The LOAEL for brain cholinesterase inhibition was *xxx mg/kg, bw/day* with a NOAEL of *xxx mg/kg bw/day*.

REPEATED DOSE NEUROTOXICITY

A. Executive Summary:

In a subchronic neurotoxicity study (MRID *[number]) [Chemical name (% a.i., batch/lot #)]* was administered to *[xx strain/species /sex/group]* at dose levels of 0, x, x, or x ppm (equivalent to 0, x, x, x mg/kg bw/day) for *(duration)*. Neurobehavioral assessment (functional observational battery and motor activity testing) was performed in *[number]* animals/sex/group *[at what time points]. [If applicable]*. Cholinesterase activity was determined by the *[?]* method in *X* rats/sex/dose, in plasma and erythrocytes *[at what time points]*, and in *[# of regions or whole]* brain *[at what time points]*. At study termination, *[how many?]* animals/sex/group were euthanized and perfused [*in situ*] for neuropathological examination. Of the perfused animals, *[how many from which groups?]* were subjected to histopathological evaluation of brain and peripheral nervous system tissues.

[any additional measures should be included in procedures section above]

Discuss findings at low, mid- and high doses. Include only major treatment related clinical signs, FOB findings, motor activity changes, body weight or brain weight changes or gross and histopathology or neuropathology, including onset and/or duration if any, or the following statement: There were no treatment related effects on mortality, clinical signs, body weight, brain weight or gross and histologic pathology or neuropathology. FOB and motor activity testing revealed no treatment-related effects. Note if there was a NOAEL for acute neurotoxicity (for Acute reference dose consideration during subsequent risk assessment.)

Based on the effects seen in this study, the LOAEL was *xxx mg/kg (based on xxx)*, with a NOAEL *of xxx mg/kg.*

[If applicable]

The LOAEL for plasma cholinesterase inhibition was *xxx mg/kg*, with a NOAEL of *xxx mg/kg*.

The LOAEL for erythrocyte cholinesterase inhibition was *xxx mg/kg*, with a NOAEL of *xxx mg/kg*.

The LOAEL for brain cholinesterase inhibition was *xxx mg/kg*, with a NOAEL of *xxx mg/kg*.

B. STUDY DESIGN:

1. Animal assignment and treatment: Animals were randomly assigned to the test groups noted in Table 1 *[stratified by body weight]*. Test substance was administered *[how, for how long?]*. Dose levels were chosen based on *[what]. [Dose selection rationale should be discussed]*

[Include additional description of study design, e.g. use of replicates, as needed, to supplement the information in the table.]

Table 1. Study Design *[change headings and units as appropriate, add or delete rows as needed]*

	Dose Group (mg/kg bw)			
Experimental Parameter	**Control**	**Low Dose**	**Mid Dose**	**High Dose**
Total number of Animals/sex/group				
Behavioral Testing (FOB, Motor Activity)				
Neuropathology				
Blood cholinesterase determination				
Brain cholinesterase determination				

2. Test Substance Preparation and Analysis: *[Indicate how test substance was prepared for administration, how it was stored, and how stability, concentration, and homogeneity were verified.]*

3. Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. RESULTS & DISCUSSION (Observations):

1. Mortality and Clinical Observations:

Table 2. Clinical observations

	Dose Level (mg/kg bw/day)			
Observation	**Control**	**Low Dose**	**Mid Dose**	**High Dose**
Males				
[observation type]				
Females				
[observation type]				

Data were extracted from *[cite report page nos.]*

Numbers represent the total number of observations/number of animals with at least one instance of the observation

n=*[give number of animals in each group]*

2. Body weight:

3. Food consumption:

4. Cholinesterase Determination:

Table 2. Blood cholinesterase activity

Data were extracted from *[cite study report page nos.]*

Values represent mean ± s.d. *[% difference from control mean]*

	Dose Level (Mg/kg Bw)			
Brain Region	**Control**	**Low Dose**	**Mid Dose**	**High Dose**
Tissue 1				
Male				
Week 3				
Week 7				
Week 13				
Female				
Week 3				
Week 7				
Week 13				
Tissue 2				
Male				
Week 3				
Week 7				
Week 13				
Female				
Week 3				
Week 7				
Week 13				

**=p<.01, *=p<.05, when compared to control mean.
n=*[*give *number of animals in each group]*

[Include all data for whole brain (if brain regions were evaluated, also include all data from cortex and hippocampus; for other regions include data from all time points if statistically significant changes were found for a particular region or if changes from baseline of 20% or greater were seen) - add extra lines to table as needed].

Table 3. Brain cholinesterase activity (U/g)
Data were extracted from *[cite study report page nos.]*
Values represent mean ± s.d. *[% difference from control mean]*
**=p<.01, *=p<.05, when compared to control mean.
n=*[*give *number of animals in each group]*

5. Neurobehavioral Assessment:
a. Functional Observational Battery (FOB): *[*The CHECKED (X) parameters were examined.
[Add and delete parameters from the following table, as needed.]

HOME CAGE OBSERVATIONS	HANDLING OBSERVATIONS	OPEN FIELD OBSERVATIONS
Posture*	Reactivity*	Mobility
Biting	Lacrimation* / chromodacryorrhea	Rearing+
Convulsions*	Salivation*	Arousal/ gereral activity level*
Tremors and twitches*	Piloerection*	Convulsions*
Abnormal Movements*	Fur appearance	Tremors*
Palpebral closure*	Palpebral closure*	Abnormal movements*
Faeces consistency	Respiratory rate+	Urination/ defecation/ Urinary staining*
	Red/crusty deposits*	Grooming
SENSORY OBSERVATIONS	Mucous membranes /eye /skin colour	Gait abnormalities/ posture*
Approach response+	Eye prominence*	Gait score*
Touch response+	Muscle tone*	Bizarre/ stereotypic behaviour*
Startle response*		Backing
Pain response*		Time to first step
Pupil response*		
Eyeblink response	**PHYSIOLOGICAL OBSERVATIONS**	**NEUROMUSCULAR OBSERVATIONS**
Forelimb extension	Body weight*	Hindlimb extensor strength
Hindlimb extension	Body temperature+	Forelimb grip strength*
Air righting reflex+		Hindlimb grip strength*
Olfactory orientation		Landing foot splay*
Reflexes (Sensory and motor)	**OTHER OBSERVATIONS**	Rotarod performance

Table 4. Functional observation battery results

Data were extracted from *[cite study report page nos.] [include units for measurements, as needed]*

Values represent incidence (or other appropriate measure)
n=*[include number of animals for all groups]*

	Dose Level (mg/kg bw)			
Observation	**Control**	**Low dose**	**Mid dose**	**High dose**
Males				
Observation -1 (state) Pretest Week 4 Week 8 Week 12				
Observation -2 (state) Pretest Week 4 Week 8 Week 12				
Females				
Observation -1 (state) Pretest Week 4 Week 8 Week 12				
Observation -2 (state) Pretest Week 4 Week 8 Week 12				

*=p<.05,** p<.01 compared with controls

b. Locomotors Activity:

Table 5. Motor activity (total activity counts for session)

	Dose Level (mg/kg bw)			
Test Day	**Control**	**Low Dose**	**Mid Dose**	**High Dose**
Males				
Pre-test				
Week 4				
Week 8				
Week 13				
Females				
Pre-test				
Week 4				
Week 8				
Week 13				

Data were extracted from *[cite study report page nos.] [Include units for measurements, as needed]*

Values represent mean ±s.d.

n=*[give number of animals for all groups]*

*=p<.05,** p<.01 compared with controls

6. Sacrifice and Pathology:

The CHECKED (X) tissues were evaluated. *[add or delete tissues as needed].*

CENTRAL NERVOUS SYSTEM	PERIPHERAL NERVOUS SYSTEM
BRAIN	**SCIATIC NERVE**
Forebrain	Mid-thigh
Center of cerebrum	Sciatic Notch
Midbrain	
Cerebellum	**OTHER**
Pons	Sural Nerve
Medulla oblongata	Tibial Nerve
SPINAL CORD	Peroneal Nerve
Cervical swelling	Lumbar dorsal root ganglion
Lumbar swelling	Lumbar dorsal root fibers
Thoracic swelling	Lumbar ventral root fibers
OTHER	Cervical dorsal root ganglion
Gasserian Ganglion	Cervical dorsal root fibers
Trigeminal nerves	Cervical ventral root fibers
Optic nerve	
Eyes	
Gastrocnemius muscle	

a. Gross pathology: *[describe results, including whether there were any changes in brain weights (if measured - provide table)]*

b. Brain weight - *[absolute and relative as appropriate, relate to any histological changes]*

Table 6: Absolute and relative brain weights

Weights (mg)	Dose Level (mg/kg bw)			
	Control	Low Dose	Mid Dose	High Dose
Males				
Body wt				
Brain wt				
Brain/body wt				
Female				
Body wt				
Brain wt				
Brain/body wt				

Data were extracted from *[cite study report page nos.]*

* Statistically different ($p < 0.05$) from the control

c. Neuropathology:

Include information as to what types of lesions were found. If neuropathological alterations were observed in the high dose group, were lower dose groups sequentially examined? If evidence of neuropathological alterations was seen, was a subjective diagnosis (dose-blind coded re-reading) conducted? If treatment-related lesions were found, include information in a table, including information regarding lesion severity; if no treatment-related lesions were found, include some information in text regarding reported incidence of lesions unrelated to treatment and in control groups. A sample table (with sample data) is included below.

Table 7. Incidence of neuropathological findings *[Tissues listed are examples, change as needed.]*

	Treatment Group			
	Male		Female	
Lesion	**Control**	**High Dose**	**Control**	**High Dose**
Sciatic Nerve -mid-thigh -notch (mid-thigh or notch)				
Sural Nerve				

Tibial Nerve				
Lumbar Roots -dorsal -ventral -(dorsal or ventral)				
Axonal degeneration -some peripheral nerve				

All lesions were graded minimal except for sciatic nerve degeneration in one control female (graded mild) MF=multifocal; all other lesions were focal.

Numbers in parentheses represent combined incidence.

Data were extracted from individual animal pathology data tables, *[cite study report page nos.]*

D. CONCLUSIONS:

Based on the effects seen in this study, the LOAEL was *xxx mg/kg bw/day (based on xxx)*, with a NOAEL *of xxx mg/kg bw/day.*

[If applicable]

The LOAEL for plasma cholinesterase inhibition was *xxx mg/kg bw/day*, with a NOAEL of *xxx mg/kg bw/day*.

The LOAEL for erythrocyte cholinesterase inhibition was *xxx mg/kg bw/day*, with a NOAEL of *xxx mg/kg bw/day*.

The LOAEL for brain cholinesterase inhibition was *xxx mg/kg, bw/day* with a NOAEL of *xxx mg/kg bw/day*.

DEVELOPMENTAL NEUROTOXICITY

A. Executive Summary:

In a developmental neurotoxicity study test substance was administered to *[# of animals]* female *[strain]* rats per dose in *[by gavage, diet, water, inhalation]* at dose levels of 0, x, x, or x mg/kg bw/day from gestation day *[#]* through postnatal day *[#]*. *(Briefly describe study procedures. Mention all critical and/or unusual procedures, e.g., direct treatment of offspring, neurobehavioral and neuropathology assessments, biochemical measures, etc.)*

[Concisely describe treatment-related toxicity, at the LOAEL and at doses greater than the LOAEL, for dams. Do not attempt to separate systemic-neurotoxicity; it is not possible to make this type of distinction based on the data available in these studies. If no toxicity was observed, state that there were no treatment-related effects, for maternal animals.]

The maternal LOAEL is *[dose]* mg/kg/day, based on *[endpoint]*. The maternal NOAEL is *[dose]* mg/kg/day.

[Concisely describe treatment-related toxicity, at the LOAEL and at doses greater than the LOAEL, for the offspring. Do not attempt to separate systemic- and developmental-neurotoxicity; it is not possible to make this type of distinction based on the data available in these studies. If no toxicity was observed, state that there were no treatment-related effects, offspring.]

The offspring LOAEL is *[dose]* mg/kg/day, based on *[endpoint]*. The offspring NOAEL is *[dose]* mg/kg/day.

The LOAEL for plasma cholinesterase inhibition is *[dose]* mg/kg/day, with a NOAEL of *[dose]* mg/kg/day. *[If applicable; list separately for maternal and offspring endpoints when available:]*

The LOAEL for erythrocyte cholinesterase inhibition is *[dose]* mg/kg/day, with a NOAEL of *[dose]* mg/kg/day.

	Dose (mg/kg/day)			
Experimental Parameter	**0**	**LDT**	**MDT**	**HDT**
Maternal Animals				
No. of maternal animals assigned				
FOB (GD #, #; LD #, #)				
Offspring				
Detailed clinical/FOB (PND -,-,-,-,-,)				

Motor activity (PND -,-,-,-)				
Auditory startle habituation (PND -, -)				
Learning and memory (PND -, -)				
Brain weight *[revise numbers if necessary]* PND 11 PND 60				
Neuropathology *[revise numbers if necessary]* PND 11 PND 60				
Blood cholinesterase determination *[if applicable]*				
Brain cholinesterase determination *[if applicable]*				

The LOAEL for brain cholinesterase inhibition is *[dose]* mg/kg/day, with a NOAEL of *[dose]* mg/kg/day.

B. STUDY DESIGN

1. Study schedule & procedure:

2. Animal Assignment: Mated females were assigned *[randomly? based upon body weight criteria?]* to dose groups as indicated in Table 1. Dams were assigned to functional observation testing as shown.

Offspring were assigned to testing subgroups at the time of litter standardization on postnatal day (PND) 4 (Table 1). *[Offspring assignment to testing must be described in detail, whether in text or in a table as illustrated. If pups were assigned to testing subsets, a column could be added to Table 1 to indicate which subset designation applies to each test.]*

Table 1. Study Design *[Add satellite groups if necessary]*

Note: The method of animal assignment should have minimized potential problems related to litter effects, i.e., by using one pup/sex/litter (or one measure/litter, e.g., mean body weight for each litter).

When allocating animals to FOB and motor activity testing, the same individual animals should have been evaluated at all scheduled time points. For the selection of animals and testing paradigms for cognitive (learning and memory) assessment, it is important to ensure that tasks

were selected and/or animals allocated so that comparable assessments of learning were made at both times, i.e., shortly after PND 21 and around PND 60. Indicate whether the same or different animals were used for assessments at the weanling and adult ages. In general, the use of separate animals at the two time points is preferred, because for many tasks, initial learning (PND 21) may confound later (PND 60) assessment of learning. If the same animals were used at both times, different tasks would likely have been necessary. The selection of the test for assessing learning should have been adequately justified regardless of whether the same or a different task was used.]

++++++

C. RESULT AND DISCUSSION (OBSERVATIONS):

	CENTRAL NERVOUS SYSTEM	X	PERIPHERAL NERVOUS SYSTEM
	BRAIN Forebrain Center of cerebrum Midbrain Cerebellum Pons Medulla oblongata		**SCIATIC NERVE** Mid-thigh Sciatic Notch
	SPINAL CORD Cervical swelling Lumbar swelling		**OTHER** Sural Nerve Tibial Nerve Peroneal Nerve Lumbar dorsal root ganglion Lumbar dorsal root fibers Lumbar ventral root fibers Cervical dorsal root ganglion Cervical dorsal root fibers Cervical ventral root fibers
	OTHER Gasserian Ganglion Trigeminal nerves Optic nerve Eyes		

1. Parental animals:

a. Mortality and clinical and functional observations:

Individual maternal body weight data were recorded weekly throughout gestation *[specify days]*, on the day of delivery, and on lactation days 11 and 21.

[Add descriptions of any other data reported, e.g., food consumption, reproduction data, pharmacokinetic data (e.g., levels of test substance and/or metabolite in milk), and/or cholinesterase activity, which were collected from maternal animals during the course of the DNT study (rather than from a pilot study).]

The CHECKED (X) tissues were evaluated for adult offspring. *[add or delete tissues as needed]*

b.) **Body weight and food consumption:**

Selected group mean body weights and food consumption values for pregnant or nursing dams were summarized in the following table. *[The data contained in this table are **MANDATORY**;*

FUNCTIONAL OBSERVATIONS	
X	Signs of autonomic function, including: 1) Ranking of degree of lacrimation and salivation, with range of severity scores from none to severe 2) Presence of absence of piloerection and exophthalamus, 3) Ranking or count of urination and defecation, including polyuria and diarrhea 4) Pupillary function such as constriction of the pupil in response to light, or a measure of pupil size 5) Degree of palpebral closure, e.g., ptosis.
X	Description, incidence, and severity of any convulsions, tremors, or abnormal movements.
X	Description and incidence of posture and gait abnormalities.
X	Description and incidence of any unusual or abnormal behaviors, excessive or repetitive actions (stereotypies), emaciation, dehydration, hypotonia or hypertonia, altered fur appearance, red or crusty deposits around the eyes, nose, or mouth, and any other observations that may facilitate interpretation of the data.

findings should be presented for gestation and lactation periods; data can be split into more than one table.]

Body weight was *[Describe findings]*.

Food consumption was *[Describe findings]*.

TABLE 3. Mean) Maternal Body Weight and Food Consumption [a]

Observations/study week	Dose (mg/kg/day)			
	Control	LDT	MDT	HDT
Gestation				
Mean body weight (g) Gestation day *[#]*				
Mean weight gain (g) Gestation days *[# - #]*				
Mean food consumption (g/animal/day) Gestation days *[# - #]*				
Lactation				
Mean body weight (g)				

Observations/study week	Dose (mg/kg/day)			
	Control	LDT	MDT	HDT
Lactation day *[#]*				
Mean weight gain (g) Lactation days *[# - #]*				
Mean food consumption (g/animal/day) Lactation days *[# - #]*				

a Data obtained from pages *(insert page #s)* in the study report.

N = *[include number of animals for all groups]*

* Statistically different from control, $p<0.05$.

** Statistically different from control, $p<0.01$.

c. Test Substance Intake: ***[MANDATORY** only for dietary studies:]* Based on maternal food consumption and body weight *[and dietary analyses results if available]*, the doses expressed as mean daily mg test substance/kg body weight during the gestation and lactation periods are presented in the following table.

TABLE 4. Mean Maternal Test Substance Intake (mg/kg body weight/day) [a]

Period	Dose (mg/kg/day)		
	LDT	MDT	HDT
Gestation			
Gestation days *[# - #]*			
Gestation days *[# - #]*			
Gestation days *[# - #]*			
Lactation			
Lactation days *[# - #]*			
Lactation days *[# - #]*			
Lactation days *[# - #]*			

a Data obtained from pages *(insert page #s)* in the study report.

d. Reproductive performance: *[Summarize any biologically relevant effects on reproductive performance]* Results for the maternal animals are summarized from the report in the following table. ***[MANDATORY**; the table should be based on report content and include any calculated reproductive indices.]*

TABLE 5. Reproductive Performance [a]

Observation	Dose (mg/kg/day)			
	Control	LDT	MDT	HDT
Number mated				
Number of litters				
Intercurrent deaths				
Mean (±SD) gestation duration (days)				
Incidence of dystocia				

a Data obtained from pages *(insert page #s)* in the study report.

* Statistically different from control, $p<0.05$.

** Statistically different from control, $p<0.01$.

e. Maternal postmortem results:

2. Offspring:

a. Viability and clinical signs: Litter size and viability (survival) results from pups during lactation are summarized from the report in the following table. *[Some form of this table is **MANDATORY**.] [Additionally, describe any post-weaning survival problems.*

TABLE 6. Litter size and viability [a]

Observation	Dose (mg/kg/day)			
	Control	LDT	MDT	HDT
Total number born				
Number born live				
Number born dead				
Sex Ratio Day 0 (% ♀)				
# Deaths Days 0-4 (%)				
# Deaths Days 4-21 (%)				
Mean litter size:				
Day 0				
Day 4 [b]				
Day 4 [c]				
Day 11				
Day 17				
Day 21				
Live birth index				
Viability index				
Lactation index				

a Data obtained from pages *(insert page #s)* in the study report.

b Before standardization (culling).

c After standardization (culling).
* Statistically different from control, p<0.05
** Statistically different from control, p<0.01
Clinical observations on offspring included *[describe findings for pups during lactation and post-weaning]*.

b. Body weight: Offspring body weights during lactation were *[Describe findings]*. Selected mean preweaning pup body weight data are presented in the following table. *[Some form of this table is **MANDATORY**.]*

TABLE 7. Mean Pre-weaning Pup Body Weights (g) [a]

Postnatal Day	Dose (mg/kg/day)							
	Control	LDT	MDT	HDT	Control	LDT	MDT	HDT
	Males				Females			
1								
4 b								
4 c								
11								
17								
21								

a Data obtained from pages *(insert page #s)* in the study report.
b Before standardization (culling).
c After standardization (culling).
* Statistically different from control, p<0.05
** Statistically different from control, p<0.01

Offspring postweaning body weights were *[Describe findings]*. Selected mean Postweaning offspring body weight data are presented in the following table. *[Some form of this table is **MANDATORY**]*.

TABLE 8. Mean (±SD) Post-weaning Pup Body Weights (g) [a]

Postnatal Day	Dose (mg/kg/day)							
	Control	LDT	MDT	HDT	Control	LDT	MDT	HDT
	Males				Females			
35								
49								
[#]								

[#]								

a Data obtained from pages *(insert page #s)* in the study report.

* Statistically different from control, $p<0.05$

** Statistically different from control, $p<0.01$

c) Developmental landmarks:

i) Sexual maturation: *[Summarize any biologically relevant effects on vaginal opening and balanopreputial separation.]* Sexual maturation was *[Describe findings]*. The data are presented in the following table. *[Some form of this table is **MANDATORY**]*.

TABLE 9. Mean (±SD) Age of Sexual Maturation (days) [a]

Parameter	Dose (mg/kg/day)			
	Control	LDT	MDT	HDT
N (M/F)				
Preputial separation (males)				
Vaginal opening (females)				

a Data obtained from pages *(insert page #s)* in the study report.

* Statistically different from control, $p<0.05$

** Statistically different from control, $p<0.01$

ii.) Physical landmarks: *[Summarize findings]* the data are presented in the following table.

TABLE 10. Mean Age of Landmark (day) [a]

Parameter	Dose (mg/kg/day)			
	Control	LDT	MDT	HDT
Males				
N				
Eye opening				
Incisor eruption				
Females				
N				
Eye opening				
Incisor eruption				

a Data obtained from pages *(insert page #s)* in the study report.

* Statistically different from control, $p<0.05$

** Statistically different from control, $p<0.01$

d) Neurobehavioral evaluations: Observations and the schedule for those observations are summarized as follows from the report. *[Detailed description of endpoints is **MANDATORY**.]*

i) Functional observational battery

Table 11. Functional Observational Battery Results (incidence) [a]

Observation	Dose (mg/kg/day)			
	Control	LDT	MDT	HDT
Males				
Type of Observation -1 -PND # -PND # -PND # -PND #				
Type of Observation -2 -PND # -PND # -PND # -PND #				
Females				
Type of Observation -1 -PND # -PND # -PND # -PND #				
Type of Observation -2 -PND # -PND # -PND # -PND #				

a Data obtained from pages *(insert page #s)* in the study report.

N = 10/sex/dose

* Statistically different from control, $p<0.05$

** Statistically different from control, $p<0.01$

ii) Motor activity testing:

TABLE 11. Mean Motor Activity Data (total activity counts for session) [a]

Test Day	Dose (mg/kg/day)			
	Control	LDT	MDT	HDT
Males				
PND 13				
PND 17				
PND 21				
PND *[60]*				
Females				
PND 13				
PND 17				
PND 21				
PND *[60]*				

a Data obtained from pages *(insert page #s)* in the study report.
N = *[include number of animals for all groups]*
[Include units for measurements, as needed.]
* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$
[Create separate tables for males and females.]

TABLE 12a. Motor Activity Sub-sessions - *[sex]* (mean ±S.D. activity counts) [a]

Sub-session		Dose (mg/kg/day)			
		Control	LDT	MDT	HDT
PND 13	1				
	2				
	3				
	4				
	5				
	6				
	7				
	8				
	9				
	10				
PND 17	1				
	2				
	3				

Sub-session		Dose (mg/kg/day)			
		Control	LDT	MDT	HDT
	4				
	5				
	6				
	7				
	8				
	9				
	10				
PND 21	1				
	2				
	3				
	4				
	5				
	6				
	7				
	8				
	9				
	10				
PND *[60]*	1				
	2				
	3				
	4				
	5				
	6				

Sub-session		Dose (mg/kg/day)			
		Control	LDT	MDT	HDT
	7				
	8				
	9				
	10				

a Data obtained from pages *(insert page #s)* in the study report.
N = *[include number of animals for all groups]*
* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$

iii) Auditory startle reflex habituation:

TABLE 13. Auditory Startle Reflex Peak Amplitude Data (mean ±S.D.) [a]

Block		Dose (mg/kg/day)			
		Control	LDT	MDT	HDT
Males					
PND 23	1				
	2				
	3				
	4				
	5				
	Total				
PND *[60]*	1				
	2				
	3				
	4				
	5				

Block		Dose (mg/kg/day)			
		Control	**LDT**	**MDT**	**HDT**
	Total				
Females					
PND 23	1				
	2				
	3				
	4				
	5				
	Total				
PND *[60]*	1				
	2				
	3				
	4				
	5				
	Total				

a Data obtained from pages *(insert page #s)* in the study report.
N = *[include number of animals for all groups]*
[Include units for measurements, as needed.]
* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$

TABLE 13b. Auditory Startle Reflex Latency Data (mean ±S.D. seconds) [a]

Block		Dose (mg/kg/day)			
		Control	LDT	MDT	HDT
Males					
PND 23	1				
	2				
	3				
	4				
	5				
	Total				
PND *[60]*	1				
	2				
	3				
	4				
	5				
	Total				
Females					
PND 23	1				
	2				
	3				
	4				
	5				
	Total				
PND *[60]*	1				
	2				
	3				

Block		Dose (mg/kg/day)			
		Control	**LDT**	**MDT**	**HDT**
	4				
	5				
	Total				

a Data obtained from pages *(insert page #s)* in the study report.
N = *[include number of animals for all groups]*
[Include units for measurements, as needed.]s
* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$

iv) Learning and memory testing:

TABLE 14. Passive Avoidance Performance at PND /#/ Offspring (mean ± S.D.) [a]

Session/Parameter		Dose (mg/kg/day)			
		Control	LDT	MDT	HDT
Males					
Session 1	Trials to criterion				
	Latency trial 1 (sec)				
	Latency trial 2 (sec)				
	Failed to learn				
Session 2	Trials to criterion				
	Latency trial 1 (sec)				
	Failed to learn				
Females					
Session 1	Trials to criterion				
	Latency trial 1 (sec)				
	Latency trial 2 (sec)				
	Failed to learn				
Session 2	Trials to criterion				
	Latency trial 1 (sec)				
	Failed to learn				

a Data extracted from pages ( ) of the study report.
N = *[include number of animals for all groups]*
[Include units for measurements, as needed.]
* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$

[Option 2: use for water M-mazes, E-mazes, or Y-mazes]

TABLE 14. Water Maze Performance in PND *[#]* Offspring (mean ± S.D.) [a]

Session/Parameter		Dose (mg/kg/day)			
		Control	LDT	MDT	HDT
Males					
Session 1	Latency trial 1 (sec)				
	Latency trial 2 (sec)				
	Trials to criterion				
	Errors per trial				
	Failed to learn				
Session 2	Latency trial 1 (sec)				
	Trials to criterion				
	Failed to learn				
Females					
Session 1	Latency trial 1 (sec)				
	Latency trial 2 (sec)				
	Trials to criterion				
	Errors per trial				
	Failed to learn				
Session 2	Latency trial 1 (sec)				
	Trials to criterion				
	Failed to learn				

a Data obtained from pages *(insert page #s)* in the study report.
N = *[include number of animals for all groups]*; values for rats who failed to learn during session 1 were not included in means for session 2.

[Include units for measurements, as needed.]

* Statistically different from control, $p<0.05$

** Statistically different from control, $p<0.01$

[Option 3: use for Morris water maze; create separate tables for males and females]

TABLE 14. Morris Water Maze Performance - *[Sex]* (mean ± S.D.) [a]

Test Day/Parameter		**Dose (mg/kg/day)**			
		Control	**LDT**	**MDT**	**HDT**
PND *[#]*					
Test day 1	Trial time (sec)				
	No. failed trials				
	No. sector entries				
Test day 2	Trial time (sec)				
	No. failed trials				
	No. sector entries				
Test day 3	Trial time (sec)				
	No. failed trials				
	No. sector entries				
Test day 4	Trial time (sec)				
	No. failed trials				
	No. sector entries				
PND *[#]*					
Test day 1	Trial time (sec)				
	No. failed trials				
	No. sector entries				
Test day 2	Trial time (sec)				

Test Day/Parameter		Dose (mg/kg/day)			
		Control	LDT	MDT	HDT
	No. failed trials				
	No. sector entries				
Test day 3	Trial time (sec)				
	No. failed trials				
	No. sector entries				
Test day 4	Trial time (sec)				
	No. failed trials				
	No. sector entries				

a Data obtained from pages *(insert page #s)* in the study report.
N = *[include number of animals for all groups]*
[Include units for measurements, as needed.]
* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$
[Option 4: use for Biel maze (also known as Cincinnati maze); if not performed as water maze, correct table accordingly; create separate tables for males and females]

TABLE 14. Biel Swimming Trials - *[Sex]* (mean ± S.D.) [a]

Test Day/Parameter		Dose (mg/kg/day)			
		Control	LDT	MDT	HDT
PND *[#]*					
Test day 1	Swimming ability (sec)				
Test day 2 Path A	Time (sec)				
	Errors				

Test Day/Parameter		Dose (mg/kg/day)			
		Control	LDT	MDT	HDT
Test day 3 Path A	Time (sec)				
	Errors				
Test day 4 Path B	Time (sec)				
	Errors				
Test day 5 Path B	Time (sec)				
	Errors				
Test day 6 Recall	Time (sec)				
	Errors				
PND *[#]*					
Test day 1	Swimming ability (sec)				
Test day 2 Path A	Time (sec)				
	Errors				
Test day 3 Path A	Time (sec)				
	Errors				
Test day 4 Path B	Time (sec)				
	Errors				
Test day 5 Path B	Time (sec)				
	Errors				
Test day 6 Recall	Time (sec)				
	Errors				

a Data obtained from pages *(insert page #s)* in the study report.

N = *[include number of animals for all groups]*

[Include units for measurements, as needed.]

Path A = forward through maze; Path B = reverse through maze; Time = mean time to escape; Error = all four feet into an incorrect channel.

* Statistically different from control, $p<0.05$

** Statistically different from control, $p<0.01$

e.) Postmortem results:

(i)Brain weights: Mean brain weight data are presented in the following table. The report noted *[Describe findings for both postnatal day 11 (or 22) and termination. Constant brain-to-body weight ratios should not be used to discount alterations in brain weight for pups of low body weight.] [Some form of this table is **MANDATORY**]*

TABLE 15. Mean Brain Weight Data [a]

Parameter	Dose (mg/kg/day)			
	Control	LDT	MDT	HDT
Males				
Day 11 (or 22)				
Terminal body weight (g)				
Brain weight (g)				
Brain-to-body weight ratio				
Termination				
Terminal body weight (g)				
Brain weight (g)				
Brain-to-body weight ratio				
Females				
Day 11 (or 22)				
Terminal body weight (g)				
Brain weight (g)				
Brain-to-body weight ratio				
Termination				
Terminal body weight (g)				
Brain weight (g)				
Brain-to-body weight ratio				

a Data obtained from pages *(insert page #s)* in the study report.

N = *[include number of animals for all groups]*

* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$

ii) Neuropathology

1) Macroscopic examination: The following findings were reported: *[Describe findings for both postnatal day 11 (or 22) and termination]*

2) Microscopic examination: The report noted the following: *[Describe qualitative findings for both postnatal day 11 (or 22) and termination. Include information as to what types of lesions were found. If neuropathological alterations were observed in the high dose group, were lower dose groups sequentially examined? If evidence of neuropathological alterations was seen, was a subjective diagnosis (dose-blind coded re-reading) conducted? If treatment-related lesions were found, include information in a table, including information regarding lesion severity; if no treatment-related lesions were found, include some information in text regarding reported incidence of lesions unrelated to treatment and in control groups.]* The qualitative histopathological findings are presented in the following table. *[Table is **MANDATORY** if there are any treatment-related findings]*

TABLE 16. Histopathology Findings

Parameter	**Dose (mg/kg/day)**			
	Control	**LDT**	**MDT**	**HDT**
Males				
Day 11 (or 22)				
[Observation]				
[Observation]				
Day Termination				
[Observation]				
[Observation]				
Females				
Day 11 (or 22)				

Parameter	Dose (mg/kg/day)			
	Control	LDT	MDT	HDT
[Observation]				
[Observation]				
Termination				
[Observation]				
[Observation]				

a Data obtained from pages *(insert page #s)* in the study report.
N = *[include number of animals for all groups]*
* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$
Morphometric evaluation, presented in the following table, revealed the following: *[Describe quantitative findings for both postnatal day 11 (or 22) pups and adult offspring at termination.] [Some form of this table is **MANDATORY**].*

TABLE 17. Mean (±SD) Morphometric Data [a]

Parameter	Dose (mg/kg/day)			
	Control	LDT	MDT	HDT
Males				
Day 11 (or 22)				
Neocortex (µm)				
Hippocampus (µm)				
Cerebellum (µm)				
Termination				
Neocortex (µm)				
Hippocampus (µm)				

Parameter	Dose (mg/kg/day)			
	Control	LDT	MDT	HDT
Cerebellum (µm)				
Females				
Day 11 (or 22)				
Neocortex (µm)				
Hippocampus (µm)				
Cerebellum (µm)				
Termination				
Neocortex (µm)				
Hippocampus (µm)				
Cerebellum (µm)				

a Data obtained from pages *[insert page #s]* in the study report.
N = *[include number of animals for all groups]*
* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$

D. CONCLUSIONS:

[Note any deficiencies and how they impact on the study results and interpretation, if at all]
[State NOAELs for maternal and offspring toxicity and basis for setting LOAELs; do not attempt to separate systemic- and developmental-neurotoxicity - it is not possible to make this type of distinction based on the data available in these studies. If cholinesterase data were measured, determine separate NOAELs/LOAELs for each compartment (brain, plasma, and erythrocyte) for dams and offspring.]

CARCINOGENICITY

A. Executive Summary:

In a carcinogenicity study test substance was administered to *[(# of animals) species, strain]*/sex/dose in *[dietary, gavage, drinking water, dermal or inhalation]* at dose levels of 0, x, x, or x ppm (equivalent to 0, x, x, x mg/kg bw/day) for *(duration)*.

[Describe toxicity briefly following instructions for exec summary paragraph 2. If there is no toxicity, state that there were no compound related effects on mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic (including tumors) pathology. Note if there was a NOAEL for clinical findings and when they occurred (for acute reference dose consideration during subsequent risk assessment.)].

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

At the doses tested, there was *(not)* a treatment related increase in tumor incidence *[specify tumor type]* when compared to controls. ***(Brief** description)*. Dosing was *(not)* considered adequate based on *(mention critical endpoint noted above)*.

B. STUDY DESIGN:

2. Animal Assignment/Dose Levels: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: STUDY DESIGN *[change heading and units as appropriate for method of administration]*

Test Group	Conc. in Diet *(units)*	Dose to animal *(units)*	Main Study # months		Interim Sac. # months	
			Male	Female	Male	Female
Control						
Low (LDT)						
Mid (MDT)						
High (HDT)						

3. Statistics- *[list parameters that were analyzed and the statistical methods used]*

C. RESULTS AND DISCUSSION (OBSERVATION):

1. Observations –

i. Clinical signs of toxicity - *[include cage side observations and clinical examinations; note when signs were first observed]*

ii. Mortality

2. Body weight -

Animals were weighed *[frequency]*.

Include a table of body weight gain, especially 0-3, 3-13,(0-13), 13-26, 26-52, 52-75, 75-104 weeks, rather than cumulative weight gain alone, especially if there is a treatment related effect. Other time points should be included as appropriate to get the point across.]

TABLE 2: Mean body weights (BW) and body weight gains (BWG)[a] *[SAMPLE - some form of this table is required when there is a treatment-related effect]*

	0 (C)	LDT	MDT	HDT
MALES Initial BW				
Final BW				
BWG Wk 1 (% C)				
BWG Wk 1-13 (%C)				
BWG Wk 13-26 (% C)				
BWG Wk 26-52 (% C)				
BWG Wk 52-75 (% C)				
Overall BWG Wk -1-75				
FEMALES Initial BW				
Final BW				
BWG Wk 1 (% C)				
BWG Wk 1-13 (%C)				
BWG Wk 13-26 (% C)				
BWG Wk 26-52 (% C)				
WG Wk 52-75 (% C)				
Overall BWG Wk -1-75				

C= control

[a] Data obtained from pages *(insert page #s)* in the study report.

* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

3. Food consumption and compound intake - *[if feeding study]*

i. Food consumption -

ii. Compound consumption (time-weighted average) *[include compound intake in table 1]* –

iii. Food efficiency *[if relevant, - relate to effects on body weight gain]*

4. Ophthalmoscopic examination - *[if done - not a guideline requirement]*

5. Blood analysis -

The CHECKED (X) parameters were examined.

a. Hematology

	Hematocrit (HCT)		Leukocyte differential count
	Hemoglobin (HGB)		Mean corpuscular HGB (MCH)
	Leukocyte count (WBC)		Mean corpusc. HGB conc.(MCHC)
	Erythrocyte count (RBC)		Mean corpusc. volume (MCV)
	Platelet count		Reticulocyte count
	Blood clotting measurements		
	(Thromboplastin time)		
	(Clotting time)		
	(Prothrombin time)		

b. Clinical Chemistry/ Biochemistry*

	ELECTROLYTES		OTHER
	Calcium		Albumin
	Chloride		Creatinine
	Magnesium		Urea nitrogen
	Phosphorus		Total Cholesterol
	Potassium		Globulins
	Sodium		Glucose
	ENZYMES		Total bilirubin
	Alkaline phosphatase (ALK)		Total protein (TP)
	Cholinesterase (ChE)		Triglycerides
	Creatine phosphokinase		Serum protein electrophoresis
	Lactic acid dehydrogenase (LDH)		
	Alanine aminotransferase (ALT/also SGPT)		
	Apartate aminotransferase (AST/also SGOT)		
	Gamma glutamyl transferase (GGT)		
	Glutamate dehydrogenase		

6. Urinalysis*

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

	Appearance		Glucose
	Volume		Ketones
	Specific gravity		Bilirubin
	pH		Blood/blood cells
	Sediment (microscopic)		Nitrate
	Protein		Urobilinogen

7. Sacrifice and Pathology

All animals that died and those sacrificed on schedule were subjected to gross pathological examination and the CHECKED (X) tissues were collected for histological examination *[note if not all collected tissues were examined - guideline requires full histopathology in control and high-dose groups as well as in animals that were sacrificed or died]*. The (XX) organs, in addition, were weighed.

DIGESTIVE SYSTEM		CARDIOVASC./HEMAT.		NEUROLOGIC
Tongue		Aorta, thoracic*		Brain (multiple sections)*+
Salivary glands*		Heart*+		Periph.nerve*
Esophagus*		Bone marrow*		Spinal cord (3 levels)*
Stomach*		Lymph nodes*		Pituitary*
Duodenum*		Spleen*+		Eyes (retina, optic nerve)*
Jejunum*		Thymus		**GLANDULAR**
Ileum*				Adrenal gland*+
Cecum*		**UROGENITAL**		Lacrimal gland
Colon*		Kidneys*+		Parathyroids*
Rectum*		Urinary bladder*		Thyroids*
Liver*+		Testes*+		**OTHER**
Gall bladder* (not rat)		Epididymides*+		Bone (sternum and/or femur)
Bile duct* (rat)		Prostate*		Skeletal muscle
Pancreas*		Seminal vesicle*		Skin*
RESPIRATORY		Ovaries*+		All gross lesions and
Trachea*		Uterus*+		
Lung*++		Mammary gland*		
Nose*				
Pharynx*				
Larynx*				

* Required for carcinogenicity studies based on Guideline 870.4200.
+Organ weight required in carcinogenicity studies.
++Organ weight required if inhalation route.

i. Organ weight - *[absolute and relative as appropriate, relate to any histological changes]*

ii. Gross pathology -

iii. Microscopic pathology - *[relate with other findings, as appropriate]*

a) Non-neoplastic –

b) Neoplastic –

D. CONCLUSIONS: *[Note any deficiencies and how they impact on the study results and interpretation, if at all. Include the following points in your discussion/conclusions section.] [Describe the significant findings and provide justification for the conclusions.]*

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

COMBINED CHRONIC TOXICITY/CARCINOGENICITY-RAT

A. Executive Summary:

In a combined chronic /carcinogenicity study test substance was administered to *[(# of animals) species, strain]*/sex/dose in *[dietary, gavage, drinking water, dermal or inhalation]* at dose levels of 0, x, x, or x ppm (equivalent to 0, x, x, x mg/kg bw/day) for *(duration)*.

[Describe toxicity briefly following instructions for exec summary paragraph 2. If there is no toxicity, state that there were no compound related effects on mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic (including tumors) pathology. Note if there was a NOAEL for clinical findings and when they occurred (for acute reference dose consideration during subsequent risk assessment.)].

The LOAEL is , based on The NOAEL is

At the doses tested, there was *(not)* a treatment related increase in tumor incidence *[specify tumor type]* when compared to controls. ***(Brief** description)*. Dosing was *(not)* considered adequate based on *(mention critical endpoint noted above)*.

B. STUDY DESIGN:

1. Animal Assignment/Dose Levels: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: STUDY DESIGN *[change heading and units as appropriate for method of administration]*

Test Group	Conc. in Diet *(units)*	Dose to animal *(units)*	Main Study # months		Interim Sac. # months	
			Male	Female	Male	Female
Control						
Low (LDT)						
Mid (MDT)						
High (HDT)						

2. Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. RESULTS AND DISCUSSION (OBSERVATIONS):

1. Clinical signs of toxicity :

1a. Cage side Observations:

1b. Clinical Examination

1c. Neurological Evaluations

2. Body weight:

[Include a table of body weight gain, especially 0-3, 3-13, (0-13), 13-26, 26-52, 52-75, 75-104 weeks, rather than cumulative weight gain alone, especially if there is a treatment related effect. Other time points should be included as appropriate to get the point across]

TABLE 2: Mean body weights (BW) and body weight gains (BWG) [a] *[SAMPLE - some form of this table is required when there is a treatment-related effect]*

g□SD	0	LDT	MDT	HDT
MALES Initial BW				
Final BW				
BWG Wk 1 (% C)				
BWG Wk 1-13 (%C)				
BWG Wk 13-26 (% C)				
BWG Wk 26-52 (% C)				
BWG Wk 52-75 (% C)				
Overall BWG Wk -1-104				
FEMALES Initial BW				
Final BW				
BWG Wk 1 (% C)				
BWG Wk 1-13 (%C)				
BWG Wk 13-26 (% C)				
BWG Wk 26-52 (% C)				
BWG Wk 52-75 (% C)				
Overall BWG Wk -1-104				

C = control

[a] Data obtained from pages *(insert page #s)* in the study report.

* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

3. Food consumption and compound intake: *[if feeding study]*

i. Food consumption -

ii. Compound consumption (time-weighted average) *[include compound intake in table 1]* -

iii. Food efficiency *[if relevant, - relate to effects on body weight gain]*

4. Ophthalmoscopic examination:

5. Blood analyses:

i. Hematology & Clinical Chemistry:

a. Hematology

Hematocrit (HCT)		Leukocyte differential count
Hemoglobin (HGB)		Mean corpuscular HGB (MCH)
Leukocyte count (WBC)		Mean corpusc. HGB conc.(MCHC)
Erythrocyte count (RBC)		Mean corpusc. volume (MCV)
Platelet count		Reticulocyte count
Blood clotting measurements		
(Thromboplastin time)		
(Clotting time)		
(Prothrombin time)		

b. Clinical Chemistry

ELECTROLYTES		**OTHER**
Calcium		Albumin
Chloride		Creatinine
Magnesium		Urea nitrogen
Phosphorus		Total Cholesterol
Potassium		Globulins
Sodium		Glucose (fasting)
ENZYMES (more than 2 hepatic enzymes)		Total bilirubin
Alkaline phosphatase (ALK)		Total protein (TP)
Cholinesterase (ChE)		Triglycerides
Creatine phosphokinase		Serum protein electrophoresis
Lactic acid dehydrogenase (LDH)		
Alanine aminotransferase (ALT/ SGPT)		
Aspartate aminotransferase (AST/ SGOT)		
Gamma glutamyl transferase (GGT)		
Sorbitol		
Glutamate dehydrogenase		

6. Urinalysis:

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

Appearance		Glucose
Volume		Ketones
Specific gravity / osmolality		Bilirubin
pH		Blood/ red blood cells
Sediment (microscopic)		Nitrate
Protein		Urobilinogen

7. Sacrifice and Pathology

All animals that died and those sacrificed on schedule were subjected to gross pathological examination and the CHECKED (X) tissues were collected for histological examination *[note if not all collected tissues were examined]*. The (XX) organs, in addition, were weighed.

DIGESTIVE SYSTEM		CARDIOVASC./HEMAT		NEUROLOGIC
Tongue		Aorta, thoracic*		Brain (multiple sections)*+
Salivary glands*		Heart*+		Periph.nerve*
Esophagus*		Bone marrow*		Spinal cord (3 levels)*
Stomach*		Lymph nodes*		Pituitary*
Duodenum*		Spleen*+		Eyes (retina, optic nerve)*
Jejunum*		Thymus		**GLANDULAR**
Ileum*				Adrenal gland*+
Cecum*		**UROGENITAL**		Lacrimal gland
Colon*		Kidneys*+		Parathyroids*
Rectum*		Urinary bladder*		Thyroids*
Liver*+		Testes*+		**OTHER**
Gall bladder* (not rat)		Epididymides*+		Bone (sternum and/or femur)
Bile duct (rat)		Prostate*		Skeletal muscle
Pancreas*		Seminal vesicle*		Skin*
RESPIRATORY		Ovaries*+		All gross lesions and
Trachea*		Uterus*+		
Lung*++		Mammary gland*		
Nose*				
Pharynx*				
Larynx*				

* Required for combined chronic/carcinogenicity studies +Organ weight required in combined chronic/carcinogenicity studies.

++Organ weight required if inhalation route.

i. Organ weight - *[absolute and relative as appropriate, relate to any histological changes]*

ii. Gross pathology -

iii. Microscopic pathology - *[relate with other findings, as appropriate]*

a) Non-neoplastic -

b) Neoplastic –

D. CONCLUSIONS: *[Note any deficiencies and how they impact on the study results and interpretation, if at all. Include the following points in your discussion/conclusions section] [Describe the significant findings and provide justification for the conclusions.]*

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

[At the doses tested, there was *(not)* a treatment related increase in tumor incidence *[specify tumor type]* when compared to controls. *(**Brief** description)*. Dosing was *(not)* considered adequate based on *(mention critical endpoint noted above)*.]

PRENATAL DEVELOPMENTAL TOXICITY - *[RODENT SPECIES]*

A. Executive Summary:

In a developmental toxicity study test substance *(% a.i., batch/lot #)]* was administered to *[(# of females) strain]* rats/dose in *[diet, water, by capsule, by gavage]* at dose levels of 0, x, x, or x mg/kg bw/day from days *[#]* through *[#]* of gestation.

[Describe maternal toxicity briefly. If none, state that there were no treatment-related effects in survival, clinical signs, body weight, food consumption, or cesarean parameters. Include effects at doses >LOAEL.]

The maternal LOAEL is mg/kg bw/day, based on *[endpoints]*.

The maternal NOAEL is mg/kg bw/day.

[Describe developmental toxicity briefly. If none, state that there were no treatment-related effects in developmental parameters. Include effects at doses > LOAEL.

The developmental LOAEL is mg/kg bw/day, based on *[endpoints].*

The developmental NOAEL is mg/kg bw/day.

B. STUDY DESIGN

1. Mating: *[describe technique used, e.g.,* sexually mature females were mated with sexually mature males *(verify males were same strain, source as female).]* Confirmation of mating was determined by *[describe, e.g., the presence of sperm in the vaginal washing; or the presence of a copulatory plug]* and was designated as day [0] of gestation.

2. Animal Assignment: Animals were assigned [*randomly?, how?]* to dose groups as indicated in Table 1 *[The information in this table is **MANDATORY**]*.

TABLE 1. Animal Assignment *[change heading / units as appropriate for method of administration]*

Dose (mg/kg bw/day)	**0**	**LDT**	**MDT**	**HDT**
# Females				

2. **Statistical analyses:** *[Statistical procedures should be described in detail for each endpoint evaluated. The litter should be considered the unit of statistical analysis. Differentiate between parametric and non-parametric analysis Describe any data transformations used. General statistical assumptions need not be stated unless there are deviations from generally applied techniques. Animals excluded from analyses should be in table footnotes.]*

3. **Indices:** The following indices were calculated from cesarean section records of animals in the study: *[Formulas or descriptions of pre- and post-implantation loss indices and any other indices as provided in the study report.]*

C. RESULTS AND DISCUSSION (OBSERVATIONS)

1. MATERNAL TOXICITY

1. Mortality and Clinical Observations: The following observations were reported: *[Describe findings along with incidences or #animals affected/# animals examined]*.

2. Body Weight - Body weight data are summarized in Table 2 and as follows: *[include, body weight gain, corrected for gravid uterine weight, as necessary.]*

TABLE 2. Mean Maternal Body Weight Gain (g) [a]

a Data obtained from pages *(insert page #s)* in the study report.

Interval	Dose in mg/kg bw/day (# of Dams)			
	Control (N)	LDT (N)	MDT (N)	HDT (N)
Pretreatment: Days # -#				
Treatment: Days # -#				
Posttreatment: Days # -#				
Corrected BW Gain				

* Statistically different ($p < 0.05$) from the control.
** Statistically different ($p < 0.01$) from the control.

3. Food Consumption - Food consumption data are summarized as follows: *[Describe findings]*. *(Include table only if needed)*.

4. Gross Pathology - Gross pathology data are summarized as follows: *[Describe findings]*.

5. Cesarean Section Data - Data are as follows: *[Describe findings]*; as summarized in Table 3. *[data should be presented as both fetal and litter incidences]*

TABLE 3 Cesarean Section Observations [a]

Observation	Dose (mg/kg bw/day)			
	0	LDT	MDT	HDT
# Animals Assigned (Mated)				
# Animals Pregnant				
Pregnancy Rate (%)				
# Nonpregnant				
Maternal Wastage				
# Died				
# Died Pregnant				
# Died Nonpregnant				
# Aborted				
# Premature Delivery				
Total # Corpora Lutea Corpora Lutea/Dam				
Total # Implantations (Implantations/Dam)				
Total # Litters				
Total # Live Fetuses (Live Fetuses/Dam)				
Total # Dead Fetuses				

(Dead Fetuses/Dam)				
Total # Resorptions				
Early				
Late				
Resorptions/Dam				
Early				
Late				
Litters with Total Resorptions				
Mean Fetal Weight (g)				
Males				
Females				
Sex Ratio (% Male)				
Preimplantation Loss (%)				
Postimplantation Loss (%)				

a Data obtained from pages *(insert page #s)* in the study report.

* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

2. DEVELOPMENTAL TOXICITY *[Special instructions for Tables 4a, b, c: generally present variations and malformations (or other classifications of anomalies) separately; if there are no treatment-related findings include only a few of the most common findings; give the total visceral, skeletal and visceral alterations when applicable.]*

1. External Examination - *[Describe noteworthy findings]*.

2. Visceral Examination - *[Describe noteworthy findings]*.

3. Skeletal Examination - *[Describe noteworthy findings]*.

TABLE 4a. External Examinations [a]

Observations [b]	**Dose (mg/kg bw/day)**			
	0	**LDT**	**MDT**	**HDT**
#Fetuses(litters) examined				
#Fetuses(litters) affected				
[Finding]	[c]			

a Data obtained from pages *(insert page #s)* in the study report.

b Some observations may be grouped together.

c Fetal (litter) incidence

* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

TABLE 4b. Visceral Examinations a

Observations [b]	**Dose (mg/kg bw/day)**			
	0	**LDT**	**MDT**	**HDT**

#Fetuses(litters) examined				
#Fetuses(litters) affected				
[Finding]	c			

a Data obtained from pages *(insert page #s)* in the study report.
b Some observations may be grouped together.
c Fetal (litter) incidence
* Statistically different ($p < 0.05$) from the control.

TABLE 4c. Skeletal Examinations [a]

Observations	**Dose (mg/kg bw/day)**			
	0	**LDT**	**MDT**	**HDT**
#Fetuses(litters) examined				
#Fetuses(litters) affected				
[Finding]				

a Data obtained from pages *(insert page #s)* in the study report.
b Some observations may be grouped together.
c Fetal (litter) incidence
* Statistically different ($p < 0.05$) from the control.
** Statistically different ($p < 0.01$) from the control.

D. CONCLUSIONS: *[Note any deficiencies and how they impact on the study results and interpretation, if at all. Include the following points in your discussion/conclusions section.]*
[Describe the significant maternal findings and provide justification for the conclusions.]
The maternal LOAEL is mg/kg bw/day, based on *[endpoints]*.
The maternal NOAEL is mg/kg bw/day.
[Describe developmental toxicity briefly.]
a. Deaths/Resorptions:
b. Altered Growth:
c. Developmental Variations:
d. Malformations:
[If none, state that there were no treatment-related effects in developmental parameters. Include effects at doses >LOAEL.]
The developmental LOAEL is mg/kg bw/day, based on *[endpoints]*.
The developmental NOAEL is mg/kg bw/day.

PRENATAL DEVELOPMENTAL TOXICITY - *[NON-RODENT SPECIES]*

A. EXECUTIVE SUMMARY:

In a developmental toxicity study (MRID *[number])* *[Chemical name (% a.i., batch/lot #)]* was administered to *[(# of females) strain]* rabbits/dose in *[diet, drinking water, by capsule, by gavage]* at dose levels of 0, x, x, or x mg/kg bw/day from days *[#]* through *[#]* of gestation.

[Describe maternal toxicity briefly. If none, state that there were no treatment-related effects in survival, clinical signs, body weight, food consumption, or cesarean parameters. Include effects at doses > LOAEL.]

The maternal LOAEL is mg/kg bw/day, based on *[endpoints]*.

The maternal NOAEL is mg/kg bw/day.

[Describe developmental toxicity briefly. If none, state that there were no treatment-related effects in developmental parameters. Include effects at doses > LOAEL.

The developmental LOAEL is mg/kg bw/day, based on *[endpoints]*.

The developmental NOAEL is mg/kg bw/day.

B. STUDY DESIGN

1. Mating: *[Describe technique used, i.e., whether natural or artificial insemination. How was mating confirmed? Verify males were same strain, source.]* The day of mating was designated as gestation day [0].

2. Animal Assignment: Animals were assigned [*randomly?, how?]* to dose groups as indicated in Table 1 *[The information in this table is **MANDATORY**]*.

TABLE 1: Animal Assignment *[change heading / units as appropriate for method of administration]*

Dose (mg/kg bw/day)	**0**	**LDT**	**MDT**	**HDT**
# Females				

3. Statistical analyses: *[Statistical procedures should be described in detail for each endpoint evaluated. The litter should be considered the unit of statistical analysis. Differentiate between parametric and non-parametric analysis. Describe any data transformations used. General statistical assumptions need not be stated unless there are deviations from generally applied techniques. Animals excluded from analyses should be in table footnotes.]*

4. Indices: The following indices were calculated from cesarean section records of animals in the study: *[Formulas or descriptions of pre- and postimplantation loss indices and any other indices as provided in the study report.]*

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. MATERNAL TOXICITY

1. Mortality and Clinical Observations: The following observations were reported: *[Describe findings along with incidences or #animals affected/# animals examined]*.

2. Body Weight - Body weight data are summarized in Table 2 and as follows: *[Also include, body weight gain, corrected for gravid uterine weight, as necessary.]*

TABLE 2 Mean Maternal Body Weight Gain (g) [a]

Interval	Dose in mg/kg bw/day (# of Dams)			
	Control (N)	LDT (N)	MDT (N)	HDT (N)
Pretreatment: Days # -#				
Treatment: Days # -#				
Post-treatment: Days # -#				
Corrected BW Gain				

a Data obtained from pages *(insert page #s)* in the study report.

* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

3. Food Consumption - Food consumption data are summarized as follows: *[Describe findings]*. *(Include table only if needed)*.

4. Gross Pathology - Gross pathology data are summarized as follows: *[Describe findings]*.

5. Cesarean Section Data - Data are as follows: *[Describe findings]*; as summarized in Table 3. *[data should be presented as both fetal and litter incidences]*

TABLE 3 Cesarean Section Observations [a] [Include ?SD with mean values, as appropriate.]

Observation	Dose (mg/kg bw/day)			
	0	LDT	MDT	HDT
# Animals Assigned (Mated)				
# Animals Pregnant				
Pregnancy Rate (%)				
# Nonpregnant				
Maternal Wastage				
# Died				
# Died Pregnant				
# Died Nonpregnant				
# Aborted				
# Premature Delivery				
Total # Corpora Lutea Corpora Lutea/Dam				
Total # Implantations (Implantations/Dam)				
Total # Litters				
Total # Live Fetuses (Live Fetuses/Dam)				
Total # Dead Fetuses				

(Dead Fetuses/Dam)				
Total # Resorptions				
Early				
Late				
Resorptions/Dam				
Early				
Late				
Litters with Total Resorptions				
Mean Fetal Weight (g)				
Males				
Females				
Sex Ratio (% Male)				
Preimplantation Loss (%)				
Postimplantation Loss (%)				

a Data obtained from pages *(insert page #s)* in the study report.

* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

DEVELOPMENTAL TOXICITY

[Special instructions for Tables 4a, b, c: generally present variations and malformations (or other classifications of anomalies) separately; if there are no treatment-related findings include only a few of the most common findings; give the total visceral, skeletal and visceral alterations when applicable.]

1. External Examination - *[Describe noteworthy findings]*.

2. Visceral Examination - *[Describe noteworthy findings]*.

3. Skeletal Examination - *[Describe noteworthy findings]*.

TABLE 4a. External Examinations [a]

Observations [b]	**Dose (mg/kg bw/day)**			
	0	**LDT**	**MDT**	**HDT**
#Fetuses(litters) examined				
#Fetuses(litters) affected				
[Finding]	( ) [c]	( )	( )	( )

a Data obtained from pages *(insert page #s)* in the study report.

b Some observations may be grouped together.

c Fetal (litter) incidence

* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

TABLE 4b. Visceral Examinations [a]

Observations [b]	**Dose (mg/kg bw/day)**			
	0	**LDT**	**MDT**	**HDT**
#Fetuses(litters) examined				
#Fetuses(litters) affected				
[Finding]	[c]			

a Data obtained from pages *(insert page #s)* in the study report.

b Some observations may be grouped together.

c Fetal (litter) incidence

* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

TABLE 4c. Skeletal Examinations [a]

Observations [b]	**Dose (mg/kg bw/day)**			
	0	**LDT**	**MDT**	**HDT**
#Fetuses(litters) examined				
#Fetuses(litters) affected				
[Finding]				

a Data obtained from pages *(insert page #s)* in the study report.
b Some observations may be grouped together.
c Fetal (litter) incidence
* Statistically different ($p < 0.05$) from the control.
** Statistically different ($p < 0.01$) from the control.

D. CONCLUSIONS: *[Note any deficiencies and how they impact on the study results and interpretation, if at all. Include the following points in your discussion/conclusions section.]*
[Describe the significant maternal findings and provide justification for the conclusions.]
The maternal LOAEL is mg/kg bw/day, based on *[endpoints]*.
The maternal NOAEL is mg/kg bw/day.
[Describe developmental toxicity briefly.]
a. Deaths/Resorptions:
b. Altered Growth:
c. Developmental Variations:
d. Malformations:
The developmental LOAEL is mg/kg bw/day, based on *[endpoints]*.
The developmental NOAEL is mg/kg bw/day.

TWO GENERATION REPRODUCTION AND FERTILITY EFFECTS STUDY

A. Executive Summary:

In a *[#]*-generation reproduction study (MRID *[number]*) *[Chemical name (% a.i., batch/lot #)]* was administered to *[(# of animals) strain, species]*/sex/dose in *[diet, water, by capsule, by gavage]* at dose levels of 0, x, x, x ppm (equivalent to 0, x, x, or x mg/kg bw/day). *(Mention number of litters per generation and other critical or unusual procedures)*

[Describe parental toxicity briefly for both males and females, including treatment-related effects at doses >LOAEL if applicable.

The parental systemic LOAEL is ppm (mg/kg bw/day in males, mg/kg bw/day in females), based on *[endpoint]*.

The parental systemic NOAEL is ppm (mg/kg bw/day in males, mg/kg bw/day in females).

B. STUDY DESIGN

1. Mating procedure: *[SAMPLE - [#] male was caged with [#] females from the same test group until sperm cells were observed in vaginal smears taken daily during the mating period. If sperm were not found after [#] days' observation, the first male was removed and [#] days later was replaced by another male with proven fertility in the same test group. (If two attempts at mating were unsuccessful the report should state that no further matings were tried. Sibling matings should also be avoided for F_1.)*

After successful mating, each pregnant female was individually placed into a cage with a solid bottom and bedding where it was kept through gestation and lactation.]

2. Study schedule: *[SAMPLE - The P parental animals were given test diets for [#] weeks before they were mated, and the F_1 parental animals were not mated until [#] weeks after they were selected from the F_1 litters. Selection of parents for the F_1 generation was made when the pups were [#] days of age, and the mated animals in the study were approximately [#] weeks of age at mating.]*

3. Animal assignment: P animals were randomly *[how]* assigned to test groups as seen in Table

TABLE 1. Animal Assignment *[include data from both generations in the table as needed]*

Test Group	Dose in Diet [a] *(units)*	Animals/group			
		P Males	P Females	F_1 Males	F_1 Females
Control					
Low (LDT)					
Mid (MDT)					
High (HDT)					

a Diets were administered from *[beginning of the study until sacrifice]*

4. Statistical analyses: *[list parameters that were analyzed and the statistical methods used]*

5. Indices:

Reproductive indices: The following reproductive indices were calculated from breeding and parturition records of animals in the study: *[Formulas or descriptions as provided in the study report.]*

Offspring viability indices: The following viability indices were calculated from lactation records of litters in the study: *[Formulas or descriptions as provided in the study report.]*

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. Parental animals: Observations and the schedule for those observations are summarized from the report. *[Description of endpoints in text or table format including: mortality and clinical signs, detailed examinations, body weight and food consumption, estrous cyclicity, sperm parameters, etc.]*

Gross necropsy consisted of external and internal examinations including the cervical, thoracic, and abdominal viscera.

The following tissues (X) were prepared for microscopic examination and weighed (XX):

a. Mortality and clinical signs: *[Discuss treatment-related mortality including cause of death and time of occurrence.]*

	Ovaries		Testes
	Uterus		Epididymides
	Vagina/cervix		Prostate
	Lesions		Seminal vesicles

The following clinical signs were observed: *[Describe findings]*. These results are summarized in Table 3.

TABLE 3. Mortality and Clinical Signs a

Observation	Dose Group			
	Control	LDT	MDT	HDT
***[P or F_1]* Generation - Males**				
***[P or F_1]* Generation - Females**				

a Data obtained from pages *(insert page #s)* in the study report.

b. Body weight and food consumption:

Body weight was *[Describe findings]*.

Food consumption was *[Describe findings]*.

Reported body weight and selected food consumption results are summarized in Table 4. *[findings should be presented for each generation and sex; data can be split into more than one table.]*

TABLE 4. Mean Body Weight and Food Consumption - Pre-mating [a]

Observations/study week	Dose Group			
	Control	LDT	MDT	HDT
***[P or F_1]* Generation Males - Pre-mating**				
Mean body weight (g) Week *[#]*				
Mean weight gain (g) Weeks *[# - #]*				
Mean food consumption (g/animal/day) Weeks *[# - #]*				
***[P or F_1]* Generation Females - Pre-mating**				
Mean body weight (g) Week *[#]*				
Mean weight gain (g) Weeks *[# - #]*				
Mean food consumption (g/animal/day) Week *[# - #]*				

a Data obtained from pages *(insert page #s)* in the study report.

* Statistically different from control, $p<0.05$.

** Statistically different from control, $p<0.01$.

Selected group mean body weights and food consumption values for pregnant or nursing dams were summarized in the report as follows. *[Table presentation is OPTIONAL; findings during gestation and lactation should be presented or discussed for each generation.]*

c. Test Substance Intake: Based on food consumption, body weight, *[and dietary analyses results]*, the doses expressed as mean daily mg test substance/kg body weight during the *[duration in weeks]* pre-mating period are presented in Table 5. The values for the *[P or F_1]* generation are considered to be representative of the test substance intake for the entire study.

TABLE 5. Mean test substance intake during premating (mg/kg body weight/day) [a]

	Male			Female		
	LDT	MDT	HDT	LDT	MDT	HDT
P						
F1						

a Data obtained from pages *(insert page #s)* in the study report.

d. Reproductive function:

a. Estrous cycle length and periodicity: *[Summarize any biologically relevant effects on the estrous cycle]* Results from the evaluation of vaginal smears indicated *[Describe findings]*. *[findings should be presented for each generation.]*

b. Sperm measures: *[Summarize any biologically relevant effects on sperm parameters (epididymis sperm counts, motility, morphology; and testicular spermatid counts).]* Results from the evaluation of sperm parameters revealed *[Describe findings]*. *[findings should be presented for each generation.]*

5. Reproductive performance: *[Summarize any biologically relevant effects on reproductive performance]* Results for the parental animals are summarized from the report in Table 6. *[findings should be presented for each generation and each litter; the table should be based on report content and include any calculated reproductive indices.]*

TABLE 6. Reproductive Performance [a] ***[Example:]***

Observation	**Dose Group (ppm)**			
	Control	**LDT**	**MDT**	**HDT**
P Generation - Litter A				
Mean (±SD) precoital interval (days)				
MALES				
Number mated				
Number fertile				
Fertility not determined				
Intercurrent deaths				
FEMALES				
Number mated				
Number fertile				
Fertility not determined				
Intercurrent deaths				
Mean (±SD) gestation interval (days)				
Number of litters				

a Data obtained from pages *(insert page #s)* in the study report.

* Statistically different from control, $p<0.05$.

** Statistically different from control, $p<0.01$.

e. Parental postmortem results:

a) Organ weights: The report noted *[Describe findings, relate to histological observations]*. Selected absolute and relative (to body weight *[brain weight])* organ weight values are presented in the following table.

b) Pathology

1) Macroscopic examination: The report noted the following observations to be related to the administration of the test substance. *[Describe findings]*

2) Microscopic examination: The report noted the following observations to be related to the administration of the test substance. *[Describe findings, relate with other findings as appropriate]*

2. OFFSPRING

a. Viability and clinical signs: The following findings were reported: *[Discuss results; describe anogenital distance results, if measured.]*

Mean litter size and viability (survival) results from pups during lactation are summarized from the report in Table 7.

TABLE 7. Litter parameters for F_1 and F_2 generations [a] *[Example; data should be presented for each generation (F_1 and F_2 pups); include mean values, as appropriate.]*

Observation	Dose Group (ppm)			
	Control	50	250	1250
F_1 Generation				
Mean implantation sites				
Number born live				
Number born dead				
Sex Ratio Day 0 (% ♀)				
# Deaths Days 0-4 (%)				
# Deaths Days 4-21 (%)				
Mean litter size Day 0				
Day 4 [b]				
Day 4 [c]				
Day 7				
Day 14				
Day 21				
Birth index				
Live birth index				
Viability index				
Lactation index				
F_2 Generation				
Mean implantation sites				
Number born live				
Number born dead				

Observation	Dose Group (ppm)			
	Control	50	250	1250
Sex Ratio Day 0 (% ♀)				
# Deaths Days 0-4 (%)				
# DeathsDays 4-21 (%)				
Mean litter size Day 0				
Day 4 [b]				
Day 4 [c]				
Day 7				
Day 14				
Day 21				
Birth index				
Live birth index				
Viability index				
Lactation index				

a Data obtained from pages *(insert page #s)* in the study report.
b Before standardization (culling)
c After standardization (culling)
* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$

The report stated that the clinical observations of offspring during lactation included *[Describe findings]*. The results of these observations are as follows.

b. Body weight: Offspring body weights were *[Describe findings]*. Selected mean pup body weight data are presented in Table 8.

TABLE 8. Mean (±SD) Litter and Pup Weights (g) [a] *[Example; data should be presented for each generation (F_1 and F_2 pups)]*

Dose Group (ppm)								
Lactation Day	0	50	250	1250	0	50	250	1250
	F_1 Litters				F_2 Litters			
1								
4 b								
4 c								
7								
14								
21								
	F_1 Pups - male				F_2 Pups - male			
1								
4 b								
4 c								
7								
21								
	F_1 Pups - female				F_2 Pups - female			
1								
4 b								
4 c								
7								

21								

a Data obtained from pages *(insert page #s)* in the study report.
b Before standardization (culling)
c After standardization (culling)
* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$

c. Sexual maturation (F_1): *[Summarize any biologically relevant effects on vaginal opening and preputial separation.]* Sexual maturation was *[Describe findings]*.

d. Offspring postmortem results:

a) Organ weights: The report noted *[Describe findings]*. Selected absolute and relative (to body weight *[brain weight])* organ weight values are presented in the following table.

b) Pathology

i) Macroscopic examination: The following findings were reported: *[Describe findings]*

ii) Microscopic examination: The report noted the following: *[Describe findings]*

D. CONCLUSIONS:

The parental systemic LOAEL is ppm (mg/kg bw/day in males, mg/kg bw/day in females), based on *[endpoint]*.

The parental systemic NOAEL is ppm (mg/kg bw/day in males, mg/kg bw/day in females).

The offspring LOAEL is ppm (mg/kg bw/day), based on *[endpoint]*. The offspring NOAEL is ppm (mg/kg bw/day).

The reproductive LOAEL is ppm (mg/kg bw/day in males, mg/kg bw/day in females), based on *[endpoint]*.

The reproductive NOAEL is ppm (mg/kg bw/day in males, mg/kg bw/day in females).

METABOLISM [*RODENT SPECIES*];

A. Executive Summary:

In a metabolism study test substance *[Chemical name (% a.i., batch/lot #), include location of radioactive label]* was administered to *[(# of animals) species, strain]*/sex/dose in *[method of exposure: eg. by gavage]* at dose levels of 0, x, x [mg/kg or other pertinent units].

Be brief (one or two paragraphs) [Describe, as appropriate: recoveries and routes of elimination of radioactivity and time frame as they relate to absorption and excretion of the compound; radioactivity in organs of concern, especially as it relates to bioaccumulation; sex and treatment group differences; and expired air radioactivity; major metabolites; other major factors.]

This metabolism study in the *(species)* is classified *[acceptable, unacceptable (guideline, non-guideline)]* and satisfies *(does not satisfy)* the guideline requirement for a metabolism study [OPPTS 870.7485, OECD 417] in *[species] [If unacceptable, why and is it upgradable. If it does not satisfy the requirement, concisely list only major deficiencies or refer to deficiency section.]*

B. STUDY DESIGN:

1. Group Arrangements

Animals were assigned *[note how assigned, e.g., random, briefly describe groups as needed]* to the test groups noted in Table 1.

TABLE 1: Dosing groups for pharmacokinetic studies for *(chemical)*

Test Group	**Dose of labeled material (mg/kg)**	**Number/sex**	**Remarks (eg. time of sacrifice)**
Oral Dose			
Treatment 2 ***[if applicable]***			
Treatment 3 ***[if applicable]***			
: :			

2. Dosing and sample collection: *[Briefly describe dosing methods and sample collection]*

a. Pharmacokinetic studies: *[give details of experiments including what was sampled (urine, feces, tissues, cage washes, bile, if appropriate) and when and how often.]*

b. Metabolite characterization studies: *[What was collected for identification, when and from how many animals (samples pooled or not), method type for identification (e.g. GCMS or TLC)].*

3. Statistics: *[list parameters that were analyzed and the statistical methods used]*

C. RESULTS AND DISCUSSION (OBSERVATIONS):

1. PHARMACOKINETIC STUDIES:

1. Preliminary experiment [*Briefly describe results]*

2. Absorption *[Briefly describe absorption, may include an optional table relating excretion of radioactivity (in urine, feces, etc.) to sampling time]*

3. Tissue distribution *[include groups that are applicable; describe distribution patterns for each treatment group. Some form of table 2 is recommended, if data are available.]*

TABLE 2: Distribution of radioactivity in rat tissues/organs after administration of C^{14}-labeled Compound XX[a].

	Percent of radioactive dose administered [or ppm equivalents]					
	Oral dose		**Treatment 2 (if applicable)**		**Treatment 3 (if applicable)**	
Tissue/organ	**Male**	**Female (if applicable)**	**Male**	**Female (if applicable)**	**Male**	**Female (if applicable)**
Organ 1						
Organ 2....						

[a] Data obtained from pages *(insert page #s)* in the study report.

[Write a brief narrative of the contents of Table 2 under the following headings]:

a) Oral Dose : As summarized in Table 2 .....

b) Treatment 2 ..... *[If Applicable]*

c) Treatment 3 ..... *[If Applicable]*

4. Excretion *[include treatment groups that are applicable) (describe excretion patterns for each treatment group. Some form of table 3 is recommended]*

TABLE 3: Recovery of radioactivity in tissues and excreta of rats after administration of C^{14}-labeled Compound XX[a].

	Percent of radioactive dose recovered					
	Oral Dose		**Treatment 2 (if applicable)**		**Treatment 3 (if applicable)**	
	Male	**Female (if applicable)**	**Male**	**Female (if applicable)**	**Male**	**Female (if applicable)**
Expired air						
Tissues						
Carcass						
Cage wash						
Urine[b]						
Feces						
Total						

[a] Data obtained from pages *(insert page #s)* in the study report.

[b]Report at appropriate intervals.

[Write a brief narrative of the contents of Table 3 under the following headings]:

a) Oral Dose: As summarized in Table 3.....

b) Treatment 2: *[If applicable]*

c) Treatment 3: *[If applicable]*

2. METABOLITE CHARACTERIZATION STUDIES:

[Give the metabolites identified, include percent of radioactive dose given, where they were identified, when if applicable, how they were identified if applicable, how much parent was present in the excreta. Some form of table 4 is recommended. When available, include summary of metabolic pathways and figures available. Mention which are major vs. minor pathways. Include the registrant=s postulated pathway as a figure or attachment, preferably electronic]

TABLE 4. Metabolite profile in excreta of rats dosed with C^{14}-labeled Compound XX[a]. ***[Metabolites must be given as percent of dose.*** *If possible the reviewer should perform the necessary conversions, include Total identified, Total unidentified, Total accounted for, Total lost or unaccounted (see below)]*

Dose	Percent of administered dose					
	Oral Dose		Treatment 2 *(If Applicable)*		Treatment 3 *(If Applicable)*	
Compound	Male	Female *(If Applicable)*	Male	Female *(If Applicable)*	Male	Female *(If Applicable)*
Parent						
Identified Metabolite 1						
Identified Metabolite 2						
Total identified						
Unidentified Metabolite X						
Unidentified Metabolite Y						
Undentified at origin or at some band						
Total unidentif.						
Total accounted for [b]						
Lost/unaccounted for [c]						
Total	100	100	100	100	100	100

[a] Data obtained from pages *(insert page #s)* in the study report.

[b] Total accounted for = (Total identified) + (Total unidentified)

[c] 100 - (Total accounted for)

C. CONCLUSIONS:

METABOLISM, DISTRIBUTION, AND EXPRESSION OF RESIDUES IN LIVESTOCK

A. Executive Summary:

[^{14}C specify radiolabel]-[active ingredient] (specific activity: xx Bq/mg) was administered to [number] laying hen at an average dose of [xx] mg/kg feed (corresponding to [xx] mg/kg bw/day). The radiolabeled compound was administered [specify route, e.g. orally] by [specify means, e.g. gelatin capsule] [once/twice] daily for [number] consecutive days. Eggs were collected twice a day and the excreta was collected once a day throughout the study period. The animals were sacrificed approximately [xx] hours following the last dose administration and the following tissues were collected for analysis: [list tissues, e.g. liver, fat, muscle, gastrointestinal (GI) tract and its contents].

[Discuss recoveries/accountabilities and routes of elimination of radioactivity; absorption and excretion of the compound; radioactivity in organs of concern (distribution/disposition), especially as it relates to bioaccumulation; extractability; major metabolites; other major factors.]

The majority of the administered dose (AD) was eliminated via excreta (xx% of the AD). An additional yy% of the AD was recovered from the GI tract and zz% of the AD from the cage wash. Throughout the study period, only xx% of the AD was transferred to eggs and less than yy% of the AD was transferred to edible tissues. The highest concentrations of residues were detected in [tissue] (xx ppm).

[Briefly summarize extraction procedures and analytical methods used to identify metabolites.]

Samples were analyzed within [xx] months of sacrifice. Freezer storage stability was investigated. Storage stability of [active ingredient] was demonstrated in [livestock matrices] for up to [xx] days/months in the study. [or [Tissue] samples were analyzed first at yy months of frozen storage, and then at zz months of frozen storage. The metabolite profiles in the chromatograms obtained from the first and second HPLC analysis were similar for [tissue] samples, thus demonstrating the stability of the analytes of interest in livestock commodities for up to zz months of frozen storage.]

[Given that samples were stored frozen for less than 6 months, storage stability data are not required.]

[Indicate whether the parent or metabolite(s) was (were) found to be the predominant residue(s) in the various matrices (include ppm equivalents and corresponding %TRR/matrix). Indicate whether any other metabolites were identified and if any were present at concentrations >10% TRR.]

[Summarize the metabolic pathway in poultry.]

The metabolic pathway of [active ingredient] in poultry involves/proceeds via…

[Include this section only if the "GLP Compliance" prompt above is answered "Significant deviations from regulatory requirements were reported."]

B. MATERIALS AND METHODS

I. MATERIALS

1. Test Material

Radiochemical purity	a-label: xx%
	b-label: xx%
Specific activity as received	a-label: xx mCi/mmol (xx mCi/mg)
	b-label: xx mCi/mmol (xx mCi/mg)
Specific activity of dose	a-label: xx mCi/mmol (xx mCi/mg)
	b-label: xx mCi/mmol (xx mCi/mg)

Position of radiolabels [Insert structures]

2. Animals

Table B.7.2.1-2. General Test Animal Information.					
Species	Breed	Age	Weight at Study Initiation (kg)	Health Status	Description of Housing/Holding Area
Hen					

II. STUDY DESIGN

Dose Regime

Table B.7.2.1-3. Test Animal Dietary Regime.				
Composition of Diet	Feed Consumption (kg/day)	Water	Acclimation Period	Pre-dosing
				Yes or No

Table B.7.2.1-4. Test Animal Dosing Regime.				
Treatment Type	Treatment Level (ppm in diet)	Vehicle	Dose (mg ai/kg bw/day)	Timing/Duration
Oral		capsule, feed, bolus, etc.		

Sampling

Table B.7.2.1-5. Sample Collection Information.			
Eggs Collected	Excreta and Cage Wash Collected*	Interval From Last Dose to Sacrifice	Tissues Harvested and Analyzed
XXX daily	XXX daily	XXX hours	

*If available.

[Briefly describe how samples were taken, parts sampled, how samples were handled after collection (shipment, storage, etc.), and any preparation that was done prior to extraction.]

Extraction and Analysis

[If available, then include a flowchart of the extraction and fractionation schemes.]

[Briefly describe the extraction, fractionation and hydrolysis strategies for each tissue including solvents used (ratios), the order of their use, the extraction procedures employed (i.e., blending, maceration, Soxhlet, etc.) and other extraction techniques.]

[Briefly describe procedures used to release bound and conjugated residues (i.e., acid, base, or enzyme hydrolysis, exhaustive extraction, etc.). Has the petitioner justified the use of severe conditions (e.g., strong acid hydrolysis in the presence of heat, etc.)?]

Identification and Characterization

[Briefly describe the methods used for identification/characterization of the residues (LSC, TLC, GLC, HPLC, etc.). If applicable, then very briefly describe difficulties with methods that fail to elucidate the nature of the residues or bound residues.]

C. RESULTS AND DISCUSSION

1. Total Radioactive Residues

Quantitation: [Briefly describe methods for determining TRR values.]

Table B.7.2.1-6. TRRs in Eggs, Tissue, and Excreta.

Matrix	A-label		B-label	
	% TRR	ppm	% TRR	ppm
Excreta				
Muscle				
Fat				
Liver				
Eggs				
GI tract				
Other				

TRRs in eggs [did/did not] appear to have reached a plateau at the end of dosing (see Table B.7.2.1-7).

Table B.7.2.1-7. TRRs in Eggs as Function of Time.

Interval		A-Label		B-Label	
		ppm	% of dose	ppm	% of dose
Day 1	AM				
	PM				
Day 2	AM				
	PM				
Day 3	AM				
	PM				
[add rows as necessary]	AM				
	PM				
Total					

Note: A graphical plot of the data may be substituted for Table B.7.2.1-7.]

2. Extraction, Characterization, and Distribution of Residues

Extraction and Characterization of Residues in Poultry

A label:

Table B.7.2.1-8. Distribution of the Parent and the Metabolites in Poultry Matrices Following Dosing with [A Label] Radiolabeled [Active Ingredient] at [Dose]. [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.2.1-x as needed to accommodate additional radiolabel positions.]

Metabolite Fraction	Excreta (TRR = xx ppm)		Fat (TRR = xx ppm)		Muscle (TRR = xx ppm)		Liver (TRR = xx ppm)		Eggs (TRR = xx ppm)	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Surface wash										
[Add a row for each identified compound]										
[Unidentified compound]										
Organosoluble										
[Add a row for each identified compound]										
[Unidentified compound]										
Aqueous soluble										
[Add a row for each identified compound]										
[Unidentified compound]										
Etc. (e.g. PES)										

B label:

Table B.7.2.1-9. Distribution of the Parent and the Metabolites in Poultry Matrices Following Dosing with [B Label] Radiolabeled [Active Ingredient] at [Dose]. [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.2.1-x as needed to accommodate additional radiolabel positions.]

Metabolite Fraction	Excreta (TRR = xx ppm)		Fat (TRR = xx ppm)		Muscle (TRR = xx ppm)		Liver (TRR = xx ppm)		Eggs (TRR = xx ppm)	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Surface wash										
[Add a row for each identified compound]										
[Unidentified compound]										
Organosoluble										
[Add a row for each identified compound]										

[Unidentified compound]										
Aqueous soluble										
[Add a row for each identified compound]										
[Unidentified compound]										
Etc. (e.g. PES)										

3. Storage Stability of Residues

[Discuss whether the petitioner demonstrated that residues are stable during storage.]

Table B. 7.2.1-10. Summary of Storage Conditions.

Matrix (RAC or Extract)	Storage Temperature (°C)	Actual Study Duration (days or months)	Interval of Demonstrated Storage Stability [specify crop/matrix if different] (days/months)

4. Identity of Residues in Poultry

A label:

[Briefly summarize the metabolites found in each matrix.]

Table B.7.2.1-11. Summary of Characterization and Identification of Radioactive Residues in Poultry Matrices Following Dosing with [A Label] Radiolabeled [Active Ingredient] at [Dose]. [Note: Create additional Tables B.7.2.1-x as needed to accommodate additional radiolabel positions.]

Compound	Muscle		Fat		Kidney		Liver		Eggs	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	%TRR	ppm
[Parent]										
[Metabolite 1]										
[Metabolite 2]										
[Metabolite 3]										
[Metabolite 4]										
Total extractable (Aqueous + organic)										
Total identified										
Total unidentified										
Total bound residues (PES)										
% Accountability										

Total (ppm)/TRR (ppm) * 100										

PES = post-extraction solids.

B label:

[Briefly summarize the metabolites found in each matrix. Are there any major differences between labels?]

Table B.7.2.1-12. Summary of Characterization and Identification of Radioactive Residues in Poultry Matrices Following Dosing with [A Label] Radiolabeled [Active Ingredient] at [Dose]. [Note: Create additional Tables B.7.2.1-x as needed to accommodate additional radiolabel positions.]

Compound	Muscle		Fat		Kidney		Liver		Eggs	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	%TRR	ppm
[Parent]										
[Metabolite 1]										
[Metabolite 2]										
[Metabolite 3]										
[Metabolite 4]										
Total extractable (Aqueous + organic)										
Total identified										
Total unidentified										
Total bound residues (PES)										
% Accountability Total (ppm)/TRR (ppm) * 100										

PES = post-extraction solids.

5. Proposed Metabolic Pathway: [Briefly describe the metabolic pathway and reactions (i.e., oxidation, hydrolysis, etc.)]

Figure B.7.2.1. Proposed Metabolic Profile of [Active ingredient] in Poultry.

[Insert metabolic profile]

Table B.7.2.1-13. Identification of Compounds from Metabolism Study (both proposed and found).

Common Name/Code [Figure B.7.2.1 ID No.]	Chemical Name	Chemical Structure

D. CONCLUSIONS

The poultry metabolism study is considered scientifically [acceptable or unacceptable]. [Briefly, summarize the results of the submitted poultry metabolism studies such as: routes or pathways, mechanisms involved and extent/degree of metabolism observed, nature, amount, and distribution of the TRRs in the poultry tissues. Conclusion should be very high level.]

LACTATING RUMINANTS (GOAT OR COW)

A. Executive Summary

[^{14}C specify radiolabel]-[active ingredient] (specific activity: xx Bq/mg) was administered to one lactating goat at an average dose of [xx] mg/kg feed (corresponding to [xx] mg/kg bw/day). The radiolabeled compound was [specify route, e.g. orally] by [specify means, e.g. gelatin capsule] [once/twice] daily for [number] consecutive days. Milk was collected twice a day and the excreta was collected once a day throughout the study period. The animal was sacrificed approximately [xx] hours following the last dose administration and the following tissues were collected for analysis: [list tissues, e.g. liver, kidney, fat, muscle, gastrointestinal (GI) tract and its contents, and bile].

[Discuss recoveries/accountabilities and routes of elimination of radioactivity; absorption and excretion of the compound; radioactivity in organs of concern (distribution/disposition), especially as it relates to bioaccumulation; extractability; major metabolites; other major factors.]

The majority of the administered dose (AD) was eliminated via urine (xx% of the AD) and feces (xx% of the AD). An additional yy% of the AD was recovered from the GI tract and zz% of the AD from the cage wash. Throughout the study period, only xx% of the AD was transferred to milk and less than yy% of the AD was transferred to edible tissues. The highest concentrations of residues were detected in [tissue] (xx ppm).

[Briefly summarize extraction procedures and analytical methods used to identify metabolites.]

Samples were analyzed within [xx] months of sacrifice. Freezer storage stability was investigated. Storage stability of [active ingredient] was demonstrated in [livestock matrices] for up to [xx] days/months in the study. [or [Tissue] samples were analyzed first at yy months of frozen storage, and then at zz months of frozen storage. The metabolite profiles in the chromatograms obtained from the first and second HPLC analysis were similar for [tissue] samples, thus demonstrating the stability of the analytes of interest in livestock commodities for up to zz months of frozen storage.]

[Given that samples were stored frozen for less than 6 months, storage stability data are not required.]

[Indicate whether the parent or metabolite(s) was (were) found to be the predominant residue(s) in the various matrices (include ppm equivalents and corresponding %TRR/matrix). Indicate whether any other metabolites were identified and if any were present at concentrations >10% TRR.]

[Summarize the metabolic pathway in ruminant.]

The metabolic pathway of [active ingredient] in ruminant involves/proceeds via…

[Include this section only if the "GLP Compliance" prompt above is answered "Significant deviations from regulatory requirements were reported."]

B. MATERIALS AND METHODS

1. MATERIALS

a. Test Material

Radiochemical purity	a-label: xx%
	b-label: xx%
Specific activity as received	a-label: xx mCi/mmol (xx mCi/mg)
	b-label: xx mCi/mmol (xx mCi/mg)
Specific activity of dose	a-label: xx mCi/mmol (xx mCi/mg)
	b-label: xx mCi/mmol (xx mCi/mg)
Position of radiolabels [Insert structures]	

b. Animals

Table B.7.2.2-2. General Test Animal Information.

Species	Breed	Age	Weight at Study Initiation (kg)	Health Status	Description of Housing/Holding Area
Goat					

2. STUDY DESIGN

Dose Regime

Table B.7.2.2-3. Test Animal Dietary Regime.

Composition of Diet	Feed consumption (kg/day)	Water	Acclimation period	Predosing
				Yes or No

Table B.7.2.2-4. Test Animal Dosing Regime.

Treatment Type	Treatment Level (ppm in diet)[1]	Vehicle	Dose (mg ai/kg bw/day)	Timing/Duration

Oral		capsule, feed, bolus, etc.		
Dermal				

[1] Dietary burden on a dry-weight basis.

Sampling

Table B.7.2.2-5. Sample Collection Information.			
Milk Collected	Urine, Feces, and Cage Wash Collected*	Interval From Last Dose to Sacrifice	Tissues Harvested and Analyzed
XXX daily	XXX daily	XXX hours	

*If available.

[Briefly describe how samples were taken, parts sampled, how samples were handled after collection (shipment, storage, etc.), and any preparation that was done prior to extraction.]

Extraction and Analysis

[If available, then include a flowchart of the extraction and fractionation schemes.]

[Briefly describe the extraction, fractionation and hydrolysis strategies for each tissue including solvents used (ratios), the order of their use, the extraction procedures employed (i.e., blending, maceration, Soxhlet, etc.) and other extraction techniques.]

[Briefly describe procedures used to release bound and conjugated residues (i.e., acid, base, or enzyme hydrolysis, exhaustive extraction, etc.). Has the petitioner justified the use of severe conditions (e.g., strong acid hydrolysis in the presence of heat, etc.)?]

Identification and Characterization

[Briefly describe the methods used for identification/characterization of the residues (LSC, TLC, GLC, HPLC, etc.). If applicable, then very briefly describe difficulties with methods that fail to elucidate the nature of the residues or bound residues.]

C. RESULTS AND DISCUSSIONS (OBSERVATIONS)

1. Total Radioactive Residues

Quantitation: [Briefly describe methods for determining TRR values.]

Table B.7.2.2-6. TRRs in Milk, Tissue, and Excreta.				
Matrix	A-label		B-label	
	% TRR	ppm	% TRR	ppm
Urine				
Feces				
Muscle				
Fat				
Kidney				
Liver				
Milk				
GI tract				
Other				

TRRs in milk [did/did not] appear to have reached a plateau at the end of dosing (see Table B.7.2.2-7).

Table B.7.2.2-7. TRRs in Milk as Function of Time.					
Interval		A-Label		B-Label	
		ppm	% of dose	ppm	% of dose
Day 1	AM				
	PM				
Day 2	AM				
	PM				
Day 3	AM				
	PM				
[add rows as necessary]	AM				
	PM				
Total					

[Note: A graphical plot of the data may be substituted for Table B.7.2.2-7.]

2. Extraction, Characterization, and Distribution of Residues

Extraction and Characterization of Residues in Ruminant

A label:

Table B.7.2.2-8. Distribution of the Parent and the Metabolites in Ruminant Excreta Following Dosing with [A Label] Radiolabeled [Active Ingredient] at [Dose]. [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.2.2-x as needed to accommodate additional radiolabel positions.]				
Metabolite Fraction	Urine (TRR = xx ppm)		Feces (TRR = xx ppm)	
	%TRR	ppm	%TRR	ppm
Surface wash				
[Add a row for each identified compound]				
[Unidentified compound]				
Organosoluble				
[Add a row for each identified compound]				
[Unidentified compound]				
Aqueous soluble				
[Add a row for each identified compound]				
[Unidentified compound]				
Total extractable (Aqueous + organic)				
Total identified				
Total unidentified				
Total bound residues (PES)				
% Accountability Total (ppm)/TRR (ppm) * 100				

PES = post-extraction solids.

Table B.7.2.2-9. Distribution of the Parent and the Metabolites in Ruminant Matrices Followi Dosing with [A Label] Radiolabeled [Active Ingredient] at [Dose]. [Note: Add rows to the table needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.2.2-x needed to accommodate additional radiolabel positions.]

Metabolite Fraction	Muscle (TRR = xx ppm)		Fat (TRR = xx ppm)		Kidney (TRR = xx ppm)		Liver (TRR = xx ppm)		Milk (TRR = ppm)	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppr
Surface wash										
[Add a row for each identified compound]										
[Unidentified compound]										
Organosoluble										
[Add a row for each identified compound]										
[Unidentified compound]										
Aqueous soluble										
[Add a row for each identified compound]										
[Unidentified compound]										

B label:

Table B.7.2.2-10. Distribution of the Parent and the Metabolites in Ruminant Excreta Following Dosing with [B Label] Radiolabeled [Active Ingredient] at [Dose]. [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.2.2-x as needed to accommodate additional radiolabel positions.]

Metabolite Fraction	Urine (TRR = xx ppm)		Feces (TRR = xx ppm)	
	%TRR	ppm	%TRR	ppm
Surface wash				
[Add a row for each identified compound]				
[Unidentified compound]				
Organosoluble				
[Add a row for each identified compound]				
[Unidentified compound]				
Aqueous soluble				
[Add a row for each identified compound]				
[Unidentified compound]				
Total extractable (Aqueous + organic)				
Total identified				

Total unidentified				
Total bound residues (PES)				
% Accountability Total (ppm)/TRR (ppm) * 100				

PES = post-extraction solids.

Table B.7.2.2-11. Distribution of the Parent and the Metabolites in Ruminant Matrices Following Dosing with [B Label] Radiolabeled [Active Ingredient] at [Dose]. [Note: Add rows to the table as needed to accommodate the fractionation/characterization scheme. Create additional Tables B.7.2.2-x as needed to accommodate additional radiolabel positions.]

Metabolite Fraction	Muscle (TRR = xx ppm)		Fat (TRR = xx ppm)		Kidney (TRR = xx ppm)		Liver (TRR = xx ppm)		Milk (TRR = xx ppm)	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Surface wash										
[Add a row for each identified compound]										
[Unidentified compound]										
Organosoluble										
[Add a row for each identified compound]										
[Unidentified compound]										
Aqueous soluble										
[Add a row for each identified compound]										
[Unidentified compound]										

C. Storage Stability of Residues

[Discuss whether the petitioner demonstrated that residues are stable during storage.]

Table B.7.2.2-12. Summary of Storage Conditions.

Matrix (RAC or Extract)	Storage Temperature (°C)	Actual Study Duration (days or months)	Interval of Demonstrated Storage Stability [specify crop/matrix if different] (days or months)

D. Identity of Residues in Ruminant

A label:

[Briefly summarize the metabolites found in each matrix.]

Table B.7.2.2-13. Summary of Characterization and Identification of Radioactive Residues in Ruminant Matrices Following Dosing with [A Label] Radiolabeled [Active Ingredient]

at [Dose]. [Note: Create additional Tables B.7.2.2-x as needed to accommodate additional radiolabel positions.]										
Compound	Muscle		Fat		Kidney		Liver		Milk	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	%TRR	ppm
[Parent]										
[Metabolite 1]										
[Metabolite 2]										
[Metabolite 3]										
[Metabolite 4]										
Total extractable (Aqueous + organic)										
Total identified										
Total unidentified										
Total bound residues (PES)										
% Accountability Total (ppm)/TRR (ppm) * 100										

PES = post-extraction solids.

B label:

[Briefly summarize the metabolites found in each matrix. Are there any major differences between labels?]

Table B.7.2.2-14. Summary of Characterization and Identification of Radioactive Residues in Ruminant Matrices Following Dosing with [B Label] Radiolabeled [Active Ingredient] at [Dose]. [Note: Create additional Tables B.7.2.2-x as needed to accommodate additional radiolabel positions.]										
Compound	Muscle		Fat		Kidney		Liver		Milk	
	% TRR	ppm	% TRR	ppm	% TRR	ppm	% TRR	ppm	%TRR	ppm
[Parent]										
[Metabolite 1]										
[Metabolite 2]										
[Metabolite 3]										
[Metabolite 4]										
Total extractable (Aqueous + organic)										

Total identified										
Total unidentified										
Total bound residues (PES)										
% Accountability Total (ppm)/TRR (ppm) * 100										

PES = post-extraction solids.

E. Proposed Metabolic Pathway

[Briefly describe the metabolic pathway and reactions (i.e., oxidation, hydrolysis, etc.).]

Figure B.7.2.2. Proposed Metabolic Profile of [Active ingredient] in Ruminant.

[Insert metabolic profile]

Table B.7.2.2-15. Identification of Compounds from Metabolism Study (both proposed and found).

Common Name/Code [Figure B.7.2.2 ID No.]	Chemical Name	Chemical Structure

D. CONCLUSIONS

[Briefly, summarize the results of the submitted ruminant metabolism studies such as: routes or pathways, mechanisms involved and extent/degree of metabolism observed, nature, amount, and distribution of the TRRs in the ruminant tissues.]

LIVESTOCK FEEDING STUDIES [LIVESTOCK (CATTLE, POULTRY, SWINE, ETC.)]

A. Executive Summary:

[Active ingredient] was administered [method of administration] to [number and breed] of [animal] for [duration] consecutive days. Dosing was made at [list dosing levels in mg/kg feed]. [Report details on depuration study, if applicable.]

Milk/egg samples were collected twice daily [provide details on sampling method]. Animals were sacrificed on Day xx within [xx] hours of last dose. Tissue samples of [liver, kidney, muscle, and fat] were taken from each sacrificed animal. All samples were maintained frozen at the testing facility, during shipping to the laboratory and were stored frozen until analysis. The maximum storage interval for samples between collection and analysis was [xx] days/months. Residues of [active ingredient] have been shown to be stable in [livestock matrices] for up to [xx] days under frozen conditions. Adequate storage stability data are therefore available to support the storage conditions and intervals for samples in the current study.

Samples in the current study were analyzed using Method [Method ID], a [describe method] to determine residues of [list analytes]. Acceptable [method validation and] concurrent recoveries were reported for [matrices] samples at fortification levels of [xx] ppm, thus validating the method. The limit of quantitation (LOQ) was [xx] ppm per analyte for [matrices].

Following a pre-slaughter interval of [xx] hours, individual sample residues ranged from xx ppm to yy ppm [list matrices and residue levels]. [Describe, qualitatively and quantitatively, the relationship between residue levels and dosing levels for the matrices addressed in the study.] Depuration results indicated that residues of [analytes(s)] will [describe depuration results, noting especially matrices where there appears to be little reduction of residues with time.]

B. Materials and Methods

1. Materials

Table B.7.8.1-1. Nomenclature for [Active Ingredient] and Metabolites of Interest.	
Common name	(active ingredient)
Identity	[CAS Chemical Name]
CAS no.	
Company experimental name	
Other synonyms (if applicable)	
Metabolite X	(for each analyte)
Identity	[CAS Chemical Name]
CAS no.	
Company experimental name	
Other synonyms (if applicable)	

2. Study Design

a. Test Procedure

Livestock

Table B.7.8.1-2. Description of Livestock Used in the Feeding Study.					
Species	Breed	Age	Weight at Study Initiation (kg)	Health Status	Description of Housing/Holding Area

Diet

Table B.7.8.1-3. Test Animal Dietary Regime.				
Composition of Diet	Feed Consumption (kg/day)	Water	Acclimation Period	Predosing

Treatment

Table B.7.8.1-4. Dosing Regime.					
Treatment Group	Treatment Type	Level of Administered Dose (mg/day)	Residue Intake in Diet (ppm)	Vehicle	Timing/ Duration

Sampling

Table B.7.8.1-5. Sample Collection.		
Treatment Group	Matrix	Interval From Last Dose to Sacrifice (hours or days)

Sample Handling and Preparation

[Briefly describe how samples were handled after collection (shipment, storage, etc.) and any preparation that was done prior to extraction.]

2. Description of Analytical Procedures

Samples of [matrices] were analyzed for residues of [analyte(s)] using the Analytical Method [ID# and Title]. [Indicate if the method was previously reviewed and/or validated and for what commodities.]

[Reference study summary if method is described in the B.5.2 section of this review, or provide a description similar to that below if it is a different method.]

Briefly, samples were extracted with [solvent system]. Extracts were cleaned up using [SPE column, partitioning, etc.] and a portion of this extract was analyzed for residues of [list analytes]

using [describe instrument/detector system]. The LOQ was [xx] ppm for each analyte. [State the LOD if available and how the LOQ and LOD were determined.]

C. RESULTS AND DISCUSSIONS (OBSERVATIONS)

Method performance was evaluated [during method validation and] by use of concurrent recovery samples by fortifying [matrix] at [xx] and [yy] ppm. [n] Samples of [livestock matrix] were fortified at [xx] ppm and individual recoveries ranged from [xx]% to [yy]% with a standard deviation of [xx]%. [n] Samples of [livestock matrix] were fortified at [yy] ppm and individual recoveries ranged from [xx]% to [yy]% with a standard deviation of [xx]%. All recoveries were within the acceptable range of 70% to 120%; therefore, the method was considered valid for the analysis of [active ingredient and metabolites] residues in [livestock] matrices (Table B.7.8.1-6). [Note Table B.7.8.1.-6 should only be included if recoveries are consistently outside the acceptable range.] The fortification levels [did/did not] bracket the measured residues.

The detector response was linear (coefficient of determination, $r^2 > xx$) within the range of [concentrations]. Representative chromatograms of control samples, fortified samples and treated samples were provided. The control chromatograms generally have no peaks of interest above the chromatographic background. [The fortified sample chromatograms contained only the analyte of interest, and peaks were symmetrical and well defined.] or [Residues in controls were ≤xx ppm. The reported residue values [were/were not] corrected for apparent residues in controls.] Metabolites were expressed in parent equivalents.

Table B.7.8.1-6. Summary of Procedural/Concurrent Recoveries of [Active Ingredient] from [Matrix][1].

Matrix	Fortification Level (ppm)	Recoveries (%)	Mean ± Std. Dev. (%)
[Analyte]			

[1] This table should be included only if recoveries are consistently outside the acceptable range.

The livestock commodity samples were stored frozen at [-xx]°C for a maximum of [xx days/months] from collection to analysis (Table B.7.8.1-7). [Table B.7.8.1-7 should only be included if storage stability data are not included in B.7.8.3, if it is included, then just cite location in monograph.]

The available freezer storage stability data indicate that residues of [active ingredient and metabolites (if applicable)] were stable when stored frozen at ≤-20°C in [livestock matrices] for up to [demonstrated period]. [Indicate if the freezer storage stability data were previously reviewed and report the demonstrated storage intervals for each matrix/analyte]; or

Freezer storage stability data were generated concurrently with the livestock feeding study. [Note: A summary table of these results should be inserted here.] Data showed that [active ingredient and metabolites (if applicable)] residues were stable in [matrices] under frozen storage for the duration of the storage period; or

No storage stability studies were conducted for milk matrices or any tissue matrices, as all samples were analyzed within 30 days of collection.

Table B.7.8.1-7. Summary of Storage Conditions[1].			
Matrix (RAC or Extract)	Storage Temperature (°C)	Actual Storage Duration (days/months)	Interval of Demonstrated Storage Stability [specify matrix if different] (days/months)

[1] Delete this table if storage stability addressed in B.7.8.3.

The results from the feeding study showed that when dosed at xx, yy, zz ppm, residues of [active ingredient and metabolites, if applicable] in [livestock matrices] ranged from [xx] ppm to [yy] ppm.

Table B.7.8.1-8. [Whole Milk/Egg] Residue Data From [Ruminant/Poultry] Feeding Study with [Active Ingredient].						
Animal Identification #	Matrix/Collection Time	Feeding Level (ppm)	Residues[1] (ppm)			
			Analyte 1	Analyte 2	Analyte 3	Total[2,3] (Mean)
			Rep 1	Rep 1	Rep 1	
			Rep 2	Rep 2	Rep 2	
			Rep 1	Rep 1	Rep 1	
			Rep 2	Rep 2	Rep 2	
			Rep 1	Rep 1	Rep 1	
			Rep 2	Rep 2	Rep 2	
			Rep 1	Rep 1	Rep 1	
			Rep 2	Rep 2	Rep 2	

[1] Expressed as parent equivalents.

[2] Total = Parent + Metabolite X [which corresponds to the residue definition for enforcement purposes].

[3] Do not include this column if the residue definition for enforcement purposes has not been determined.

Table B.7.8.1-9. Tissue Residue Data From [Ruminant/Poultry] Feeding Study with [Active Ingredient].						
Animal Identification #	Tissue/Collection Time	Feeding Level (ppm)	Residues[1] (ppm)			
			Analyte 1	Analyte 2	Analyte 3	Total[2,3] (Mean)
			Rep 1	Rep 1	Rep 1	
			Rep 2	Rep 2	Rep 2	
			Rep 1	Rep 1	Rep 1	
			Rep 2	Rep 2	Rep 2	
			Rep 1	Rep 1	Rep 1	
			Rep 2	Rep 2	Rep 2	
			Rep 1	Rep 1	Rep 1	
			Rep 2	Rep 2	Rep 2	

[1] Expressed as parent equivalents.
[2] Total = Parent + Metabolite X [which corresponds to the residue definition for enforcement purposes].
[3] Do not include this column if the residue definition for enforcement purposes has not been determined.
[Note: When the residue definition (RD) is different for tolerance/enforcement and risk assessment, the residues corresponding to the RD for risk assessment are reported in the dietary exposure assessment (risk assessment) template only.]
[DO NOT include the following table if the RDs are not determined at the time of the primary review. This table will be included only in the overview document (Level D Review) if the RDs are not determined. The statistics are compiled only for the RDs, not for each individual analyte.]

Table B.7.8.1-10. Summary of Residue Data From [Ruminant/Poultry] Feeding Study with [Active Ingredient].

Matrix	Feeding Level (ppm)	[Specify which residues, e.g. Combined Residues of A and B] Residues[1] (ppm)						Maximum Tissue Residue: Feeding Level Ratio[2]
		n	Min.	Max.	Median	Mean	Std. Dev.	

[1] Expressed as parent equivalents.
[2] Referred to as the transfer coefficient (TC) or transfer factor (Tf); to be used in the calculation of residues anticipated at the dietary burden.

FIGURE B.7.8.1-1. [Active Ingredient] Residues in [Whole Milk/Eggs] as a Function of Time. Residues are Maximum Values for Each Treatment Group.
[Provide Figure 7.8.1-1 if doing so will facilitate the description and interpretation of the residue profile across time.]

FIGURE B.7.8.1-2. Linear Regression of Maximum Residues on Feeding Level.
[Provide Figure B.7.8.1-2 if doing so will facilitate the description and interpretation of the residue profile across feeding level.]

Depuration Period

Table B.7.8.1-11. Summary of Residues of [Active ingredient] in [Whole Milk/Eggs] and Tissues of a [Species] From the Depuration Study.

Matrix	Study Day	Animal #	Residues (ppm)

FIGURE B.7.8.1-3. Depuration Curve for Residues of [Active ingredient] in [Whole Milk/Eggs].

[Provide Figure B.7.8.1-3 if doing so will facilitate the description and interpretation of the residue profile across depuration time.]

Feeding [active ingredient] at levels of at least [xx] ppm in the feed resulted in quantifiable residues of [analytes] in [matrices]. Analysis of [milk/eggs] indicates that residues reached a plateau by the [xx]th day of treatment. Ratios of residues in tissue to that in feed [were/were not] relatively consistent across feeding levels. [Discuss linearity of tissue:feed ratios as appropriate for the data]. Residues accumulated to the highest level in [matrix]. [Discuss similarity/difference in residue levels across the matrices.] Following removal of the test substance from the diet, residue levels in the tissue [remained relatively constant/decreased rapidly/decreased slowly] in [matrices].

D. CONCLUSIONS

The [livestock] feeding study is considered scientifically [acceptable or unacceptable]. The results of the study show that [describe the feeding level-residue relationship for the various matrices]. Depuration data indicate that the level of [active ingredient] residues in [matrices] [describe behavior] after [active ingredient] is removed from the diet. Adequate storage stability and method performance data are available to support the results of the feeding study.

***IN VITRO* BACTERIAL GENE MUTATION *(Bacterial system, Salmonella typhimurium; E. coli)*/ mammalian activation gene mutation assay**

(Mutagenicity: AMES Test, 2 In Vitro, 1 In Vivo]

A. Executive Summary:

In a reverse gene mutation assay in bacteria (MRID *[number]*), strains *[specify]* of *S. typhimurium [or other acceptable bacterial strains, i.e., E. coli wp2 (pKM101) and WP2uvrA(pKM101)]* were exposed to *[Chemical name, (% a.i., batch/lot #), include solvent if appropriate]* at concentrations of in the presence and absence of mammalian metabolic activation *[specify] in the plate incorporation or pre-incubation procedure [specify]*.

(Chemical name) was tested *[up to cytotoxic (or insoluble) concentrations or limit concentration (5000 g/plate or 5 L/plate), include other details as appropriate]*. *(quantitate if positive for number of revertants e.g., a dose related increase to 782 revertants at the highest concentration vs. 110 revertants in control for strain TA 100)*. The positive controls induced *(did not induce)* the appropriate responses in the corresponding strains.

There was *(no) evidence (or a concentration related positive response)* of induced mutant colonies over background.

B. MATERIALS AND METHODS

1. Control Materials:	
Negative:	*[e.g., culture medium]*
Solvent (final conc=n):	
Positive:	Nonactivation: Sodium azide _____ g/plate TA100, TA1535 2-Nitrofluorene _____ g/plate TA98, TA1538 9-Aminoacridine ____ g/plate TA97, TA1537 Other (list):
	Activation: 2-Aminoanthracene (2-anthramine) _____ g/plate usually all strains Other (list):

2. Activation: S9 derived from *[mark those that apply with x]*			
induced	Aroclor 1254	Rat	Liver
non-induced	Phenobarbitol	Mouse	Lung
	None	Hamster	Other *[name]*
	Other *[name]*	Other *[name]*	

Describe S9 mix composition *[if purchased, give details]*:

3. Test organisms: *S. typhimurium* strains *[mark those that apply with x]*				
TA97	TA98	TA100	TA102	TA104
TA1535	TA1537	TA1538	list any others	
Properly maintained?			Yes	No
Checked for appropriate genetic markers (*rfa* mutation, R factor)?			Yes	No

4. Test compound concentrations used: *[preliminary cytotoxicity test, if performed and main assay]*

Nonactivated conditions:

Activated conditions:

[Note: list strains used and number of replicates per dose, per strain, per condition along with doses]

C. RESULTS & DISCUSSIONS (OBSERVATIONS) *[Report results of analytical determination if performed]*

A. PRELIMINARY CYTOTOXICITY ASSAY: *[include concentration ranges, activation and nonactivation; strain(s) used; reported results, e.g., cytotoxicity indices (effect on background lawn; reduction in revertant) and solubility]*

B. MUTAGENICITY ASSAY: *[reported results, e.g., induction of revertant - individual plate counts and/or summary given; appropriateness of positive and background (concurrent and/or historical) revertant levels; number of concentration levels used; number of replicate plates; include representative table(s), if appropriate]*

D. CONCLUSION:

IN VITRO MAMMALIAN CYTOGENETICS ASSAY

A. Executive Summary:

In a mammalian cell cytogenetics assay *[Chromosome aberration or SCE]*(MRID *[number]*), *[cell type, e.g., CHO/V79/L5178Y cell cultures/primary lymphocyte cultures]* were exposed to *[Chemical name, (% a.i., batch/lot #), include solvent if appropriate]* at concentrations of 0, x, x, x □g/mL with and/or without metabolic activation *[specify]* for *[give duration of exposure]*.

Chemical name was tested *(up to cytotoxic or precipitating concentrations, or limit concentration, 5000 □g/mL). [include other details as appropriate, quantitate if positive (e.g. a dose related increase to 80% cells with aberrations at the top concentration, or large increase in deletions, rearrangements, etc. vs controls]*. Positive controls induced (did *not* induce) the appropriate response.

There was *(no) evidence (or a concentration related positive response)* of *[Chromosome aberration or SCE]* **induced over background.**

B. MATERIALS AND METHODS

1. Control Materials:		
	Negative control:	*[e.g., culture medium]*
	Solvent control (final conc=n):	
	Positive control:	Nonactivation: (concentrations / solvent)
		Activation: (concentrations / solvent)

2. Activation: S9 derived from *[mark those with x that apply]*							
	induced		Aroclor 1254		Rat		Liver
	non-induced		Phenobarbitol		Mouse		Lung
			None		Hamster		Other (name)
			Other (name)		Other (name)		

Describe S9 mix composition: *[if purchased, give details]*

3. Test cells: mammalian cells in culture *[identify cell line or primary cell culture (if human lymphocytes, describe subjects, e.g., donor's health, status, sex, smoker]*				
	V79 cells (Chinese hamster lung fibroblasts)			
	Human lymphocytes			
	Chinese hamster ovary (CHO) cells			
Media: (identify)				
Properly maintained?		Yes		No
Periodically checked for *Mycoplasma* contamination?		Yes		No
Periodically checked for karyotype stability?		Yes		No

4. Test compound concentrations used: *[For preliminary cytotoxicity test, if performed, and main assay]*		
	Nonactivated conditions:	
	Activated conditions:	

5. TEST PERFORMANCE

1. Preliminary Cytotoxicity Assay *[if performed, describe method; i.e., cell cycle kinetics, mitotic index, trypan blue, monolayer confluency, cloning efficience]*:

2. Cytogenetic Assay:

a.	**Cell exposure time:**	Test Material	Solvent Control	Positive Control
	Non-activated: Activated:	h h	h h	h h

b.	**Spindle inhibition**	
	Inhibition used/concentration:	
	Administration time:	x hours (before cell harvest)

c.	**Cell harvest time after termination of treatment:**	Test Material	Solvent Control	Positive Control
	Non-activated: Activated:	h h	h h	h h

d. Details of slide preparation: *[Describe briefly]*

e. Metaphase analysis

No. of cells examined per dose:				
Scored for structural?		Yes		No
Scored for numerical?		Yes If Y, list *[e.g., polyploid, endoreduplicated cells, etc.]*		No
Coded prior to analysis?		Yes		No

f. Statistical analysis: *[list parameters that were analyzed and the statistical methods]*

C. RESULTS & DISCUSSIONS (OBSERVATIONS) [*Report results of analytical determination if performed]*

1. PRELIMINARY CYTOTOXICITY ASSAY: *[reported results, e.g., include dose range, solubility, and evidence of cytotoxicity, rationale for exposure, harvest times and high dose with and without activation]*

2. *CYTOGENETIC or SCE* ASSAY:

[Reported results, e.g., include appropriateness of negative, solvent and positive control frequencies; appropriateness of dose levels; statistical evaluation; types of structural aberrations for significant dose levels; include representative table, if appropriate]

C. CONCLUSION

IN VITRO* MAMMALIAN CELLS GENE MUTATION ASSAY *(name cell type used)

Executive Summary:

In a mammalian cell gene mutation assay *[specify locus]* (MRID *[number]*), *[cell type]* cells cultured *in vitro* were exposed to *[Chemical name, (% a.i., batch/lot #), include solvent if appropriate]* at concentrations of x, x, x, x g/mL in the presence and absence of mammalian metabolic activation *[specify]* for *[give duration of exposure]*.

Chemical name was tested *[up to cytotoxic/insoluble/limit concentrations (i.e., 5000 g/mL, 5 L/mL, or 0.01 M), include other details as appropriate. Some quantitation here e.g., induced mutation frequency of $582x10^{-6}$ vs. $78x10^{-6}$ in controls at the top concentration]*. The positive controls *(did/did not)* induce the appropriate response. **There was *(no) evidence (or a concentration related positive response)* of induced mutant colonies over background.**

A. MATERIALS AND METHODS

1. Control Materials:		
	Negative control:	*[e.g., culture medium]*
	Solvent control (final conc=n):	
	Positive control:	Nonactivation:(concentrations / solvent)
		Activation: (concentrations / solvent)

2. Activation: S9 derived from *[mark those with x that apply]*							
	induced		Aroclor 1254		Rat		Liver
	non-induced		Phenobarbitol		Mouse		Lung
			None		Hamster		Other *[name]*
			Other *[name]*		Other *[name]*		

Describe S9 mix composition: *[if purchased, give details]*

3. Test cells: mammalian cells in culture *[mark those with x that apply]*			
	mouse lymphoma L5178Y cells		V79 cells (Chinese hamster lung fibroblasts)
	Chinese hamster ovary (CHO) cells		list any others
Media: *[Identify]*			
Properly maintained?		Yes	No
Periodically checked for Mycoplasma contamination?		Yes	No
Periodically checked for karyotype stability?		Yes	No

Periodically "cleansed" against high spontaneous background?		Yes		No	

	4.**Locus Examined:**		**Thymidine kinase (TK)**		**Hypoxanthine-guanine-phosphoribosyl transferase (HGPRT)**		**Na^+/K^+ ATPase**
	Selection agent:		bromodeoxyuridine (BrdU) *[give conc=n]*		8-azaguanine (8-AG) *[conc=n]*		ouabain*[conc=n]*
			fluorodeoxyuridine (FdU)		6-thioguanine (6-TG)		
			trifluorothymidine (TFT)				
	[Other? (details)]						

5. Test compound concentrations used: *[For preliminary cytotoxicity test, if performed, and main assay]*		
	Nonactivated conditions:	
	Activated conditions:	

6. Test performance

1. Cell treatment:

a. Cells were exposed to test compound, negative/solvent or positive controls for ____ hours (nonactivated) ___ hours (activated).

b. After washing, cells were cultured for ___ days (expression period) before cell selection.

c. After expression, ___ cells/dish (_ dishes/ group) were cultured for __ days in selection medium to determine numbers of mutants and ___ cells/dish (__ dishes/group) were cultured for ___ days without selective agent to determine cloning efficiency.

[If mouse lymphoma cells, include information regarding colony sizing]

7. Statistical Methods: *[list parameters that were analysed and the statistical methods used]*

C. RESULTS & DISCUSSIONS (OBSERVATIONS) *[Report results of analytical determination if performed]*

A. PRELIMINARY CYTOTOXICITY ASSAY

[include concentration ranges, activation and nonactivation; reported results, e.g., cytotoxicity and solubility, rationale for dose selection for main study]

B. MUTAGENICITY ASSAY *[reported results, e.g., induction of mutant colonies - individual colony counts and/or summary given; mutant frequencies per 10^6 survivors; positive and background mutant frequencies; inclusion of concentration levels used; number of cultures per concentration; levels of cytotoxicity obtained; appropriateness of cloning efficiencies; include representative table, if appropriate].*

D. CONCLUSION

IN VIVO MAMMALIAN BONE MARROW ERYTHROCYTES MICRONUCLEUS ASSAY

A. Executive Summary:

In a *(strain)* mouse *[or rats or other acceptable mammalian species]* bone marrow micronucleus assay (MRID *[number]*), *(number/sex/dose)* were treated *[route]* with *Chemical name (% a.i., batch/lot #)* at doses of 0, x, x, or x mg/kg bw. Bone marrow cells were harvested at *(list hours)* post-treatment. The vehicle was *(state vehicle)*. *(Note the route of exposure and if acute or multiple dosing)*

There were *(no)* signs of toxicity *(list if present)* during the study. *[Note, the signs of cytotoxicity, if present, and the quantitative evidence for a positive micronucleus response, if any]*. Chemical name was *(not)* tested at an adequate dose *(based on)*. The positive control induced the appropriate response.

B. MATERIALS AND METHODS

a. Test compound:										
	Dosing:		once		twice (24 hrs apart)			Other *(describe)*		
	Sampling (after last dose):*[mark all that are appropriate]*,		6 hr		12 hr		24 hr	48 hr		72 hr
	Other *[describe]*:									

b. Negative and/or vehicle control:										
	Dosing:		once		twice (24 hrs apart)			Other *(describe)*		
	Sampling (after last dose):*[mark all that are appropriate]*,		6 hr		12 hr		24 hr	48 hr		72 hr
	Other *[describe]*:									

c. Positive control:	

	Dosing:		once		twice (24 hrs apart)				Other *(describe)*		
	Sampling (after last dose):*[mark all that are appropriate]*,		6 hr		12 hr		24 hr		48 hr		72 hr
	Other *[describe]*:										

d. Tissues and Cells Examined:		
	Bone marrow OR other (identify):	
	No. of polychromatic erythrocytes (PCE) examined per animal:	
	No. of normochromatic erythrocytes (NCE; more mature RBCs) examined per animal:	
	Other (if other cell types examined, describe):	

e. Details of slide preparation: *[Describe briefly; were slides coded?]*

f. Evaluation Criteria: *[Describe]*

g. **Statistical methods:** *[list parameters that were analyzed and the statistical methods]*

C. RESULTS & DISCUSSIONS (OBSERVATIONS) *[Report results of analytical determination if performed]*

1. PRELIMINARY TOXICITY ASSAY: *[reported results, e.g., include dose range; signs of toxicity - e.g., MTD considerations; clinical signs; number of animals, rationale for dose selection for micronucleus assay]*

2. MICRONUCLEUS ASSAY: *[reported results, e.g., include in life animal observations, induction of micronuclei; appropriateness of negative, solvent and positive control micronucleus frequencies; ratio of PCE/NCE; sex differences (if any); appropriateness of dose levels and route; statistical evaluation; include representative table, if appropriate]*

D. DISCUSSION AND CONCLUSIONS:

UNSCHEDULED DNA SYNTHESIS IN MAMMALIAN LIVER CELL CULTURES;

A. Executive Summary:

In an unscheduled DNA synthesis, primary rat hepatocyte cultures were exposed to *[Chemical name, (% a.i., batch/lot #), include solvent if appropriate]* at concentrations of 0, x, x, or x □g/mL for *(duration of exposure)*.

Chemical name was tested *[up to cytotoxic or precipitating concentrations, or limit concentration, 5000 □g/mL. (Include other details as appropriate, quantitation if positive e.g. there was a significant increase in number of cells in repair (60% at top concentration vs 1% in controls))]*.

The positive controls induced *(did not induce)* the appropriate response.

There was *(no)* evidence *(or a dose related positive response)* that unscheduled DNA synthesis, as determined by radioactive tracer procedures [nuclear silver grain counts] was induced.

B. MATERIALS AND METHODS

1. Cell Preparation:

a. Perfusion Technique:

b. Hepatocyte Harvest/Culture Preparation:

2. TEST PERFORMANCE *[(NOTE: If cells other than hepatocytes are tested, information regarding the S9 activated phase of testing must be included)]*

1. Cytotoxicity Assay: *[if conducted, briefly describe procedure]*

2. UDS Assay:

a. Treatment:

b. Preparation of Autoradiographs/Grain Development:

c. Grain Counting: *[include number of cells scored per dose, derivation of net nuclear grains, whether % cells in repair were scored]*

e. Statistical Analysis: *[list parameters that were analyzed and the statistical methods]*

C. RESULTS AND DISCUSSIONS (OBSERVATIONS): *[Report results of analytical determination if performed]*

1. PRELIMINARY CYTOTOXICITY ASSAY: *[include concentration ranges; reported results, e.g., cytotoxicity and solubility, rationale for dose selection for main study]*

2. UDS assay: *[reported results, e.g., net nuclear grain counts and/or summary; appropriateness of positive controls and background levels (concurrent and/or historical); number of concentration levels evaluated; number of replicates -- 100 cells/group (50 cells/slide); include representative table, if appropriate]*

D. CONCLUSIONS:

IMMUNOTOXICITY STUDY

A. Executive Summary:

In an Immunotoxicity study test substance was administered to *[(# of animals) species, strain]*/sex/dose in *[diet, water, by capsule, by gavage]* at dose levels of 0, x, x, x ppm (0, x, x, x mg/kg bw/day). *[Briefly describe protocol, including parameters examined and test groups used for each parameter].*

[Describe toxicity briefly following instructions for exec summary paragraph 2. If there is no toxicity, state that there were no compound related effects in mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, gross pathology, histopathology, or Immunotoxicity. (Note if there was a NOAEL for clinical findings (for acute reference dose consideration during subsequent risk assessment.)].

The LOAEL for Immunotoxicity is , based on the NOAEL for Immunotoxicity is

B. STUDY DESIGN:

1. Animal assignment: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1. *[Note whether animals were further subdivided into separate groups, and if applicable, indicate treatment for each of those groups.]*

TABLE 1: Study design *[change heading and units as appropriate for method of administration]*

Test Group	Conc. in Diet *(units)*	Dose to Animal *(units)*	# Male	# Female
Control				
Low				
Mid				
High				
Positive control				

2. Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. RESULTS & DISCUSSIONS (OBSERVATIONS):

1. Observations:

1. Clinical signs of toxicity –

2. Mortality -

2. Body weight:

3. Food/water consumption and compound intake:

1. Food consumption -

2. Water consumption -

3. Compound consumption *[time-weighted average] [include compound intake in table 1]* -

4. Food efficiency *[if relevant]* - *[relate to any changes in bodyweight]*

4. Gross Necropsy

1. Organ weight - *[absolute and relative thymus and spleen weights, as appropriate, relate to any histological changes, if available]*

2. Histology - *[not a guideline requiremen*

5. Immunotoxicity:

a. Antibody plaque-forming cell (PFC) assay:

Immunotoxicity findings for the antibody plaque-forming cell assay are summarized in Table #. *[Was there suppression of the humoral immune response? Was spleen cell number/viability affected by exposure? Was antibody-forming cell response affected - expressed as specific activity (AFC/10^6 spleen cells) or total activity (AFC/spleen)?] e.g., the data suggest that under the conditions of this study, XXXX [compound name] did/did not suppress the humoral immune response in a dose-dependent manner in that it did/did not significantly alter the IgM antibody-forming cell response to the T-dependent antigen, sheep erythrocytes.*

[Briefly summarize positive control results. e.g., was sensitivity of the assay adequately demonstrated? Was there a decrease in spleen cell number and suppression of the antibody-forming cell response as indicated by specific activity (AFC/10^6 spleen cells) and total activity (AFC/spleen)?]

TABLE #: Antibody plaque-forming cell (PFC) assay [a] *[change heading and units as appropriate]*

Test Group (n = #)	Spleen Cells (x 10^7)	Specific Activity (IgM AFC/10^6 spleen cells)	Total Spleen Activity (IgM AFC/spleen (x 10^3))
Male			
Control			
Low			
Mid			
High			
Positive Control *(name e.g. Cyclophosphamide)*			
Female			
Control			
Low			
Mid			
High			
Positive Control *(name e.g. Cyclophosphamide)*			

[a] Data obtained from pages ( ) in the study report.

* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

OR

b. Enzyme-Linked Immunosorbent Assay (ELISA):

c. NK cell Assay: ***[Optional assay according to EPA guideline]***

Immunotoxicity findings for the NK cell assay are summarized in Table #.

[Were significant effects observed on natural killer cell activity - when evaluated using lytic units, when evaluated as specific activity (lytic activity/10^7 spleen cells) or as total spleen activity (lytic units/spleen)?]

[Briefly summarize positive control results. e.g., was sensitivity of the assay adequately demonstrated?]

TABLE #: Natural Killer Cell Assay [a] *[change heading and units as appropriate]*

Test Group (n = #)	**Effector: Target Ratio** [b] **e.g.,**						**LU/10^7 cells** [c] **(Specific activity)**	**LU/spleen** [c] **(Total activity)**
	6.25: 1	*12.5: 1*	*25: 1*	*50: 1*	*100: 1*	*200: 1*		
Male								
Control								
Low								
Mid								
High								
Positive Control *(name)*								
Female								
Control								
Low								
Mid								
High								
Positive Control *(name)*								

[a] Data obtained from pages ( ) in the study report

[b] Values are expressed as percent cytotoxicity

[c] Values expressed as lytic unit (LU) where LU is defined as the number of splenocytes required to kill 10% of the target cells

Effector cells: NK cells. Target cells: YAC-1 lymphoma cells

* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

d. Enumeration total B cells, total T cells and T cell subpopulations:

Immunotoxicity findings for the spleen cell proliferation assay are summarized in Table #.

[Were significant effects observed on B cell (CD45+), total T cell (CD5+), T helper cell (CD4+) or T suppressor/cytotoxic cell (CD8+) numbers? In spleen cell numbers?]

[Briefly summarize positive control results. E.g. was sensitivity of the assay adequately demonstrated?]

TABLE #: Spleen Cells, T Cell, T Cell Subset and B Cell Enumeration (absolute values)[a] *[change heading and units as appropriate]*

Test Group (n = #)	Spleen cells ($x10^7$)	T Cell [b]	T Cell Subsets[b]		T Cell Suppressor Cells [b]	B Cell [b]
			e.g. Cytotoxic T Cells	*T Cell Suppressor Cells*		
Male						
Control						
Low						
Mid						
High						
Positive Control *(name)*						
Female						
Control						
Low						
Mid						
High						
Positive Control *(name)*						

[a] Data obtained from pages ( ) in the study report.
[b] Values expressed as the absolute number per spleen x 10^6.
* Statistically different ($p < 0.05$) from the control.
** Statistically different ($p < 0.01$) from the control.

e. Other: *[describe findings, include tables if needed]*

D. CONCLUSION:

Acute Avian Toxicity {Chicken, Pigeon, Quail, Duck etc}

A. Executive Summary:

The acute oral toxicity of {test material} to X-d-old {common name and scientific name} was assessed over ....days. {Test material} was administered to the birds {enter the number of birds per treatment} by {method} at [Indicate doses used} mg ai/kg bw. The ...day-acute oral LD_{50} was ....mg a.i/kg bw. The ...day NOAEL of {test material} to the {species}, based on {endpoint} was ....mg a.i/kg bw. Describe toxicity briefly including mortality, behavioral abnormalities, and other signs of toxicity. If there was no toxicity, state that there was no compound related toxicity effect.

Results Synopsis

LD_{50}: {.....mg a..i./kg bw} 95% C.I.: {.... to ... mg a.i./kg bw} Probit Slope: {.....}

NOAEL:{.....mg a.i./kg bw}

Endpoint(s) Affected: {.....}

B. MATERIALS AND METHODS

1. Test Organism:

Species (common and scientific names): EPA recommends using either northern bobwhite [*Colinus virginianus*] or mallard [*Anas platrhynchos*]. Species that can be used in addition to northern bobwhite or mallard but are not preferred as an alternative include: pigeon [*Columba livia*], Japanese quail [*Coturnix coturnix japonica*], ring-necked pheasant [*Phasianus colchicus*], and red-legged partridge [*Alectoris rufa*], may be tested. If species other than the northern bobwhite or mallard are used,it is important that they are responsive to the conditions of the test and do not avoid exposure to the test material through fasting.

Age at study initiation: young adults of both sexes, not yet mated, and at least 16 weeks old at time of dosing.

Weight at study initiation: (mean and range): Birds are typically uniform in size and weight and phenotypically indistinguishable from *wild birds*

Source:

2. STUDY DESIGN:

1. Experimental Conditions

a) Range-finding study: If a range-finding study was conducted, briefly outline the test concentrations and other relevant conditions. Indicate the results from the preliminary study that were used to determine the conditions for the definitive study.

b) Definitive Study

Table X. Experimental Parameters

Parameter	Details	Remarks
Conditions (same as test or not): Feeding: Health (any mortality observed):		
Pen size and construction materials		

Parameter	Details	Remarks
Test duration		
Dose preparation (Indicate method of confirmation of dose)		
Dose levels Nominal: Measured:		
Solvent/vehicle, if used Type: Amount/bw:		
Number of birds per groups/treatment Negative control: Solvent/vehicle control: Treated:		
Test conditions Temperature: Relative humidity: Photoperiod:		
Reference chemical, if used Name: Concentrations tested:		

2. Observations:

Table X: Observations

Criteria	Details	Remarks
Parameters measured (mortality/individual body weight at test initiation and termination/ mean feed consumption/ others)		

Indicate if the test material was regurgitated		
Groups on which necropsies were performed		
Observation intervals		
Were raw data included?		

Statistics:
List the parameters

that were analyzed and the statistical tests that were performed. A copy of the statistical methods from the study may be attached.

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. MORTALITY:

Briefly summarize mortality; indicate if there was a dose-response effect; slope values, if provided. Compare with reference chemical toxicity test endpoints.

Table X: Effect of {Test Material} on Mortality of {Test Organism}

2. SUBLETHAL TOXICITY ENDPOINTS:

Briefly summarize behavioral abnormalities; other signs of toxicity (body weight loss, food consumption, organ effects, etc.). Indicate effects that were related to the chemical properties of the test material. Compare the sub-lethal effects with that of the reference chemical.

Table X: Sub-lethal Effect of {Test Material} on {Test Organism},

Treatment (mg a.i./kg bw)	**Observation**						
	body weight			**food consumption**			**other endpoint**
	day 0	**day x1**	**day x2**	**day 0**	**day x1**	**day x2**	**% affected**
Negative control							
Test dose 1							
Test dose 2							
Test dose 3							
Test dose n							
NOAEL							
EC_{50}							
effect							

Reference chemical	NOAEL	
	LD_{50}	

D. CONCLUSIONS:

Indicate the acceptability classification. Provide the major conclusions, e.g., values for LD_{50} (95% confidence interval), probit slope (95% confidence interval), NOAEL, and sub-lethal effects.

REPEATED DOSE AVIAN TOXICITY

A. Executive Summary:

The acute dietary toxicity of {test material} to X-d-old {common name and scientific name} was assessed over X days. {Test material} was administered to the birds {enter the number of birds per treatment} in the diet at {indicate concentrations} mg a.i/kg dw of diet. The.... day acute dietary LC_{50} was..... mg a.i/kg diet. The ....day NOAEC of {test material} based on {endpoint} was.....mg a.i/kg diet.
Briefly describe toxicity including mortality, behavioral abnormalities, and other signs. Describe any avoidance of treated diet and its relation to the test material. If there was no toxicity, state that there were no compound-related effects.

Results Synopsis

Test Organism Size/Age (mean weight):

LC_{50}: {.....mg a.i./kg diet} 95% C.I.: {.....to ..... mg a.i./kg diet}

Probit slope: {.....}

NOAEC: {..... mg a.i./kg diet} Endpoint(s) Affected { .....}

Sub-lethal effects:

B. MATERIALS AND METHODS

1. **Test organism**:

Species (common and scientific names):
EPA/OECD recommends using either northern bobwhite [*Colinus virinianus*] or mallard [*Anas pltyrhynchos*]. Other species which can be used in addition to northern bobwhite or mallard but preferably not as an alternative include: pigeon [*Columba livia*], Japanese quail [*Coturnix coturnix japonica*], ring-necked pheasant [*Phasianus colchicus*], and red-legged partridge [*Alectoris rufa*] may be tested. If species other than the northern bobwhite or mallard are used, it is important that they are responsive to the conditions of the test and do not avoid exposure to the test material through fasting.
Age at study initiation:
EPA recommends 10-14 days old for northern bobwhite and 5 days old for mallards; OECD recommends 10-17 days old
Weight at study initiation: (mean and range)

Source:

2. **STUDY DESIGN:**

1. Experimental Conditions
a. Range-finding Study: If a range-finding study was conducted, briefly outline the test concentrations and

other relevant conditions. Indicate the results from the preliminary study that were used to determine the conditions for the definitive study.

b. Definitive Study

Table X . Experimental Parameters

Table X. Experimental Parameters

Parameter	Details	Remarks
Conditions (same as test or not): Feeding: Health (any mortality observed):		
Pen size and construction materials		
Test duration		
Dose preparation (Indicate method of confirmation of dose)		
Dose levels Nominal: Measured:		
Solvent/vehicle, if used Type: Amount/bw:		
Number of birds per groups/treatment Negative control: Solvent/vehicle control: Treated:		
Test conditions Temperature: Relative humidity: Photoperiod:		
Reference chemical, if used Name: Concentrations tested:		

2. Observations:

Table X: Observations

Parameters	Details	Remarks
Parameters measured (mortality/body weight/ mean feed consumption/ others)		
Indicate the stability and homogeneity of test chemical in the diet		
Indicate if the test material was regurgitated		
Treatments on which necropsies were performed		
Observation intervals		
Were raw data included?		

3. Statistics:

List the parameters that were analyzed and the statistical tests that were performed. A copy of the statistical methods from the study may be attached.

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. MORTALITY: Briefly summarize mortality; indicate if there was a dose-response effect; report the slope values, if provided. Provide measured concentration of test material, if determined. Compare with reference chemical toxicity test endpoints.

Table X: Effect of {Test Material} on Mortality of {Test Organism}

Treatment (mg a.i./ kg diet) [indicate if measured or nominal conc. were used]		**No. of birds per treatment**	**Cumulative mortality**				
			day 1	**day 2**	**day 3**	**day 4**	**day n**
Solvent/vehicle control							
Test concentration 1							
Test concentration 2							
Test concentration 3							
Test concentration n							
NOAEC							
LC_{50}							
Reference chemical	mortality						
	LC_{50}						
	NOAEC						

2. SUB-LETHAL TOXICITY ENDPOINTS:

Briefly summarize behavioral abnormalities and other signs of toxicity (body weight loss, decreased food consumption, organ effects, and other relevant findings). Indicate effects that were related to the chemical properties of the test material. Indicate if there was food avoidance and its relation to test material. Compare the sub-lethal effects with that of the reference chemical. If there was no toxicity, state there were no compound-related effects.

Table X: Sub-lethal Effect of {Test Material} on {Test Organism, If Reported

Treatment (mg a.i./kg diet [record measured and nominal conc. used]	**Observation**						
	Body weight		**Food consumption**		**Other endpoint**		
	day 0	**day x1**	**day xn**	**day 0**	**day x1**	**day xn**	**% affected**
Negative control							
Test dose 1							
Test dose 2							
Test dose 3							
Test dose n							
NOAEC							

Treatment (mg a.i./kg diet [record measured and nominal conc. used]		Observation						
		Body weight		Food consumption		Other endpoint		
		day 0	day x1	day xn	day 0	day x1	day xn	% affected
EC_{50}								
Reference chemical	NOAEC							
	EC_{50}							

D. CONCLUSIONS: Indicate the acceptability classification of the study. Provide the major conclusions, *e.g.*, values for

LC_{50}: _____ mg a.i./kg diet 95% C.I.: _____-_____mg a.i./kg diet

NOAEC: mg a.i./kg diet

sublethal effects:

AVIAN REPRODUCTIVE TOXICITY

A. EXECUTIVE SUMMARY:

The (one-generation) reproductive toxicity of (test material) to groups of (indicate the number) pairs of .....-day-old (species) was assessed over ..... days. (Test material) was administered to the birds in the diet at (indicate test concentrations)..... mg ai/kg diet. The NOAEC of (test material) to the (species) was determined to be ..... mg ai/kg diet based on (the reproductive parameters) at the ..... mg ai/kg diet level (LOAEC) when compared to the control.

Describe toxicity to parental generation, including behavioral abnormalities and other signs of toxicity. Describe any avoidance of treated diet, differences in weight gain among treated groups as compared to the control group, and any other symptoms reported in the study.

Describe toxicity on reproductive parameters, including effects on egg production, hatching and growth of hatchlings.

Results

Test Organism Size/Age(mean weight):

NOAEC:{.....mg a.i./kg diet}

LOAEC:{.....mg a.i./kg diet} Endpoint(s) Affected:{.....}

B. MATERIALS AND METHODS

1. Test organism:

Parameter	Details	Remarks
Species (common and scientific names):		
Age at study initiation:		
Body weight: (mean and range)		
Source of test birds:		

2. STUDY DESIGN:

1. Experimental Conditions

a. Range-finding Study:

If a range-finding study was conducted, briefly outline the test concentrations and other relevant conditions. Indicate the results from the preliminary study that were used to determine the conditions for the definitive study.

b. Definitive Study

Table X . Experimental Parameters

Parameter	Details	Remarks
Acclimation Period: Conditions (same as test or not): Feeding: Health (any mortality observed):		
Test duration (weeks) Pre-laying exposure: Egg-laying exposure: Withdrawal period, if applicable:		
Pen (for parental and offspring) Size: Construction materials: Number:		
Number of birds per pen (male:female)		
Number of pens per group/treatment Negative control: Solvent control: Treated:		
Test concentrations (mg ai/kg diet) Nominal: Measured:		
Maximum field residue anticipated from maximum application rate on product label; state source of information for determining residue level		
Solvent/vehicle, if used Type: Amount:		
Was detailed description and nutrient analysis of the basal diet provided (Yes/No)		
Preparation of test diet		

Parameter	Details	Remarks
Indicate whether stability and homogeneity of test material in diet was determined (Yes/No)		
Were concentrations in diet verified by chemical analysis?		
Did chemical analysis confirm that diet was stable and homogeneous?		
Feeding and husbandry		
Test conditions (pre-laying) Temperature: Relative humidity: Photoperiod:		
Egg collection and storage Collection interval: Storage temperature: Storage humidity:		
Were eggs candled for cracks prior to setting for incubation?		
Were eggs set weekly?		
When was candling done for fertility?		
When were the eggs transferred to the hatcher?		
Hatching conditions Temperature: Humidity: Photoperiod:		
Day the hatched eggs were removed and counted		
Were egg shells washed and dried for at least 48 hrs before measuring?		

Parameter	Details	Remarks
Egg shell thickness No. of eggs used: Intervals: Mode of measurement:		
Reference chemical, if used		

Table X: Observations

Parameter	Details	Remarks
Parameters measured		
Parental: (mortality, body weight, mean feed consumption) Egg collection and subsequent development: (no. of eggs laid, no. of eggs cracked, shell thickness, no. of eggs set, no. of viable embryos, no. of live 3-week embryos, no. hatched, no. of 14-day survivors, average weight of 14-d old survivors, mortality, gross pathology, others)		
Indicate if the test material was regurgitated		
Observation intervals (for various parameters)		
Were raw data included?		

3. STATISTICS: List the parameters that were analyzed and the statistical tests that were performed. A copy of the statistical methods from the study may be attached.

C. RESULTS AND DISCUSSIONS

1. MORTALITY: Briefly summarize mortality; indicate if there was a dose-response effect; slope values, if provided. Compare with reference chemical mortality.

Table X: Effect of {Test Material} on Mortality of {Species}

Treatment (mg a.i./kg diet) [record measured and nominal conc. used]	Observation Period					
	Day x		Day x		Day x	
	No. Dead		No. Dead		No. Dead	
	Male	Female	Male	Female	Male	Female
Control						
Vehicle control						
Test concentration 1						
Test concentration 2						
Test concentration 3						
Test concentration n						

2. REPRODUCTIVE AND OTHER ENDPOINTS:

Describe the toxicity to parental generation, including the effect on food consumption and body weight and any observation of food repellency or food palatability. Describe briefly the various reproductive effects of the chemical, including the time of onset of symptoms, duration and severity of effects, and numbers affected, if applicable. Indicate the most sensitive reproductive endpoints, the results of gross necropsies, and compare with the reference chemical.

Table X. Reproductive and Other Parameters –

Results for each test group (use similar tables for reference chemical, if used); indicate the units of measurement

Parameter	Control	Test conc. 1	Test conc. 2	Test conc. 3	Test conc. n	NOAEC / LOAEC
No. eggs laid/pen						
No. eggs laid/hen/day						
% of eggs cracked						
No. eggs set						
Shell thickness (mm " SD)						
No. viable embryos						
No. live 3-week embryos						
No. of hatchling/hen						
No. of normal hatchlings						
Hatchling weight (g)						
No. 14-day old survivors						
14-day old survivors weight (g)						
Mean food consumption (g)						
Weight of adult females at test initiation: at onset of egg laying/other:						
Weight of adult males at test initiation: at onset of egg laying/other:						
Gross pathology						
Other, if any						

D. CONCLUSIONS:

NOAEC: {.....mg a.i./kg diet}

LOAEC: {.....mg a.i./kg diet} Endpoint(s) Affected: {.....}

Effect on reproductive parameters and the most sensitive end point:

ACUTE TOXICITY TO FISH

A. EXECUTIVE SUMMARY:

In a 96-hr acute toxicity study, {common name and scientific name} were exposed to {test chemical} at {nominal and/or measured} concentrations of {control, solvent control, x_1, x_2, x_3.....x_n mg a.i/L} under static/static renewal/flow-through conditions. The 96-hr LC_{50} was .....mg a.i/L. The NOAEC based on mortality/sub-lethal effects, was .... mg a.i/L (optional). Sublethal effects {list effects} were observed in the groups exposed to {list corresponding concentration(s)} of {test material}. Based on the results of this study, {test material} would be classified as {toxicity classification} to {test species} in accordance with U.S. EPA's classification system.

MATERIALS AND METHODS

1. Test organism:

Species

Age at test initiation: {mean and range in days}

Weight at study initiation: {mean and range}

Length at study initiation: {mean and range}

Source:

STUDY DESIGN:

Experimental Conditions

a) Range-finding Study: If a range-finding study was conducted, briefly outline the test concentrations and other relevant conditions. Indicate the results from the preliminary study that were used to determine the conditions for the definitive study.

b) Definitive Study:

Table X. Experimental Parameters

Parameter	Details	Remarks
Acclimation Period: Conditions: (same as test or not) Feeding: Health: (any mortality observed)		
Duration of the test		
Test condition static/static renewal/flow-through Type of dilution system for flow-through method. Renewal rate for static renewal		
Aeration, if any		
Test vessel Material: (glass/stainless steel) Size: Fill volume: Loading:		

Parameter	Details	Remarks
Source of dilution water Quality:		
Water parameters Hardness (freshwater) pH Dissolved oxygen Total Organic Carbon Particulate matter Metals Pesticides Chlorine Alkalinity Conductivity COD (when testing cationic compounds) Temperature {Salinity for marine or estuarine species} Intervals of water quality measurement		
Test concentrations: Nominal (corrected/uncorrected): Measured:		
Solvent (type and concentration if used)		
Number of replicates/group Negative control: Positive control: treatments:		
Number of organisms / replicate/group: Negative control: Positive control: Treatments:		
Biomass loading rate		
Lighting		
Feeding		
Recovery of chemical Level of Quantitation Level of Detection Method recoveries % of nominal		

Parameter	Details	Remarks
Stability of chemical in the test system		
Variability of chemical in the test system		
Positive control {if used, indicate the chemical and concentrations}		
Other parameters, if any		

2. Observations:

Table X: Observations

Parameter	Details	Remarks
Parameters measured including the sub-lethal effects/toxicity symptoms		
Observation intervals		
Were raw data included?		
Other observations, if any		

Statistics:

List the parameters that were analyzed and the statistical tests that were performed. A copy of the statistical methods from the study may be attached.

C. RESULTS and DISCUSSIONS (OBSERVATIONS):

A. MORTALITY:

Briefly summarize mortality; indicate if there was a concentration-response effect; probit slope of concentration-response curve, if it can be calculated.

Table X: Effect of {Test Material} on Mortality of {Test Organism}.

Treatment (mg a.i./L) [record measured and nominal conc. used]	No. of fish at start of study	Observation period							
		24-hr		48-hr		72-hr		96-hr	
		No. Dead	% mortality	No. Dead	% mortality	No. Dead	% mortality	No. Dead	% mortality
Negative control (dilution water only)									
Positive control, if used (indicate carrier concentration)									
Test concentration 1									
Test concentration 2									
Test concentration 3									
Test concentration 4									
Test concentration 5									
Test concentration n									
NOAEC									

LC_{50}									
Probit slope, if applicable									

B. NON-LETHAL TOXICITY ENDPOINTS:

Briefly summarize behavioral abnormalities or other signs of toxicity. Indicate effects that were related to the chemical properties of the test material. Compare the sub-lethal effects with that of the reference chemical.

Table X: Sub-lethal Effect of {Test Material} on {Test Organism}.

Treatment (mg a.i./L) [record measured and nominal concentrations used]	**Observation period**											
	Endpoint 1 (% affected)				**Endpoint 2 (% affected)**				**Endpoint 3 (% affected)**			
	24 h	**48 h**	**72 h**	**96 h**	**24 h**	**48 h**	**72 h**	**96 h**	**24 h**	**48 h**	**72 h**	**96 h**
Negative control (dilution water only), if used												
Positive control, if used (indicate carrier concentration) % sub-lethal effect: EC_{50}												
Test concentration 1												
Test concentration 2												
Test concentration 3												
Test concentration n												
NOAEC												

D. CONCLUSIONS:

Provide the major conclusions, e.g., values for LC_{50} and NOAEC.

ACUTE HONEYBEES TOXICITY (Oral & Contact)

A. Executive Summary:

In a *[#]*-day *[oral or dietary]* toxicity and pathogenicity study, *[common name (scientific name)]* were exposed to a *[single OR #]* dose of *[dose amount]* of *[formulation, note its potency, biological activity or concentration per unit weight or volume]* (containing % *a.i. name*) by *[indicate exposure method]*. *[Include other pertinent details such as the controls used.*

The *[#]*-day LD50 was *[=, > or <] [insert LC50 in appropriate units]* (95% C.I. *-if applicable*). *[If the study included sublethal test endpoints and/or sublethal effects were observed and/or additional subchronic testing was triggered include the following text (otherwise-delete):* The EC50 based on sublethal effects, were *[insert EC50 in appropriate units.]* The NOEC value, based on mortality *[and sublethal effects]*, was *[=, > or <] [insert NOEC in appropriate units]*.

This study is classified as *[acceptable, unacceptable, and supplemental]*. This study was *[not]* conducted in accordance with the guideline recommendations for a *[oral or dietary]* toxicity and pathogenicity study for honey bees in the *[species]*.

B. MATERIALS AND METHODS:

1. Test Organism:

Species (common and scientific names): *[Indicate the species used.]*

Age at test initiation: *[Give the age of the test organisms.]*

Strain/Source: [Report the strain, supplier and/or source of the test organism.]

Date of collection: *[Insert the date of collection, if applicable.]*

2. STUDY DESIGN AND METHODS:

a. Experimental Methods and Conditions

Acclimation:

Duration:

Feeding:

Water:

Temperature:

Relative humidity:

b. Test chamber - description and size:

c. Route(s) of exposure:[Describe route of exposure and topical application apparatus, if applicable.]

d. Dose levels / test concentrations:

e. Preparation of dose or test concentration:

f. Confirmation of MPCA viability: [Describe methods used to confirm the concentration and/or viability of the MPCA in the dosing suspensions.]

g. Positive control / reference material: *[if used]* **[Insert a description of the reference material, with the number of arthropods treated and frequency of testing (if not concurrent).]**

h. Number of bees per chamber:

i. ***Control(s): Treatment(s):***

j. Number of replicates (chambers) per treatment:

k. Recovery of MPCA from bees: *[if applicable]* **[Describe methods used to recover the MPCA from collected samples.]**

l. Feeding: [Describe the feeding regime used during the experiment.]

m. Test Conditions Temperature: Humidity: Lighting:

n. **Duration of the study:**

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

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. Parameters measured including sub-lethal effects/toxicity symptoms:

[List the parameters measured during the experiment, e.g., mortality, survival, abnormal behaviour or appearance, fecundity, growth inhibition, concentration of the MPCA in the test suspensions. Provide references to data summary tables, if used.]

Observation/measurement intervals:

[List time points for each parameter measurement and observation.]

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

TABLE *[#].* Viability of *[test substance]* in the *[dosing suspension/diet]* administered to honey bees (*Apis mellifera*) in a *[contact, acute oral or dietary]* test.

Dose Group	**Nominal Concentration *[units]***	**Measured Concentration *[units]***
Solvent/vehicle control		
Inactivated control		
Sterile filtrate control		
Maximum hazard dose		
Negative control		

3. 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.]

TABLE *[#]*. Effect of *[test material]* on cumulative mortality of honey bees (*Apis mellifera*) in a *[contact, acute oral or dietary]* test.

Treatments *[indicate if nominal or measured (measured should be used, if provided)]*		**No. of Bees**	**Observation Period**					
			Day x1		***Day x2***		***Day n***	
			No. Dead	**% Mortality**	**No. Dead**	**% Mortality**	**No. Dead**	**% Mortality**
Negative control								
Solvent control, if used								
test concentration 1								
test concentration 2								
test concentration3								
test concentration 4								
test concentration n								
LD50/LC50 *[insert [>] if greater than]*								
NOEL/NOEC *[insert [>] if greater than]*								
Reference chemical	*Mortality (% or No.)*							
	LD50: LC50:	*[insert [>] if greater than]*						
	NOEL NOEC	*[insert [>] if greater than]*						

[a Use superscript and footnote to indicate values that are statistically significantly different from control.]

4. SUB-LETHAL TOXICITY EFFECTS:

[Include if any sub-lethal effects are observed- Briefly summarize behavioural abnormalities or other signs of toxicity. Indicate effects that were related to the t*est-material. Compare sub-lethal effects with control treatment and/or the reference chemical. 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 *[#]*. Effect of *[test material]* on *[endpoint]* of honey bees (*Apis mellifera*) in a *[contact, acute oral or dietary]* test.

Treatments *[indicate if nominal or measured (measured should be used, if provided)]*		**Observation Period**					
		Day x1		***Day x2***		***Day n***	
		endpoint 1	**% Affected**	***endpoint 2***	**% Affected**	***endpoint n***	**% Affected**
Negative control							
Solvent control, if used							
test concentration 1							
test concentration 2							
test concentration3							
test concentration 4							
test concentration n							
ED50/EC50 or other sublethal endpoint *[insert [>] if greater than]*							
NOEL/NOEC *[insert [>] if greater than]*							
Reference chemical	*LC50/ LC50*	*[insert [>] if greater than]*					
	NOEL/ NOEC	*[insert [>] if greater than]*					

CONCLUSIONS

Values for LD50, LC50, LT50, EC50, NOEL, NOEC, Probit slope, Endpoint(s) Affected: etc. were [=, > or <] insert final dose concentration/level (in appropriate units).]

ACUTE TOXICITY TO EARTHWORMS

A. Executive Summary:

In a..... day acute toxicity study, earthworms {species} were exposed to {test chemical} at {0, x1, x2, x3,...x_n mg a.i./kg dry weight of soil/artificial substrate}. The reference chemical used was..... (name) at x mg a.i/kg d w of the soil/substrate. The ..... day LC_{50} was..... mg a.i/kg dw of soil/substrate. The..... day EC_{50} was ..... mg a.i/kg dw of soil/substrate. The..... day NOAEC, based on [indicate parameter used] was x mg a.i./kg d.w. of soil/substrate. The LOAEC, based on [indicate parameter used] was x mg a.i./kg d.w. of soil/substrate. The {a.i.} is considered to be {non-toxic/toxic} to earthworms up to/above a concentration of {X} mg a.i./kg d.w of soil/substrate.

Briefly describe the mortality and other toxic effects that were observed. If toxicity or abnormalities were not observed, state that there were no compound related toxicity effects.

Results Synopsis

Test Organism Size/Age (mean weight or length):

Test Type (Flow-through, Static, Static Renewal):

LC_{50}: {.....mg a..i./kg dw soil} 95% C.I.: {.... to ... mg a.i./kg dw soil}

NOAEL: {.....mg a.i./kg dw soil}

Probit Slope: {.....} 95% C.I.: {.... to ... }

EC_{50}: {.....mg a.i./kg dw soil} 95% C.I.: {.... to ... mg a.i./kg dw soil}

Endpoint(s) Affected: {.....}

B. MATERIALS AND METHODS

1. Test organism:

Species: {common and scientific names} :OECD recommend *Eisenia fetida andrei* (Bouche). The earthworms should weigh 300-600 mg at the beginning of the test.

Age at test initiation: (mean and range)

Weight at study initiation: (mean and range)

Source:

2. STUDY DESIGN:

1. Experimental Conditions

a. Range-finding Study: If a range-finding study was conducted, briefly outline the test concentrations and other relevant conditions. Indicate the results from the preliminary study that were used to determine the conditions for the definitive study.

b. Definitive Study

1. Soil: Indicate if an artificial or natural soil was used. If an artificial soil is used, provide the composition, pH and moisture content. If a natural soil was used, complete the following table.

Table X: Physicochemical Properties of Natural Soil

Property	**Value**	**Remarks**
For natural soil: Texture: % sand % silt % clay Textural classification: For artificial substrate (provide composition):		
pH (__:__ soil:water)		
Organic carbon (%)		
Moisture (%)		

Table X . Experimental Design

Parameter	Value	Remarks
Acclimation: Duration: Conditions (state if same as the test conditions): Health:		
Soil [fresh or stored]		
Test Container Material Size Amount of soil/substrate		
No. of replicates: Per treatment group: Per control:		
No. of earthworms per treatment		.
Solvents used or not (if yes report the name and concentration)		
Rates of application: Nominal: Measured:		
Reference chemical (if used) name: Concentration:		

Parameter	Value	Remarks
Test conditions: Temperature Lighting conditions Moisture		
Duration of the study		

2. Observations:

Table X: Observations

Parameters	**Details**	**Remarks**
Observation intervals		
Parameters measured including the sublethal effects/toxicity symptoms		
Were raw data included?		
Other observations, if any		

3. Statistics: List the parameters that were analyzed and the statistical tests that were performed. A copy of the statistical methods from the study may be attached.

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. MORTALITY: Briefly summarize mortality; dose response relationship and slope of dose-response curve, if provided; compare with reference toxicity end points.

Table X: Effect of {Test Material} on Mortality of {Species}

Treatment (mg a.i./kg soil) [record measured and nominal conc. used]	Observation period					
	Day x		Day x		Day x	
	No Dead	% mortality	No Dead	% mortality	No Dead	% mortality
Control						
Test concentration 1						
Test concentration 2						
Test concentration 3						
Test concentration n						
NOAEC						
LOAEC						
LC_{50}						
Reference chemical (% mortality; LC_{50})						

2. SUB-LETHAL TOXICITY ENDPOINTS:

Briefly summarize signs of sub-lethal toxicity. Indicate any results related to the chemical properties of the test material.

Table X: Sub-lethal Effect of {Test Material} on {Species}. [Indicate if average weight used]

Treatment (mg a.i./kg soil) [indicate if measured or nominal conc. used]	Observation period					
	Day x		Day x		Day x	
	weight	% loss	weight	% loss	weight	% loss
Control						
Test concentration 1						
Test concentration 2						
Test concentration 3						
Test concentration n						
NOAEC						
LOAEC						
EC_{50}						
Reference chemical (% mortality; LC_{50})						

CONCLUSIONS:

Provide the major conclusions, e.g., values for EC_{50}, LC_{50}. NOAEC, and LOAEC.

TOXICOLOGY SCRTINY TEMPLATE

[9(3)TI-New Source)]

1. GENERAL INFORMATIONS:

1.	Application Details (category etc.)		
2.	Test Substance/Chemical Details (Common Name, IUPAC Name, CAS N. Batch N.)		
3.	Assay Purity/Active ingredient Content %		
4.	Type of Pesticides (Insecticide/ Fungicide/ Herbicide etc.)		
5.	Decoding Certificates details		
6.	Product Schedule Inclusion Details		
7.	Source of Technical Material In case of TI-New source: information on registered source and its chemical composition. (Including RC decision or CR etc.)		
8.	In case of formulation, status of technical registration (including RC decision or CR)		
9.	Source of manufacturer and supplier		

2. RTT PERMIT

RTT PERMIT DETAILS						
Permit Number	Name of The Insecticide/Chemical	Quantity Approved	Name of The Importer	Name of The Manufacturer	Source of Procurement	Purpose of Import

3. LABEL & LEAFLET

LABEL AND LEAFLET							
Chemical Composition	Precautions	Symptoms of Poisoning	Cautionary Statement	First Aid	Antidote	Toxicity Triangle	Pictogram Details

4. TEST SUBSTANCE & FORMULATION

1.	Physicochemical property		
2.	Adjuvants details		
3.	Compatibility		

1. STUDY DETAILS (Applicable for all studies)

S. No.	Parameters							
1.	Study Report No. & Type							
2.	Sponsor (Name and Address)							
3.	Test Facility (Name and Address)							
4.	Test Guideline (OECD/EPA etc.)							
5.	Study Initiation Date							
6.	Study Completion Date							
7.	CoA Attached (Yes/No)							
8.	IAEC No.							
9.	NGCMA GLP Certificate (Validity up to)							

2. STUDY DESIGN/METHODOLOGY (Applicable for all studies)

S. No.	Parameters						
1.	Species/Strain						
2.	No. and sex of animals per dose						
3.	Age and Body weight range at dosing						
4.	Doses/concentrations						
5.	Vehicle & positive control						
6.	Route of administration						
7.	Fasting Details (Duration)						
8.	Housing conditions (Temperature, Relative Humidity, Light cycle)						
9.	Diet and water report (source)						
10.	Feed analysis certificate						
11.	Acclimatization period and grouping						
12.	Dosing Schedule/ Single or repeated,						
13.	Rationale for dose selection						
14.	Homogeneity Analysis: *[range]*						

	Stability Analysis: *[range of values]* **Concentration Analysis:** *[range of values]*						
15.	**Recovery Period (days)**						
16.	**Any deviation from protocol or amendments**						

1. ACUTE ORAL TOXICITY RAT

Executive Summary:

In an acute oral toxicity study groups (#/sex) of strain, species (source), (age, weight) were given a single oral dose of (formulation/technical, note a.i. and %) in (vehicle or undiluted test article) at doses of??? or??mg/kg bw. Animals were then observed for (#) days.

Study Endpoints:

Oral LD_{50} = mg/kg bw

Toxicity based on the LD_{50} in males or females whichever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV.

Dose (mg/kg b.w)	Mortality/Number Tested Males/ Females	Morbidity/Number Tested Males/ Females	Survived/ Number Tested Males/ Females

Statistics/If any: The oral LD_{50} was calculated using the

Observations:

A. Morality: as noted in table.
B. Clinical observations including signs & symptoms:
C. Gross Necropsy/ pathological findings:
D. Weight changes:

Conclusions:

2. ACUTE DERMAL TOXICITY RAT

Executive Summary:

In an acute dermal toxicity study, groups (#/sex) of strain, species (source), (age, weight) were dermally exposed to (formulation/technical, note a.i. and %) in (vehicle or undiluted test article) to (% or amount of body surface area) at doses of, or mg/kg bw. Test sites were covered with a(n) occlusive/semi-occlusive dressing for (#) hours. Animals were then observed for (#) days.

Study Endpoints:

Dermal LD_{50} = mg/kg bw
Toxicity based on the LD_{50} in males or females whichever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV.

Dose (mg/kg b.w)	**Mortality/Number Tested Males/ Females**	**Morbidity/Number Tested Males/ Females**	**Survived/ Number Tested Males/ Females**

Statistics/If any: The Dermal LD_{50} was calculated using the
Observations:

A. **Morality:** as noted in table.
B. **Clinical observations including signs & symptoms:**
C. **Gross Necropsy/ pathological findings:**
D. **Weight changes:**

Conclusions:

3. ACUTE INHALATIONAL TOXICITY RAT

Executive Summary:

In an acute inhalation toxicity study, groups (#/sex) of strain, species (source), (age, weight) were exposed (nose only, head only or whole body) via the inhalation route to (formulation/technical, note a.i. and %) in (name of vehicle or undiluted test article) for [#] hours at concentrations of mg/L. Animals were then observed for [#] days.

Study Endpoints:

LC_{50} = mg/L

Toxicity: based on (males or females whichever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV.

Nominal Conc. (mg/L)	Actual Conc. (Gravimetric/ Analytical) (mg/L)	MMAD	GSD	Mortality/Number Tested	Morbidity/Number Tested	Survived/ Number Tested
				Males/ Females	Males/ Females	Males/ Females

Test Atmosphere /Chamber Description:

Chamber Volume:	
Airflow:	
Temperature:	
Relative Humidity:	
Time to Equilibrium:	

Test the atmosphere concentration:
Particle size determination:
Statistics/if any: The LC_{50} was calculated using the
Observations:

A. **Morality:** as noted in table.
B. **Clinical observations including signs & symptoms:**
C. **Gross Necropsy/ pathological findings:**
D. **Weight changes:**

Conclusions:

4. ACUTE EYE IRRITATION RABBIT

Executive Summary:

In an acute eye irritation study, (volume or weight of test material applied) of (formulation/technical, note a.i. and %) in (name of vehicle if appropriate, or undiluted test material) was instilled into the conjunctival sac of (which eye) of (#/sex), (strain), (species - rabbits) (source, age, weight) for [#] hours. (Note if eyes were washed) Animals were then observed for *[#]* days. Irritation was scored by the method as per guideline.
In this study, formulation/technical is not an eye irritant OR is minimally, mildly, moderately, severely, or extremely irritating to the eye based on GHS/EPA Toxicity Category I, II, III, IV.

	Number "positive"/number tested							
	Hours				**Days**			
Observations	1	**24**	**48**	**72**	**4**	**7**	**14**	**21**
Corneal Opacity								
Iritis								
Redness								
Chemosis								
Discharge								
Conjunctivae:								

Clinical observations including ocular signs & symptoms/ reactions:
Conclusion:

5. ACUTE DERMAL IRRITATION/PRIMARY SKIN IRRITATION RABBIT

Executive Summary:

In a primary skin irritation study, (#/sex) strain, species (source), (age, weight) were dermally exposed to (volume or weight of test material applied) of (formulation/technical, note a.i. and %) in (name of vehicle or undiluted test material) to (% or amount of body surface area - state location of test site). Test sites were covered with a(n) occlusive/semi-occlusive dressing for (#) hours. Animals were then observed for [#] days. Irritation was scored by the method of (cite method).

In this study, formulation/technical is not a dermal irritating OR is corrosive to the skin based on. GHS/EPA Toxicity Category I, II, III, IV.

	Number "positive"/number tested			
	Hours			
Observations	1	**24**	**48**	**72**
Erythema and Eschar Formation				
Oedema				

Observations:

Results:

Conclusions:

6. SKIN SENSITIZATION GUINEA PIG/LLNA

Executive Summary:

In a dermal sensitization study with (formulation/technical, note a.i. and %) in (name of vehicle if appropriate or undiluted test article), strain, species (source)(age, weight) were tested using the method of (cite study type). Identify positive control material. List clinical signs (systemic and local for LLNA) and mortality. Necropsy results for LLNA **if significant**.

Results and discussion:

A. **Reactions and duration:**

B. **Positive control:**

C. **Conclusions:**

OBSERVATIONS FOR MAXIMIZATION TEST (GPMT) AND BUEHLER TEST:

a. **Justification for positive control other than mentioned in guideline:**

b. **Dose Range Finding Study (DRFS) result:**

c. **Treatment and control skin reaction observation**

Group		Skin reaction observation (dermal scoring)		
		21 hours of patch removal	Approx. 48 hours post challenge application	Approx. 72 hours post challenge application
Treatment group	Male			
Naïve control				
Treatment group	Female			
Naïve control				

0 = no visible change 1 = discrete or patchy erythema 2 = moderate and confluent erythema 3 = intense erythema and swelling

d. **Result of positive control for reliability check:**

e. **Clinical observations if any,**

histopathological examination	
skin fold thickness	

OBSERVATIONS FOR LOCAL LYMPH NODE ASSAY (LLNA) TEST:

Observations	Results
Dose Range Finding Study (DRFS) result:	
Clinical Observations	
Body weights changes	
Ear erythema measurements	
Ear thickness measurements	
Statistical tool used	
DPM of positive control (mean and associated error term)	
Stimulation index of positive control (concurrent/ historical)	
DPM of treatment group (mean and associated error term)	
Stimulation index of treatment group	
DPM of vehicle control group (mean and associated error term)	
Stimulation index of Vehicle control group (if any)	

DPM: Disintegration Per Minute

REPEATED DOSE 28-DAY ORAL TOXICITY-Rodent

A. Executive Summary:

In a 28-day oral toxicity study test substance (technical/formulation was administered to *[(# of animals) species, strain]*/sex/dose in *[diet, water, by gavage]* at dose levels of 0, x, x, or x ppm (equivalent to 0, x, x, x mg/kg bw/day).

[Describe toxicity briefly following instructions for exec summary paragraph 2. If there is no toxicity, state that there were no compound related effects on mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology.

Note: *if there was a NOAEL for clinical findings and when they occurred (for acute reference dose consideration during subsequent risk assessment.)].*

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

B. STUDY DESIGN:

Animal assignment: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design *[change heading and units as appropriate for method of administration]*

Test Group	Conc. in Diet *(units)*	Dose to Animal *(units)*	# Male	# Female
Control				
Low				
Mid				
High				

Dose selection rationale:

The dose levels were selected based on the results from *[state study type(s)]* where *[route]* - administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available.]*

Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. RESULT & DISCUSSION (Observations):

1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*

2. Mortality:
3. Neurological Evaluations - The following evaluations (measurements) were performed on day *[insert treatment day: [list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*
4. Body weight and weight gain: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment-related effect]*
5. Food consumption and compound intake *[if feeding study]*:
a. Food consumption:
b. Compound consumption: *[time-weighted average] [include compound intake in table 1]* -
c. Food efficiency: *[if relevant]* - *[relate to any changes in body weight]*
6. Ophthalmoscopic examination:
7. Blood analyses: [Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]:
a. Hematology: [relate to any histological findings]
Hematology:

Hematocrit (HCT)*		Leukocyte differential count*
Hemoglobin (HGB)*		Mean corpuscular HGB (MCH)*
Leukocyte count (WBC)*		Mean corpusc. HGB conc.(MCHC)*
Erythrocyte count (RBC)*		Mean corpusc. volume (MCV)*
Platelet count*		Reticulocyte count
Blood clotting measurements*		
(Thromboplastin time)		
(Clotting time)		
(Prothrombin time)		

b. Clinical Chemistry: [relate to any histological findings]
Blood was collected *[were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.

Clinical Chemistry:

ELECTROLYTES		OTHER
Calcium		Albumin*
Chloride		Creatinine*
Magnesium		Urea nitrogen*
Phosphorus		Total Cholesterol*

Potassium*		Globulins	
Sodium*		Glucose*	
ENZYMES		Total bilirubin	
Alkaline phosphatase (ALK)*		Total protein (TP)*	
Cholinesterase (ChE)		Triglycerides	
Creatine phosphokinase		Serum protein electrophoresis	
Lactic acid dehydrogenase (LDH)			
Alanine aminotransferase (ALT/also SGPT)*			
Aspartate aminotransferase (AST/also SGOT)*			
Sorbitol dehydrogenase*			
Gamma glutamyl transferase (GGT)*			
Glutamate dehydrogenase			

8. Urinalysis:

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

Appearance*		Glucose	
Volume*		Ketones	
Specific gravity/osmolality*		Bilirubin	
pH*		Blood/blood cells*	
Sediment (microscopic)		Nitrate	
Protein*		Urobilinogen	

* Recommended for 90-day oral rodent studies

9. Gross and histopathology: [Tables are recommended for treatment-related findings; limit text to integration of findings, highlights]

1. Organ weight - [absolute and relative as appropriate, relate to any histological changes]
2. Gross pathology -
3. Microscopic pathology - [relate with other findings, as appropriate]

D. CONCLUSION:

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.]

7. REPEATED DOSE 90-DAY ORAL TOXICITY-RODENT

A. Executive Summary:

In a 90-day oral toxicity study test substance (technical/formulation was administered to *[(# of animals) species, strain]*/sex/dose in *[diet, water, by gavage]* at dose levels of 0, x, x, or x ppm (equivalent to 0, x, x, x mg/kg bw/day).

[Describe toxicity briefly following instructions for exec summary paragraph 2. If there is no toxicity, state that there were no compound related effects on mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology.

Note: *if there was a NOAEL for clinical findings and when they occurred (for acute reference dose consideration during subsequent risk assessment.)].*
The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

B. STUDY DESIGN:
1. Animal assignment: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.
TABLE 1: Study design ***[change heading and units as appropriate for method of administration]***

Test Group	Conc. in Diet *(units)*	Dose to Animal *(units)*	# Male	# Female
Control				
Low				
Mid				
High				

2. Dose selection rationale:
The dose levels were selected based on the results from *[state study type(s)]* where *[route]* - administration of up to *[dose]* resulted in *[state effects]. [Use data from range-finding study if available.]*
3. Statistics - *[list parameters that were analyzed and the statistical methods used]*
C. RESULT & DISCUSSION (Observations):
1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*
2. Mortality:
3. Neurological Evaluations - The following evaluations (measurements) were performed on day *[insert treatment day*: *[list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*
4. Body weight and weight gain: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment-related effect]*
5. Food consumption and compound intake *[if feeding study]*:
a. Food consumption:
b. Compound consumption: *[time-weighted average] [include compound intake in table 1]* -
c. Food efficiency: *[if relevant] - [relate to any changes in body weight]*
6. Ophthalmoscopic examination:
7. Blood analyses: [Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]:
a. Hematology: [relate to any histological findings]
Hematology:

Hematocrit (HCT)*		Leukocyte differential count*
Hemoglobin (HGB)*		Mean corpuscular HGB (MCH)*

Leukocyte count (WBC)*		Mean corpusc. HGB conc.(MCHC)*
Erythrocyte count (RBC)*		Mean corpusc. volume (MCV)*
Platelet count*		Reticulocyte count
Blood clotting measurements*		
(Thromboplastin time)		
(Clotting time)		
(Prothrombin time)		

b. Clinical Chemistry: [relate to any histological findings]
Blood was collected *[were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.

Clinical Chemistry:

ELECTROLYTES		**OTHER**
Calcium		Albumin*
Chloride		Creatinine*
Magnesium		Urea nitrogen*
Phosphorus		Total Cholesterol*
Potassium*		Globulins
Sodium*		Glucose*
ENZYMES		Total bilirubin
Alkaline phosphatase (ALK)*		Total protein (TP)*
Cholinesterase (ChE)		Triglycerides
Creatine phosphokinase		Serum protein electrophoresis
Lactic acid dehydrogenase (LDH)		
Alanine aminotransferase (ALT/also SGPT)*		
Aspartate aminotransferase (AST/also SGOT)*		
Sorbitol dehydrogenase*		
Gamma glutamyl transferase (GGT)*		
Glutamate dehydrogenase		

8. Urinalysis:

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

Appearance*		Glucose
Volume*		Ketones
Specific gravity/osmolality*		Bilirubin
pH*		Blood/blood cells*

Sediment (microscopic)		Nitrate	
Protein*		Urobilinogen	

* Recommended for 90-day oral rodent studies

9. **Gross and histopathology**: [Tables are recommended for treatment-related findings; limit text to integration of findings, highlights]

1. Organ weight - [absolute and relative as appropriate, relate to any histological changes]
2. Gross pathology -
3. Microscopic pathology - [relate with other findings, as appropriate]

D. CONCLUSION:

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.]

8. REPEATED DOSE DERMAL TOXICITY (28-DAY)-RAT/RABBIT

Executive Summary:

In a 28-day dermal toxicity study test substance was applied to the shaved skin of *[(# of animals) species, strain]*/sex/dose at dose levels of 0, x, x, x mg/kg bw/day, 6 hours/day for 5 days/week during a 28-day period.

[Describe toxicity briefly. If there is no toxicity, state that there were no compound related effects in mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology. Note if there was a LOAEL/NOAEL for clinical findings (for acute reference dose consideration during subsequent risk assessment)].

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

B. STUDY DESIGN:

1. Animal assignment: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design *[change heading and units as appropriate for method of administration]*

Test Group	Conc. in Diet *(units)*	Dose to Animal *(units)*	# Male	# Female
Control				
Low				
Mid				
High				

2. Dose selection rationale:
The dose levels were selected based on the results from *[state study type(s)]* where *[route]* - administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available.]*
3. Statistics - *[list parameters that were analyzed and the statistical methods used]*
C. RESULT & DISCUSSION (Observations):
1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*
2. Mortality:
3. Neurological Evaluations - The following evaluations (measurements) were performed on day *[insert treatment day*: *[list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*
4. Dermal irritation:
5. Body weight and weight gain: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment-related effect]*
6. FOOD CONSUMPTION AND COMPOUND INTAKE *[if feeding study]*:
a. Food consumption:
b. Compound consumption: *[time-weighted average] [include compound intake in table 1]* -
c. Food efficiency: *[if relevant]* - *[relate to any changes in body weight]*
7. Ophthalmoscopic examination:
8. Blood analyses: [Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]:
a. Hematology: [relate to any histological findings]
Hematology:

Hematocrit (HCT)*		Leukocyte differential count*
Hemoglobin (HGB)*		Mean corpuscular HGB (MCH)*
Leukocyte count (WBC)*		Mean corpusc. HGB conc.(MCHC)*
Erythrocyte count (RBC)*		Mean corpusc. volume (MCV)*
Platelet count*		Reticulocyte count

Blood clotting measurements*		
(Thromboplastin time)		
(Clotting time)		
(Prothrombin time)		

b. Clinical Chemistry: [relate to any histological findings]
Blood was collected *[were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.

Clinical Chemistry:

ELECTROLYTES		**OTHER**
Calcium		Albumin*
Chloride		Creatinine*
Magnesium		Urea nitrogen*
Phosphorus		Total Cholesterol*
Potassium*		Globulins
Sodium*		Glucose*
ENZYMES		Total bilirubin
Alkaline phosphatase (ALK)*		Total protein (TP)*
Cholinesterase (ChE)		Triglycerides
Creatine phosphokinase		Serum protein electrophoresis
Lactic acid dehydrogenase (LDH)		
Alanine aminotransferase (ALT/also SGPT)*		
Aspartate aminotransferase (AST/also SGOT)*		
Sorbitol dehydrogenase*		
Gamma glutamyl transferase (GGT)*		
Glutamate dehydrogenase		

9. Urinalysis:

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

Appearance*		Glucose
Volume*		Ketones
Specific gravity/osmolality*		Bilirubin
pH*		Blood/blood cells*
Sediment (microscopic)		Nitrate
Protein*		Urobilinogen

* Recommended for 90-day oral rodent studies

10. **Gross and histopathology**: [Tables are recommended for treatment-related findings; limit text to integration of findings, highlights]

1. Organ weight - [absolute and relative as appropriate, relate to any histological changes]
2. Gross pathology -
3. Microscopic pathology - [relate with other findings, as appropriate]

All animals that died and those sacrificed on schedule were subjected to gross pathological examination and the CHECKED (X) tissues were collected for histological examination *[note if not all collected tissues were examined]*. The (XX) organs, in addition, were weighed.

DIGESTIVE SYSTEM		**CARDIOVASCULAR/ HEMATOLOGY**		**NEUROLOGIC**
Tongue		Aorta*		Brain*+
Salivary glands*		Heart*+		Peripheral nerve*
Esophagus*		Bone marrow*		Spinal cord (3 levels)*
Stomach*		Lymph nodes*		Pituitary*
Duodenum*		Spleen*+		Eyes (optic nerve)*
Jejunum*		Thymus*+		**GLANDULAR**
Ileum*				Adrenal gland*+
Cecum*		**UROGENITAL**		Lacrimal gland
Colon*		Kidneys*+		Parathyroid*
Rectum*		Urinary bladder*		Thyroid*
Liver*+		Testes*+		**OTHER**
Gall bladder (not rat)*		Epididymides*+		Bone (sternum and/or femur)
Bile duct (rat)		Prostate*		Skeletal muscle
Pancreas*		Seminal vesicles*		Skin*
RESPIRATORY		Ovaries*+		All gross lesions and
Trachea*		Uterus*+		

Lung*		Mammary gland*		
Nose*				
Pharynx*				
Larynx*				

+ Organ weights required for rodent studies.

D. CONCLUSION:

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

10. REPEATED DOSE DERMAL TOXICITY (90-DAY) RAT/RABBIT

A. Executive Summary:

In a 90-day dermal toxicity study the test substance was applied to the shaved skin of *[(# of animals) species, strain]*/sex/dose at dose levels of 0, x, x, x mg/kg bw/day, 6 hours/day for 5 days/week during a 90-day period.

[Describe toxicity briefly. If there is no toxicity, state that there were no compound related effects in mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology. Note if there was a LOAEL/NOAEL for clinical findings (for acute reference dose consideration during subsequent risk assessment)].

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

B. STUDY DESIGN:

1. Animal assignment: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design *[change heading and units as appropriate for method of administration]*

Test Group	Conc. in Diet *(units)*	Dose to Animal *(units)*	# Male	# Female
Control				
Low				
Mid				

High				

2. Dose selection rationale:

The dose levels were selected based on the results from *[state study type(s)]* where *[route]* - administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available.]*

3. Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. RESULT & DISCUSSION (Observations):

1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*

2. Mortality:

3. Neurological Evaluations - The following evaluations (measurements) were performed on day *[insert treatment day*: *[list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*

4. Dermal irritation:

5. Body weight and weight gain: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment-related effect]*

6. FOOD CONSUMPTION AND COMPOUND INTAKE *[if feeding study]*:

a. Food consumption:

b. Compound consumption: *[time-weighted average] [include compound intake in table 1]* -

c. Food efficiency: *[if relevant]* - *[relate to any changes in body weight]*

7. Ophthalmoscopic examination:

8. Blood analyses: [Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]:

a. Hematology: [relate to any histological findings]

Hematology:

Hematocrit (HCT)*		Leukocyte differential count*
Hemoglobin (HGB)*		Mean corpuscular HGB (MCH)*
Leukocyte count (WBC)*		Mean corpusc. HGB conc.(MCHC)*
Erythrocyte count (RBC)*		Mean corpusc. volume (MCV)*
Platelet count*		Reticulocyte count
Blood clotting measurements*		
(Thromboplastin time)		
(Clotting time)		

(Prothrombin time)		

b. Clinical Chemistry: [relate to any histological findings]

Blood was collected *[were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.

Clinical Chemistry:

ELECTROLYTES		**OTHER**
Calcium		Albumin*
Chloride		Creatinine*
Magnesium		Urea nitrogen*
Phosphorus		Total Cholesterol*
Potassium*		Globulins
Sodium*		Glucose*
ENZYMES		Total bilirubin
Alkaline phosphatase (ALK)*		Total protein (TP)*
Cholinesterase (ChE)		Triglycerides
Creatine phosphokinase		Serum protein electrophoresis
Lactic acid dehydrogenase (LDH)		
Alanine aminotransferase (ALT/also SGPT)*		
Aspartate aminotransferase (AST/also SGOT)*		
Sorbitol dehydrogenase*		
Gamma glutamyl transferase (GGT)*		
Glutamate dehydrogenase		

9. Urinalysis:

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

Appearance*		Glucose
Volume*		Ketones
Specific gravity/osmolality*		Bilirubin
pH*		Blood/blood cells*
Sediment (microscopic)		Nitrate
Protein*		Urobilinogen

* Recommended for 90-day oral rodent studies

10. **Gross and histopathology**: [Tables are recommended for treatment-related findings; limit text to integration of findings, highlights]

1. Organ weight - [absolute and relative as appropriate, relate to any histological changes]
2. Gross pathology -
3. Microscopic pathology - [relate with other findings, as appropriate]

All animals that died and those sacrificed on schedule were subjected to gross pathological examination and the CHECKED (X) tissues were collected for histological examination *[note if not all collected tissues were examined]*. The (XX) organs, in addition, were weighed.

DIGESTIVE SYSTEM		**CARDIOVASCULAR/ HEMATOLOGY**		**NEUROLOGIC**
Tongue		Aorta*		Brain*+
Salivary glands*		Heart*+		Peripheral nerve*
Esophagus*		Bone marrow*		Spinal cord (3 levels)*
Stomach*		Lymph nodes*		Pituitary*
Duodenum*		Spleen*+		Eyes (optic nerve)*
Jejunum*		Thymus*+		**GLANDULAR**
Ileum*				Adrenal gland*+
Cecum*		**UROGENITAL**		Lacrimal gland
Colon*		Kidneys*+		Parathyroid*
Rectum*		Urinary bladder*		Thyroid*
Liver*+		Testes*+		**OTHER**
Gall bladder (not rat)*		Epididymides*+		Bone (sternum and/or femur)
Bile duct (rat)		Prostate*		Skeletal muscle
Pancreas*		Seminal vesicles*		Skin*
RESPIRATORY		Ovaries*+		All gross lesions and masses*
Trachea*		Uterus*+		
Lung*		Mammary gland*		
Nose*				
Pharynx*				
Larynx*				

+ Organ weights required for rodent studies.

D. CONCLUSION:

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

11. REPEATED DOSE INHALATION TOXICITY (28-DAY)-RAT

A. Executive Summary:

In a sub-chronic inhalation toxicity study test substance was administered to *[(# of animals) species, strain]*/sex/concentration by dynamic *[nose only, head only or whole body]* exposure at concentrations of 0, x, x, x mg/L for x hours per day, x days/week for a total of x days *(include concentrations in units reported in the study as well as mg/L conversion).*

[Describe toxicity briefly. If there is no toxicity, state that there were no compound related effects in mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology. Note if there was a LOAEL/NOAEL for clinical findings (for acute reference dose consideration during subsequent risk assessment)].

The LOAEL is mg/L/day, based on the NOAEL is mg/L/day.

B. STUDY DESIGN:

1. Animal assignment

Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design

Test group	Nominal Conc. (mg/L)	Analytical Conc. (mg/L)	MMAD	GSD	Rats/sex
Control					
Low (LCT)					
Mid (MCT)					
High (HCT)					

2. Dose selection rationale

The dose levels were selected based on the results from *[state study type(s)]* where *[route-* administration of up to *[dose]* resulted in *[state effects]. [Use data from range-finding study if available.]*

3. Generation of the test atmosphere / chamber description:

Time to equilibrium was.

Analytical Chemistry.

Test atmosphere concentration *[give method and results]*. Results are in table 1 above.
Particle size determination [*give method and results]*. Results are in table 1 above.
2. **Statistics** - *[list parameters that were analyzed and the statistical methods used]*
C. RESULT & DISCUSSION (Observations):
1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*
2. Mortality:
3. Neurological Evaluations - The following evaluations (measurements) were performed on day *[insert treatment day*: *[list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*
4. Body weight and weight gain: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment-related effect]*
5. FOOD CONSUMPTION AND COMPOUND INTAKE *[if feeding study]*:
a. Food consumption:
b. Compound consumption: *[time-weighted average] [include compound intake in table 1]* -
c. Food efficiency: *[if relevant] - [relate to any changes in body weight]*
6. Ophthalmoscopic examination:
7. Blood analyses: [Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]:
a. Hematology: [relate to any histological findings]
Hematology:

Hematocrit (HCT)*		Leukocyte differential count*
Hemoglobin (HGB)*		Mean corpuscular HGB (MCH)*
Leukocyte count (WBC)*		Mean corpusc. HGB conc.(MCHC)*
Erythrocyte count (RBC)*		Mean corpusc. volume (MCV)*
Platelet count*		Reticulocyte count
Blood clotting measurements*		
(Thromboplastin time)		
(Clotting time)		
(Prothrombin time)		

b. Clinical Chemistry: [relate to any histological findings]

Blood was collected *[were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.

Clinical Chemistry:

ELECTROLYTES		**OTHER**
Calcium		Albumin*
Chloride		Creatinine*
Magnesium		Urea nitrogen*
Phosphorus		Total Cholesterol*
Potassium*		Globulins

Sodium*		Glucose*
ENZYMES		Total bilirubin
Alkaline phosphatase (ALK)*		Total protein (TP)*
Cholinesterase (ChE)		Triglycerides
Creatine phosphokinase		Serum protein electrophoresis
Lactic acid dehydrogenase (LDH)		
Alanine aminotransferase (ALT/also SGPT)*		
Aspartate aminotransferase (AST/also SGOT)*		
Sorbitol dehydrogenase*		
Gamma glutamyl transferase (GGT)*		
Glutamate dehydrogenase		

8. Urinalysis:

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

	Appearance*		Glucose
	Volume*		Ketones
	Specific gravity/osmolality*		Bilirubin
	pH*		Blood/blood cells*
	Sediment (microscopic)		Nitrate
	Protein*		Urobilinogen

* Recommended for 90-day oral rodent studies

9. Gross and histopathology: [Tables are recommended for treatment-related findings; limit text to integration of findings, highlights]

1. Organ weight - [absolute and relative as appropriate, relate to any histological changes]
2. Gross pathology -
3. Microscopic pathology - [relate with other findings, as appropriate]

All animals that died and those sacrificed on schedule were subjected to gross pathological examination and the CHECKED (X) tissues were collected for histological examination *[note if not all collected tissues were examined]*. The (XX) organs, in addition, were weighed.

DIGESTIVE SYSTEM		**CARDIOVASCULAR/ HEMATOLOGY**		**NEUROLOGIC**
Tongue		Aorta*		Brain*+
Salivary glands*		Heart*+		Peripheral nerve*
Esophagus*		Bone marrow*		Spinal cord (3 levels)*
Stomach*		Lymph nodes*		Pituitary*
Duodenum*		Spleen*+		Eyes (optic nerve)*
Jejunum*		Thymus*+		**GLANDULAR**
Ileum*				Adrenal gland*+

Cecum*		**UROGENITAL**		Lacrimal gland
Colon*		Kidneys*+		Parathyroid*
Rectum*		Urinary bladder*		Thyroid*
Liver*+		Testes*+		**OTHER**
Gall bladder (not rat)*		Epididymides*+		Bone (sternum and/or femur)
Bile duct (rat)		Prostate*		Skeletal muscle
Pancreas*		Seminal vesicles*		Skin*
RESPIRATORY		Ovaries*+		All gross lesions and masses*
Trachea*		Uterus*+		
Lung*		Mammary gland*		
Nose*				
Pharynx*				
Larynx*				

+ Organ weights required for rodent studies.

D. CONCLUSION:

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

12. *IN VITRO* BACTERIAL GENE MUTATION *(Bacterial system, Salmonella typhimurium; E. coli)/* mammalian activation gene mutation assay

(Mutagenicity: AMES Test, 2 In Vitro, 1 In Vivo]

A. Executive Summary:

In a reverse gene mutation assay in bacteria (MRID *[number]*), strains *[specify]* of *S. typhimurium [or other acceptable bacterial strains, i.e., E. coli wp2 (pKM101) and WP2uvrA(pKM101)]* were exposed to *[Chemical name, (% a.i., batch/lot #), include solvent if appropriate]* at concentrations of in the presence and absence of mammalian metabolic activation *[specify] in the plate incorporation or pre-incubation procedure [specify]*.

(Chemical name) was tested *[up to cytotoxic (or insoluble) concentrations or limit concentration (5000 g/plate or 5 L/plate), include other details as appropriate]*. *(quantitate if positive for number of revertants e.g., a dose related increase to 782 revertants at the highest concentration vs. 110 revertants in control for strain TA 100)*. The positive controls induced *(did not induce)* the appropriate responses in the corresponding strains.

There was *(no) evidence (or a concentration related positive response)* of induced mutant colonies over background.

B. MATERIALS AND METHODS

1. Control Materials:		
	Negative:	*[e.g., culture medium]*
	Solvent (final conc=n):	
	Positive:	Nonactivation: Sodium azide _____ g/plate TA100, TA1535 2-Nitrofluorene _____ g/plate TA98, TA1538 9-Aminoacridine ___ g/plate TA97, TA1537 Other (list):
		Activation: 2-Aminoanthracene (2-anthramine) g/plate usually all strains Other (list):

2. Activation: S9 derived from *[mark those that apply with x]*							
	induced		Aroclor 1254		Rat		Liver
	non-induced		Phenobarbitol		Mouse		Lung
			None		Hamster		Other *[name]*
			Other *[name]*		Other *[name]*		

Describe S9 mix composition *[if purchased, give details]*:

3. Test organisms: *S. typhimurium* strains *[mark those that apply with x]*							
	TA97		TA98		TA100	TA102	TA104
	TA1535		TA1537		TA1538	list any others	
Properly maintained?						Yes	No
Checked for appropriate genetic markers (*rfa* mutation, R factor)?						Yes	No

4. Test compound concentrations used: *[preliminary cytotoxicity test, if performed and main assay]*

Nonactivated conditions:

Activated conditions:

[Note: list strains used and number of replicates per dose, per strain, per condition along with doses]

C. RESULTS & DISCUSSIONS (OBSERVATIONS) *[Report results of analytical determination if performed]*

A. PRELIMINARY CYTOTOXICITY ASSAY: *[include concentration ranges, activation and nonactivation; strain(s) used; reported results, e.g., cytotoxicity indices (effect on background lawn; reduction in revertant) and solubility]*

B. MUTAGENICITY ASSAY: *[reported results, e.g., induction of revertant - individual plate counts and/or summary given; appropriateness of positive and background (concurrent and/or historical) revertant levels; number of concentration levels used; number of replicate plates; include representative table(s), if appropriate]*

D. CONCLUSION:

13. IN VITRO MAMMALIAN CYTOGENETICS ASSAY

A. Executive Summary:

In a mammalian cell cytogenetics assay *[Chromosome aberration or SCE]*(MRID *[number]*), *[cell type, e.g., CHO/V79/L5178Y cell cultures/primary lymphocyte cultures]* were exposed to *[Chemical name, (% a.i., batch/lot #), include solvent if appropriate]* at concentrations of 0, x, x, x □g/mL with and/or without metabolic activation *[specify]* for *[give duration of exposure]*.

Chemical name was tested *(up to cytotoxic or precipitating concentrations, or limit concentration, 5000 □g/mL). [include other details as appropriate, quantitate if positive (e.g. a dose related increase to 80% cells with aberrations at the top concentration, or large increase in deletions, rearrangements, etc. vs controls]*. Positive controls induced (did *not* induce) the appropriate response.

There was *(no) evidence (or a concentration related positive response)* of *[Chromosome aberration or SCE]* induced over background.

B. MATERIALS AND METHODS

1. Control Materials:	
Negative control:	*[e.g., culture medium]*
Solvent control (final conc=n):	
Positive control:	Nonactivation: (concentrations / solvent)
	Activation: (concentrations / solvent)

2. Activation: S9 derived from *[mark those with x that apply]*			
induced	Aroclor 1254	Rat	Liver
non-induced	Phenobarbitol	Mouse	Lung
	None	Hamster	Other (name)
	Other (name)	Other (name)	

Describe S9 mix composition: *[if purchased, give details]*

3. Test cells: mammalian cells in culture *[identify cell line or primary cell culture (if human lymphocytes, describe subjects, e.g., donor's health, status, sex, smoker]*				
V79 cells (Chinese hamster lung fibroblasts)				
Human lymphocytes				
Chinese hamster ovary (CHO) cells				
Media: (identify)				
Properly maintained?		Yes		No
Periodically checked for *Mycoplasma* contamination?		Yes		No
Periodically checked for karyotype stability?		Yes		No

4. Test compound concentrations used: *[For preliminary cytotoxicity test, if performed, and main assay]*		
	Nonactivated conditions:	
	Activated conditions:	

5. TEST PERFORMANCE

1. Preliminary Cytotoxicity Assay *[if performed, describe method; i.e., cell cycle kinetics, mitotic index, trypan blue, monolayer confluency, cloning efficience]*:

2. Cytogenetic Assay:

a.	**Cell exposure time:**	Test Material	Solvent Control	Positive Control
	Non-activated:	h	h	h
	Activated:	h	h	h

b.	**Spindle inhibition**	
	Inhibition used/concentration:	
	Administration time:	x hours (before cell harvest)

c.	**Cell harvest time after termination of treatment:**	Test Material	Solvent Control	Positive Control
	Non-activated:	h	h	h
	Activated:	h	h	h

d. Details of slide preparation: *[Describe briefly]*

e. Metaphase analysis

No. of cells examined per dose:				
Scored for structural?		Yes		No
Scored for numerical?		Yes If Y, list *[e.g., polyploid, endoreduplicated cells, etc.]*		No
Coded prior to analysis?		Yes		No

f. Statistical analysis: *[list parameters that were analyzed and the statistical methods]*

C. RESULTS & DISCUSSIONS (OBSERVATIONS) [*Report results of analytical determination if performed]*

1. PRELIMINARY CYTOTOXICITY ASSAY: *[reported results, e.g., include dose range, solubility, and evidence of cytotoxicity, rationale for exposure, harvest times and high dose with and without activation]*

2. *CYTOGENETIC or SCE* ASSAY:

[Reported results, e.g., include appropriateness of negative, solvent and positive control frequencies; appropriateness of dose levels; statistical evaluation; types of structural aberrations for significant dose levels; include representative table, if appropriate]

D. CONCLUSION

14. IN VITRO MAMMALIAN CELLS GENE MUTATION ASSAY *(name cell type used)*

Executive Summary:

In a mammalian cell gene mutation assay *[specify locus]* (MRID *[number]*), *[cell type]* cells cultured *in vitro* were exposed to *[Chemical name, (% a.i., batch/lot #), include solvent if appropriate]* at concentrations of x, x, x, x g/mL in the presence and absence of mammalian metabolic activation *[specify]* for *[give duration of exposure]*.

Chemical name was tested *[up to cytotoxic/insoluble/limit concentrations (i.e., 5000 g/mL, 5 L/mL, or 0.01 M), include other details as appropriate. Some quantitation here e.g., induced mutation frequency of $582x10^{-6}$ vs. $78x10^{-6}$ in controls at the top concentration]*. The positive controls *(did/did not)* induce the appropriate response. **There was *(no) evidence (or a concentration related positive response)* of induced mutant colonies over background.**

A. MATERIALS AND METHODS

1. Control Materials:	
Negative control:	*[e.g., culture medium]*
Solvent control (final conc=n):	
Positive control:	Nonactivation:(concentrations / solvent)
	Activation: (concentrations / solvent)

2. Activation: S9 derived from *[mark those with x that apply]*							
	induced		Aroclor 1254		Rat		Liver
	non-induced		Phenobarbitol		Mouse		Lung
			None		Hamster		Other *[name]*
			Other *[name]*		Other *[name]*		

Describe S9 mix composition: *[if purchased, give details]*

3. Test cells: mammalian cells in culture *[mark those with x that apply]*			
	mouse lymphoma L5178Y cells		V79 cells (Chinese hamster lung fibroblasts)
	Chinese hamster ovary (CHO) cells		list any others
Media: *[Identify]*			
Properly maintained?	Yes		No
Periodically checked for Mycoplasma contamination?	Yes		No
Periodically checked for karyotype stability?	Yes		No
Periodically "cleansed" against high spontaneous background?	Yes		No

4.**Locus Examined:**		**Thymidine kinase (TK)**	**Hypoxanthine-guanine-phosphoribosyl transferase (HGPRT)**	**Na^+/K^+ ATPase**
	Selection agent:	bromodeoxyuridine (BrdU) *[give conc=n]*	8-azaguanine (8-AG) *[conc=n]*	ouabain*[conc=n]*
		fluorodeoxyuridine (FdU)	6-thioguanine (6-TG)	
		trifluorothymidine (TFT)		
	[Other? (details)]			

5. Test compound concentrations used: *[For preliminary cytotoxicity test, if performed, and main assay]*	
Nonactivated conditions:	
Activated conditions:	

6. Test performance

1. Cell treatment:

a. Cells were exposed to test compound, negative/solvent or positive controls for ___ hours (nonactivated) hours (activated).
b. After washing, cells were cultured for ___ days (expression period) before cell selection.
c. After expression, ____ cells/dish (__ dishes/ group) were cultured for ____ days in selection medium to determine numbers of mutants and __ cells/dish (_ dishes/group) were cultured for __ days without selective agent to determine cloning efficiency.
[If mouse lymphoma cells, include information regarding colony sizing]

7. Statistical Methods: *[list parameters that were analysed and the statistical methods used]*

C. RESULTS & DISCUSSIONS (OBSERVATIONS) *[Report results of analytical determination if performed]*

A. PRELIMINARY CYTOTOXICITY ASSAY

[include concentration ranges, activation and nonactivation; reported results, e.g., cytotoxicity and solubility, rationale for dose selection for main study]

B. MUTAGENICITY ASSAY *[reported results, e.g., induction of mutant colonies - individual colony counts and/or summary given; mutant frequencies per 10^6 survivors; positive and background mutant frequencies; inclusion of concentration levels used; number of cultures per concentration; levels of cytotoxicity obtained; appropriateness of cloning efficiencies; include representative table, if appropriate].*

D. CONCLUSION

14. IN VIVO MAMMALIAN BONE MARROW ERYTHROCYTES MICRONUCLEUS ASSAY

A. Executive Summary:

In a *(strain)* mouse *[or rats or other acceptable mammalian species]* bone marrow micronucleus assay (MRID *[number]*), *(number/sex/dose)* were treated *[route]* with *Chemical name (% a.i., batch/lot #)* at doses of 0, x, x, or x mg/kg bw. Bone marrow cells were harvested at *(list hours)* post-treatment. The vehicle was *(state vehicle)*. *(Note the route of exposure and if acute or multiple dosing)*
There were *(no)* signs of toxicity *(list if present)* during the study. *[Note, the signs of cytotoxicity, if present, and the quantitative evidence for a positive micronucleus response, if any]*. Chemical name was *(not)* tested at an adequate dose *(based on)*. The positive control induced the appropriate response.

B. MATERIALS AND METHODS

a. Test compound:										
	Dosing:		once		twice (24 hrs apart)			Other *(describe)*		
	Sampling (after last dose):*[mark all that are appropriate]*,		6 hr		12 hr		24 hr	48 hr		72 hr
	Other *[describe]*:									

b. Negative and/or vehicle control:										
	Dosing:		once		twice (24 hrs apart)			Other *(describe)*		
	Sampling (after last dose):*[mark all that are appropriate]*,		6 hr		12 hr		24 hr	48 hr		72 hr
	Other *[describe]*:									

c. Positive control:											
	Dosing:		once		twice (24 hrs apart)			Other *(describe)*			
	Sampling (after last dose):*[mark all that are appropriate]*,		6 hr		12 hr		24 hr		48 hr		72 hr
	Other *[describe]*:										

d. Tissues and Cells Examined:	
	Bone marrow OR other (identify):
	No. of polychromatic erythrocytes (PCE) examined per animal:
	No. of normochromatic erythrocytes (NCE; more mature RBCs) examined per animal:
	Other (if other cell types examined, describe):

e. Details of slide preparation: *[Describe briefly; were slides coded?]*

f. Evaluation Criteria: *[Describe]*

g. **Statistical methods:** *[list parameters that were analyzed and the statistical methods]*

C. RESULTS & DISCUSSIONS (OBSERVATIONS) *[Report results of analytical determination if performed]*

1. PRELIMINARY TOXICITY ASSAY: *[reported results, e.g., include dose range; signs of toxicity - e.g., MTD considerations; clinical signs; number of animals, rationale for dose selection for micronucleus assay]*

2. MICRONUCLEUS ASSAY: *[reported results, e.g., include in life animal observations, induction of micronuclei; appropriateness of negative, solvent and positive control micronucleus frequencies; ratio of PCE/NCE; sex differences (if any); appropriateness of dose levels and route; statistical evaluation; include representative table, if appropriate]*

D. DISCUSSION AND CONCLUSIONS:

15. SCHEDULED DNA SYNTHESIS IN MAMMALIAN LIVER CELL CULTURES;

A. Executive Summary:

In an unscheduled DNA synthesis, primary rat hepatocyte cultures were exposed to *[Chemical name, (% a.i., batch/lot #), include solvent if appropriate]* at concentrations of 0, x, x, or x □g/mL for *(duration of exposure)*.
Chemical name was tested *[up to cytotoxic or precipitating concentrations, or limit concentration, 5000 □g/mL. (Include other details as appropriate, quantitation if positive e.g. there was a significant increase in number of cells in repair (60% at top concentration vs 1% in controls))]*. The positive controls induced *(did not induce)* the appropriate response.
There was *(no)* evidence *(or a dose related positive response)* that unscheduled DNA synthesis, as determined by radioactive tracer procedures [nuclear silver grain counts] was induced.

B. MATERIALS AND METHODS

1. Cell Preparation:

a. Perfusion Technique:

b. Hepatocyte Harvest/Culture Preparation:

2. TEST PERFORMANCE *[(NOTE: If cells other than hepatocytes are tested, information regarding the S9 activated phase of testing must be included)]*

1. Cytotoxicity Assay: *[if conducted, briefly describe procedure]*

2. UDS Assay:

a. Treatment:

b. Preparation of Autoradiographs/Grain Development:

c. Grain Counting: *[include number of cells scored per dose, derivation of net nuclear grains, whether % cells in repair were scored]*

e. Statistical Analysis: *[list parameters that were analyzed and the statistical methods]*

C. RESULTS AND DISCUSSIONS (OBSERVATIONS): *[Report results of analytical determination if performed]*

1. PRELIMINARY CYTOTOXICITY ASSAY: *[include concentration ranges; reported results, e.g., cytotoxicity and solubility, rationale for dose selection for main study]*

2. UDS assay: *[reported results, e.g., net nuclear grain counts and/or summary; appropriateness of positive controls and background levels (concurrent and/or historical); number of concentration levels evaluated; number of replicates -- 100 cells/group (50 cells/slide); include representative table, if appropriate]*

D. CONCLUSIONS:

16. AVIAN ACUTE ORAL TOXICITY {Chicken, Pigeon, Quail, Duck etc.}

A. Executive Summary:

The acute oral toxicity of {test material} to X-d-old {common name and scientific name} was assessed over ....days. {Test material} was administered to the birds {enter the number of birds per treatment} by {method} at [Indicate doses used} mg ai/kg bw. The ...day-acute oral LD_{50} was ....mg a.i/kg bw. The ...day NOAEL of {test material} to the {species}, based on {endpoint} was ....mg a.i/kg bw. Describe toxicity briefly including mortality, behavioral abnormalities, and other signs of toxicity. If there was no toxicity, state that there was no compound related toxicity effect.

Results Synopsis

LD_{50}: {.....mg a..i./kg bw} 95% C.I.: {.... to ... mg a.i./kg bw} Probit Slope: {.....}

NOAEL:{.....mg a.i./kg bw}

Endpoint(s) Affected: {.....}

B. MATERIALS AND METHODS

1. Test Organism:

Species (common and scientific names): EPA recommends using either northern

Bobwhite [*Colinus virginianus*] or mallard [*Anas platrhynchos*]. Species that can be used in addition to northern bobwhite or mallard but are not preferred as an alternative include: pigeon [*Columba livia*], Japanese quail [*Coturnix coturnix japonica*], ring-necked pheasant [*Phasianus colchicus*], and red-legged partridge [*Alectoris rufa*], may be tested. If species other than the northern bobwhite or mallard are used,it is important that they are responsive to the conditions of the test and do not avoid exposure to the test material through fasting.

Age at study initiation: young adults of both sexes, not yet mated, and at least 16 weeks old at time of dosing.

Weight at study initiation: (mean and range): Birds are typically uniform in size and weight and phenotypically indistinguishable from *wild birds*

Source:

2. STUDY DESIGN:

1. Experimental Conditions

a) Range-finding study: If a range-finding study was conducted, briefly outline the test concentrations and other relevant conditions. Indicate the results from the preliminary study that were used to determine the conditions for the definitive study.

b) Definitive Study

Table X. Experimental Parameters

Parameter	Details	Remarks
Conditions (same as test or not): Feeding: Health (any mortality observed):		
Pen size and construction materials		
Test duration		
Dose preparation (Indicate method of confirmation of dose)		
Dose levels Nominal: Measured:		
Solvent/vehicle, if used Type: Amount/bw:		
Number of birds per groups/treatment Negative control: Solvent/vehicle control: Treated:		
Test conditions Temperature: Relative humidity: Photoperiod:		
Reference chemical, if used Name: Concentrations tested:		

2. Observations:

Table X: Observations

Criteria	Details	Remarks
Parameters measured (mortality/individual body weight at test initiation and termination/ mean feed consumption/ others)		
Indicate if the test material was regurgitated		
Groups on which necropsies were performed		
Observation intervals		
Were raw data included?		

3. Statistics:

List the parameters that were analyzed and the statistical tests that were performed. A copy of the statistical methods from the study may be attached.

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. MORTALITY:

Briefly summarize mortality; indicate if there was a dose-response effect; slope values, if provided. Compare with reference chemical toxicity test endpoints.

Table X: Effect of {Test Material} on Mortality of {Test Organism}

Treatment (mg a.i./kg bw)		No. of Birds	Cumulative Mortality				
			day 1	day 2	day 3	day 4	day n
Solvent/vehicle control							
Test dose 1							
Test dose 2							
Test dose 3							
Test dose n							
NOEL							
LD_{50}							
Reference chemical	Mortality						
	LD_{50}						
	NOAEL						

2. SUBLETHAL TOXICITY ENDPOINTS:

Briefly summarize behavioral abnormalities; other signs of toxicity (body weight loss, food consumption, organ effects, etc.). Indicate effects that were related to the chemical properties of the test material. Compare the sub-lethal effects with that of the reference chemical.

Table X: Sub-lethal Effect of {Test Material} on {Test Organism},

Treatment (mg a.i./kg bw)		Observation						
		body weight			food consumption			other endpoint
		day 0	day x1	day x2	day 0	day x1	day x2	% affected
Negative control								
Test dose 1								
Test dose 2								
Test dose 3								
Test dose n								
NOAEL								
EC_{50}								
Reference chemical	effect							
	NOAEL							
	LD_{50}							

D. CONCLUSIONS:

Indicate the acceptability classification. Provide the major conclusions, e.g., values for LD_{50} (95% confidence interval), probit slope (95% confidence interval), NOAEL, and sub-lethal effects.

17. REPEATED DOSE AVIAN TOXICITY (Dietary)

A. Executive Summary:

The acute dietary toxicity of {test material} to X-d-old {common name and scientific name} was assessed over X days. {Test material} was administered to the birds {enter the number of birds per treatment} in the diet at {indicate concentrations} mg a.i/kg dw of diet. The.... day acute dietary LC_{50} was..... mg a.i/kg diet. The ....day NOAEC of {test material} based on {endpoint} was.....mg a.i/kg diet. Briefly describe toxicity including mortality, behavioral abnormalities, and other signs. Describe any avoidance of treated diet and its relation to the test material. If there was no toxicity, state that there were no compound-related effects.

Results Synopsis

Test Organism Size/Age (mean weight):

LC_{50}: {.....mg a.i./kg diet} 95% C.I.: {.....to ..... mg a.i./kg diet}

Probit slope: {.....}

NOAEC: {..... mg a.i./kg diet} Endpoint(s) Affected { .....}

Sub-lethal effects:

B. MATERIALS AND METHODS

Test organism:

Species (common and scientific names):

EPA/OECD recommends using either northern bobwhite [*Colinus virinianus*] or mallard [*Anas pltyrhynchos*]. Other species which can be used in addition to northern bobwhite or mallard but preferably not as an alternative include: pigeon [*Columba livia*], Japanese quail [*Coturnix coturnix japonica*], ring-necked pheasant [*Phasianus colchicus*], and red-legged partridge [*Alectoris rufa*] may be tested. If species other than the northern bobwhite or mallard are used, it is important that they are responsive to the conditions of the test and do not avoid exposure to the test material through fasting.

Age at study initiation:

EPA recommends 10-14 days old for northern bobwhite and 5 days old for mallards; OECD recommends 10-17 days old

Weight at study initiation: (mean and range)

Source:

1. **STUDY DESIGN:**
   1. **Experimental Conditions**
   a. **Range-finding Study:** If a range-finding study was conducted, briefly outline the test concentrations and other relevant conditions. Indicate the results from the preliminary study that were used to determine the conditions for the definitive study.
   b. Definitive Study

Table X. Experimental Parameters

Parameter	Details	Remarks
Conditions (same as test or not): Feeding: Health (any mortality observed):		
Pen size and construction materials		
Test duration		
Dose preparation (Indicate method of confirmation of dose)		
Dose levels Nominal: Measured:		
Solvent/vehicle, if used Type: Amount/bw:		
Number of birds per groups/treatment Negative control: Solvent/vehicle control: Treated:		
Test conditions Temperature: Relative humidity: Photoperiod:		
Reference chemical, if used Name: Concentrations tested:		

2. Observations:

Table X: Observations

Parameters	Details	Remarks
Parameters measured (mortality/body weight/ mean feed consumption/ others)		
Indicate the stability and homogeneity of test chemical in the diet		
Indicate if the test material was regurgitated		
Treatments on which necropsies were performed		
Observation intervals		
Were raw data included?		

3. Statistics:

List the parameters that were analyzed and the statistical tests that were performed. A copy of the statistical methods from the study may be attached.

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. MORTALITY: Briefly summarize mortality; indicate if there was a dose-response effect; report the slope values, if provided. Provide measured concentration of test material, if determined. Compare with reference chemical toxicity test endpoints.

Table X: Effect of {Test Material} on Mortality of {Test Organism}

Treatment (mg a.i./ kg diet) [indicate if measured or nominal conc. were used]		**No. of birds per treatment**	**Cumulative mortality**				
			day 1	**day 2**	**day 3**	**day 4**	**day n**
Solvent/vehicle control							
Test concentration 1							
Test concentration 2							
Test concentration 3							
Test concentration n							
NOAEC							
LC_{50}							
Reference chemical	mortality						
	LC_{50}						
	NOAEC						

2. SUB-LETHAL TOXICITY ENDPOINTS:

Briefly summarize behavioral abnormalities and other signs of toxicity (body weight loss, decreased food consumption, organ effects, and other relevant findings). Indicate effects that were related to the chemical properties of the test material. Indicate if there was food avoidance and its relation to test material. Compare the sub-lethal effects with that of the reference chemical. If there was no toxicity, state there were no compound-related effects.

Table X: Sub-lethal Effect of {Test Material} on {Test Organism, If Reported

Treatment (mg a.i./kg diet [record measured and nominal conc. used]		**Observation**						
		Body weight		**Food consumption**		**Other endpoint**		
		day 0	**day x1**	**day xn**	**day 0**	**day x1**	**day xn**	**% affected**
Negative control								
Test dose 1								
Test dose 2								
Test dose 3								
Test dose n								
NOAEC								
EC_{50}								
Reference chemical	NOAEC							
	EC_{50}							

D. CONCLUSIONS: Indicate the acceptability classification of the study. Provide the major conclusions, *e.g.*, values for

LC_{50}: _____ mg a.i./kg diet 95% C.I.: _____-_____mg a.i./kg diet

NOAEC: mg a.i./kg diet

Sub-lethal effects:

18. ACUTE TOXICITY TO FISH

A. EXECUTIVE SUMMARY:

In a 96-hr acute toxicity study, {common name and scientific name} were exposed to {test chemical} at {nominal and/or measured} concentrations of {control, solvent control, x_1, x_2, x_3.....x_n mg a.i/L} under static/static renewal/flow-through conditions. The 96-hr LC_{50} was .....mg a.i/L. The NOAEC based on mortality/sub-lethal effects, was .... mg a.i/L (optional). Sublethal effects {list effects} were observed in the groups exposed to {list corresponding concentration(s)} of {test material}. Based on the results of this study, {test material} would be classified as {toxicity classification} to {test species} in accordance with U.S. EPA's classification system.

B. MATERIALS AND METHODS

1. Test organism:

Species

Age at test initiation: {mean and range in days}

Weight at study initiation: {mean and range}

Length at study initiation: {mean and range}

Source:

STUDY DESIGN:

Experimental Conditions

a) Range-finding Study: If a range-finding study was conducted, briefly outline the test concentrations and other relevant conditions. Indicate the results from the preliminary study that were used to determine the conditions for the definitive study.

b) Definitive Study:

Table X . Experimental Parameters

Parameter	Details	Remarks
Acclimation Period: Conditions: (same as test or not) Feeding: Health: (any mortality observed)		
Duration of the test		
Test condition static/static renewal/flow-through Type of dilution system for flow-through method. Renewal rate for static renewal		
Aeration, if any		
Test vessel Material: (glass/stainless steel) Size: Fill volume: Loading:		
Source of dilution water Quality:		
Water parameters Hardness (freshwater) pH Dissolved oxygen Total Organic Carbon Particulate matter Metals Pesticides Chlorine Alkalinity Conductivity COD (when testing cationic compounds) Temperature {Salinity for marine or estuarine species} Intervals of water quality measurement		

Parameter	Details	Remarks
Test concentrations: Nominal (corrected/uncorrected): Measured:		
Solvent (type and concentration if used)		
Number of replicates/group Negative control: Positive control: treatments:		
Number of organisms / replicate/group: Negative control: Positive control: Treatments:		
Biomass loading rate		
Lighting		
Feeding		
Recovery of chemical Level of Quantitation Level of Detection Method recoveries % of nominal		
Stability of chemical in the test system		
Variability of chemical in the test system		
Positive control {if used, indicate the chemical and concentrations}		
Other parameters, if any		

2. Observations:

Table X: Observations

Parameter	Details	Remarks
Parameters measured including the sublethal effects/toxicity symptoms		
Observation intervals		
Were raw data included?		
Other observations, if any		

Statistics:

List the parameters that were analyzed and the statistical tests that were performed. A copy of the statistical methods from the study may be attached.

C. RESULTS and DISCUSSIONS (OBSERVATIONS):

A. MORTALITY:

Briefly summarize mortality; indicate if there was a concentration-response effect; probit slope of concentration-response curve, if it can be calculated.

Table X: Effect of {Test Material} on Mortality of {Test Organism}.

Treatment (mg a.i./L) [record measured and nominal conc. used]	No. of fish at start of study	Observation period							
		24-hr		48-hr		72-hr		96-hr	
		No. Dead	% mortality	No. Dead	% mortality	No. Dead	% mortality	No. Dead	% mortality
Negative control (dilution water only)									
Positive control, if used (indicate carrier concentration)									
Test concentration 1									
Test concentration 2									
Test concentration 3									
Test concentration 4									
Test concentration 5									
Test concentration n									
NOAEC									
LC_{50}									
Probit slope, if applicable									

B. NON-LETHAL TOXICITY ENDPOINTS:

Briefly summarize behavioral abnormalities or other signs of toxicity. Indicate effects that were related to the chemical properties of the test material. Compare the sub-lethal effects with that of the reference chemical.

Table X: Sub-lethal Effect of {Test Material} on {Test Organism}.

Treatment (mg a.i./L) [record measured and nominal concentrations used]	Observation period											
	Endpoint 1 (% affected)				Endpoint 2 (% affected)				Endpoint 3 (% affected)			
	24 h	48 h	72 h	96 h	24 h	48 h	72 h	96 h	24 h	48 h	72 h	96 h
Negative control (dilution water only), if used												
Positive control, if used (indicate carrier concentration) % sub-lethal effect: EC_{50}												
Test concentration 1												
Test concentration 2												
Test concentration 3												
Test concentration n												
NOAEC												

D. CONCLUSIONS:

Provide the major conclusions, e.g., values for LC_{50} and NOAEC.

19. ACUTE HONEYBEES TOXICITY (Oral & Contact)

A. Executive Summary:

In a *[#]*-day *[oral or dietary]* toxicity and pathogenicity study, *[common name (scientific name)]* were exposed to a *[single OR #]* dose of *[dose amount]* of *[formulation, note its potency, biological activity or concentration per unit weight or volume]* (containing % *a.i. name*) by *[indicate exposure method]*. *[Include other pertinent details such as the controls used.*

The *[#]*-day LD50 was *[=, > or <] [insert LC50 in appropriate units]* (95% C.I. *-if applicable*). *[If the study included sublethal test endpoints and/or sublethal effects were observed and/or additional subchronic testing was triggered include the following text (otherwise-delete):* The EC50 based on sublethal effects, were *[insert EC50 in appropriate units.]* The NOEC value, based on mortality *[and sublethal effects]*, was *[=, > or <] [insert NOEC in appropriate units]*.

This study is classified as *[acceptable, unacceptable, and supplemental]*. This study was *[not]* conducted in accordance with the guideline recommendations for a *[oral or dietary]* toxicity and pathogenicity study for honey bees in the *[species]*.

B. MATERIALS AND METHODS:

1. Test Organism:
Species (common and scientific names): *[Indicate the species used.]*
Age at test initiation: *[Give the age of the test organisms.]*
Strain/Source: [Report the strain, supplier and/or source of the test organism.]
Date of collection: *[Insert the date of collection, if applicable.]*
2. STUDY DESIGN AND METHODS:
a. Experimental Methods and Conditions
Acclimation:
Duration:
Feeding:
Water:
Temperature:
Relative humidity:
b. Test chamber - description and size:
c. Route(s) of exposure:[Describe route of exposure and topical application apparatus, if applicable.]
d. Dose levels / test concentrations:
e. Preparation of dose or test concentration:
f. Confirmation of MPCA viability: [Describe methods used to confirm the concentration and/or viability of the MPCA in the dosing suspensions.]
g. Positive control / reference material: *[if used]* **[Insert a description of the reference material, with the number of arthropods treated and frequency of testing (if not concurrent).]**
h. Number of bees per chamber:
i. ***Control(s): Treatment(s):***
j. Number of replicates (chambers) per treatment:

k. **Recovery of MPCA from bees:** *[if applicable]* **[Describe methods used to recover the MPCA from collected samples.]**
l. **Feeding: [Describe the feeding regime used during the experiment.]**
m. **Test Conditions** Temperature: Humidity: Lighting:
n. **Duration of the study:**
o. **Other methods or conditions, if any:**

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. Parameters measured including sub-lethal effects/toxicity symptoms:

[List the parameters measured during the experiment, e.g., mortality, survival, abnormal behavior or appearance, fecundity, growth inhibition, concentration of the MPCA in the test suspensions. Provide references to data summary tables, if used.]

Observation/measurement intervals:

[List time points for each parameter measurement and observation.]

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

TABLE *[#].* Viability of *[test substance]* in the *[dosing suspension/diet]* administered to honey bees (*Apis mellifera*) in a *[contact, acute oral or dietary]* test.

Dose Group	Nominal Concentration *[units]*	Measured Concentration *[units]*
Solvent/vehicle control		
Inactivated		
Sterile filtrate control		
Maximum hazard dose		
Negative control		

3. 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.]

TABLE *[#]*. Effect of *[test material]* on cumulative mortality of honey bees (*Apis mellifera*) in a *[contact, acute oral or dietary]* test.

Treatments *[indicate if nominal or measured (measured should be used, if provided)]*		**No. of Bees**	**Observation Period**					
			Day x1		***Day x2***		***Day n***	
			No. Dead	**% Mortality**	**No. Dead**	**% Mortality**	**No. Dead**	**% Mortality**
Negative control								
Solvent control, if used								
test concentration 1								
test concentration 2								
test concentration3								
test concentration 4								
test concentration n								
LD50/LC50 *[insert [>] if greater than]*								
NOEL/NOEC *[insert [>] if greater than]*								
Reference chemical	*Mortality (% or No.)*							
	LD50: LC50:	*[insert [>] if greater than]*						
	NOEL NOEC	*[insert [>] if greater than]*						

[a Use superscript and footnote to indicate values that are statistically significantly different from control.]

4. SUB-LETHAL TOXICITY EFFECTS:

[Include if any sub-lethal effects are observed- Briefly summarize behavioural abnormalities or other signs of toxicity. Indicate effects that were related to the t*est-material. Compare sub-lethal effects with control treatment and/or the reference chemical. 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 *[#].* Effect of *[test material]* on *[endpoint]* of honey bees (*Apis mellifera*) in a *[contact, acute oral or dietary]* test.

Treatments *[indicate if nominal or measured (measured should be used, if provided)]*		**Observation Period**					
		Day x1		***Day x2***		***Day n***	
		endpoint 1	**% Affected**	***endpoint 2***	**% Affected**	***endpoint n***	**% Affected**
Negative control							
Solvent control, if used							
test concentration 1							
test concentration 2							
test concentration3							
test concentration 4							
test concentration n							
ED50/EC50 or other sublethal endpoint *[insert [>] if greater*							
NOEL/NOEC *[insert [>] if greater*							
Reference chemical	*LC50/ LC50*	*[insert [>] if greater than]*					
	NOEL/ NOEC	*[insert [>] if greater than]*					

D. CONCLUSIONS

Values for LD50, LC50, LT50, EC50, NOEL, NOEC, Probit slope, Endpoint(s) Affected: etc. were [=, > or <] insert final dose concentration/level (in appropriate units).]

20. ACUTE TOXICITY TO EARTHWORM

A. Executive Summary:

In a..... day acute toxicity study, earthworms {species} were exposed to {test chemical} at {0, x1, x2, x3,...x_n mg a.i./kg dry weight of soil/artificial substrate}. The reference chemical used was..... (name) at x mg a.i/kg d w of the soil/substrate. The ..... day LC_{50} was..... mg a.i/kg dw of soil/substrate. The..... day EC_{50} was ..... mg a.i/kg dw of soil/substrate. The..... day NOAEC, based on [indicate parameter used] was x mg a.i./kg d.w. of soil/substrate. The LOAEC, based on [indicate parameter used] was x mg a.i./kg d.w. of soil/substrate. The {a.i.} is considered to be {non-toxic/toxic} to earthworms up to/above a concentration of {X} mg a.i./kg d.w of soil/substrate.

Briefly describe the mortality and other toxic effects that were observed. If toxicity or abnormalities were not observed, state that there were no compound related toxicity effects.

Results Synopsis

Test Organism Size/Age (mean weight or length):

Test Type (Flow-through, Static, Static Renewal):

LC_{50}: {.....mg a..i./kg dw soil} 95% C.I.: {.... to ... mg a.i./kg dw soil}

NOAEL: {.....mg a.i./kg dw soil}

Probit Slope: {.....} 95% C.I.: {.... to ... }

EC_{50}: {.....mg a.i./kg dw soil} 95% C.I.: {.... to ... mg a.i./kg dw soil}

Endpoint(s) Affected: {.....}

B. MATERIALS AND METHODS

1. Test organism:

Species: {common and scientific names} :OECD recommend *Eisenia fetida andrei* (Bouche). The earthworms should weigh 300-600 mg at the beginning of the test.

Age at test initiation: (mean and range)

Weight at study initiation: (mean and range)

Source:

2. STUDY DESIGN:

1. Experimental Conditions

a. Range-finding Study: If a range-finding study was conducted, briefly outline the test concentrations and other relevant conditions. Indicate the results from the preliminary study that were used to determine the conditions for the definitive study.

b. Definitive Study

1. Soil: Indicate if an artificial or natural soil was used. If an artificial soil is used, provide the composition, pH and moisture content. If a natural soil was used, complete the following table.

Table X: Physicochemical Properties of Natural Soil

Property	**Value**	**Remarks**
For natural soil: Texture: % sand % silt % clay Textural classification: For artificial substrate (provide composition):		
pH (__:__ soil:water)		
Organic carbon (%)		
Moisture (%)		

Table X . Experimental Design

Parameter	Value	Remarks
Acclimation: Duration: Conditions (state if same as the test conditions): Health:		
Soil [fresh or stored]		
Test Container Material Size Amount of soil/substrate		
No. of replicates: Per treatment group: Per control:		
No. of earthworms per treatment		
Solvents used or not (if yes report the name and concentration)		
Rates of application: Nominal: Measured:		

Parameter	Value	Remarks
Reference chemical (if used) name: Concentration:		
Test conditions: Temperature Lighting conditions Moisture		
Duration of the study		

2. Observations:

Table X: Observations

Parameters	**Details**	**Remarks**
Observation intervals		
Parameters measured including the sublethal effects/toxicity symptoms		
Were raw data included?		
Other observations, if any		

3. **Statistics:** List the parameters that were analyzed and the statistical tests that were performed. A copy of the statistical methods from the study may be attached.

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. MORTALITY: Briefly summarize mortality; dose response relationship and slope of dose-response curve, if provided; compare with reference toxicity end points.

Table X: Effect of {Test Material} on Mortality of {Species}

Treatment (mg a.i./kg soil) [record measured and nominal conc. used]	Observation period					
	Day x		Day x		Day x	
	No Dead	% mortality	No Dead	% mortality	No Dead	% mortality
Control						
Test concentration 1						
Test concentration 2						
Test concentration 3						
Test concentration n						
NOAEC						
LOAEC						
LC_{50}						
Reference chemical (% mortality; LC_{50})						

2. SUB-LETHAL TOXICITY ENDPOINTS:

Briefly summarize signs of sub-lethal toxicity. Indicate any results related to the chemical properties of the test material.

Table X: Sub-lethal Effect of {Test Material} on {Species}. [Indicate if average weight used]

Treatment (mg a.i./kg soil) [indicate if measured or nominal conc. used]	Observation period					
	Day x		Day x		Day x	
	weight	% loss	weight	% loss	weight	% loss
Control						
Test concentration 1						
Test concentration 2						
Test concentration 3						
Test concentration n						
NOAEC						
LOAEC						
EC_{50}						
Reference chemical (% mortality; LC_{50})						

D. CONCLUSIONS: Provide the major conclusions, e.g., values for EC_{50}, LC_{50}. NOAEC, and LOAEC.

TOXICOLOGY SCRTINY TEMPLATE

[9(3)FIM, FI, & Ethephon)]

1. GENERAL INFORMATIONS:

1.	Application Details (Category etc.)		
2.	Test Substance/Chemical Details (Common Name, IUPAC Name, CAS N. Batch N.)		
3.	Assay Purity/Active Ingredient Content %		
4.	Type of Pesticides (Insecticide/ Fungicide/ Herbicide etc.)		
5.	Decoding Certificates details		
6.	Product Schedule Inclusion Details		
7.	Source of Technical Material In case of TI-New source: information on registered source and its chemical composition. (Including RC decision or CR etc.)		
8.	In case of formulation, status of technical registration (including RC decision or CR)		
9.	Source of manufacturer and supplier		

2. RTT PERMIT

RTT PERMIT DETAILS						
Permit Number	Name of The Insecticide/Chemical	Quantity Approved	Name of The Importer	Name of The Manufacturer	Source of Procurement	Purpose of Import

3. LABEL AND LEAFLET

LABEL AND LEAFLET							
Chemical Composition	Precautions	Symptoms of Poisoning	Cautionary Statement	First Aid	Antidote	Toxicity Triangle	Pictogram Details

4. TEST SUBSTANCE & FORMULATION

1.	Physicochemical property		
2.	Adjuvants details		
3.	Compatibility		

1. STUDY DETAILS (Applicable for acute and Ecotox Studies)

S. No.	Parameters							
1.	Study Report No. & Type							
2.	Sponsor (Name and Address)							
3.	Test Facility (Name and Address)							
4.	Test Guideline (OECD/EPA etc.)							
5.	Study Initiation Date							
6.	Study Completion Date							
7.	CoA Attached (Yes/No)							
8.	IAEC No.							
9.	NGCMA GLP Certificate (Validity up to)							

2. STUDY DESIGN/METHODOLOGY (Applicable for Acute and Ecotox Studies)

S. No.	Parameters						
1.	Species/Strain						
2.	No. and sex of animals per dose						
3.	Age and Body weight range at dosing						
4.	Doses/concentrations						
5.	Vehicle & positive control						
6.	Route of administration						
7.	Fasting Details (Duration) pre-dose						
8.	Housing conditions (Temperature, Relative Humidity, Light cycle)						
9.	Diet and water report (source)						
10.	Feed analysis certificate						
11.	Acclimatization period and grouping						
12.	Dosing Schedule/ Single or repeated						
13.	Rationale for dose selection						
14.	Homogeneity/ Stability Analysis/ Concentration Analysis						
15.	Any deviation from protocol or amendments						

1. ACUTE ORAL TOXICITY RAT

Executive Summary:

In an acute oral toxicity study groups (#/sex) of strain, species (source), (age, weight) were given a single oral dose of (formulation/technical, note a.i. and %) in (vehicle or undiluted test article) at doses of??? or??mg/kg bw. Animals were then observed for (#) days.

Study Endpoints:

Oral LD_{50} = mg/kg bw

Toxicity based on the LD_{50} in males or females whichever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV.

Dose (mg/kg b.w)	Mortality/Number Tested Males/ Females	Morbidity/Number Tested Males/ Females	Survived/ Number Tested Males/ Females

Statistics/If any: The oral LD_{50} was calculated using the

Observations:

Morality: as noted in table.
Clinical observations including signs & symptoms:
Gross Necropsy/ pathological findings:
Weight changes:

Conclusions:

2. ACUTE DERMAL TOXICITY RAT

Executive Summary:

In an acute dermal toxicity study, groups (#/sex) of strain, species (source), (age, weight) were dermally exposed to (formulation/technical, note a.i. and %) in (vehicle or undiluted test article) to (% or amount of body surface area) at doses of, or mg/kg bw. Test sites were covered with a(n) occlusive/semi-occlusive dressing for (#) hours. Animals were then observed for (#) days.

Study Endpoints:

Dermal LD_{50} = mg/kg bw
Toxicity based on the LD_{50} in males or females whichever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV.

Dose (mg/kg b.w)	Mortality/Number Tested Males/ Females	Morbidity/Number Tested Males/ Females	Survived/ Number Tested Males/ Females

Statistics/If any: The Dermal LD_{50} was calculated using the
Observations:

A. **Morality:** as noted in table.
B. **Clinical observations including signs & symptoms:**
C. **Gross Necropsy/ pathological findings:**
D. **Weight changes:**

Conclusions:

3. ACUTE INHALATIONAL TOXICITY RAT

Executive Summary:

In an acute inhalation toxicity study, groups (#/sex) of strain, species (source), (age, weight) were exposed (nose only, head only or whole body) via the inhalation route to (formulation/technical, note a.i. and %) in (name of vehicle or undiluted test article) for [#] hours at concentrations of mg/L. Animals were then observed for [#] days.

Study Endpoints:

LC_{50} = mg/L

Toxicity: based on (males or females whichever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV.

Nominal Conc. (mg/L)	Actual Conc. (Gravimetric/ Analytical) (mg/L)	MMAD	GSD	Mortality/Number Tested	Morbidity/Number Tested	Survived/ Number Tested
				Males/ Females	Males/ Females	Males/ Females

TEST ATMOSPHERE /CHAMBER DESCRIPTION:

Chamber Volume:	
Airflow:	
Temperature:	
Relative Humidity:	
Time to Equilibrium:	

Test the atmosphere concentration:
Particle size determination:
Statistics/if any: The LC_{50} was calculated using the
Observations:

A. **Morality:** as noted in table.
B. **Clinical observations including signs & symptoms:**
C. **Gross Necropsy/ pathological findings:**
D. **Weight changes:**

Conclusions:

4. ACUTE EYE IRRITATION RABBIT

Executive Summary:

In an acute eye irritation study, (volume or weight of test material applied) of (formulation/technical, note a.i. and %) in (name of vehicle if appropriate, or undiluted test material) was instilled into the conjunctival sac of (which eye) of (#/sex), (strain), (species - rabbits) (source, age, weight) for [#] hours. (Note if eyes were washed) Animals were then observed for *[#]* days. Irritation was scored by the method as per guideline.
In this study, formulation/technical is not an eye irritant OR is minimally, mildly, moderately, severely, or extremely irritating to the eye based on GHS/EPA Toxicity Category I, II, III, IV.

	Number "positive"/number tested							
	Hours				**Days**			
Observations	1	**24**	**48**	**72**	**4**	**7**	**14**	**21**
Corneal Opacity								
Iritis								
Redness								
Chemosis								
Discharge								
Conjunctivae:								

Clinical observations including ocular signs & symptoms/ reactions:
Conclusion:

5. ACUTE DERMAL IRRITATION/PRIMARY SKIN IRRITATION RABBIT

Executive Summary:

In a primary skin irritation study, (#/sex) strain, species (source), (age, weight) were dermally exposed to (volume or weight of test material applied) of (formulation/technical, note a.i. and %) in (name of vehicle or undiluted test material) to (% or amount of body surface area - state location of test site). Test sites were covered with a(n) occlusive/semi-occlusive dressing for (#) hours. Animals were then observed for [#] days. Irritation was scored by the method of (cite method).

In this study, formulation/technical is not a dermal irritating OR is corrosive to the skin based on. GHS/EPA Toxicity Category I, II, III, IV.

	Number "positive"/number tested			
	Hours			
Observations	1	**24**	**48**	**72**
Erythema and Eschar Formation				
Oedema				

Observations:

Results:

Conclusions:

6. SKIN SENSITIZATION GUINEA PIG/LLNA

Executive Summary:

In a dermal sensitization study with (formulation/technical, note a.i. and %) in (name of vehicle if appropriate or undiluted test article), strain, species (source)(age, weight) were tested using the method of (cite study type). Identify positive control material. List clinical signs (systemic and local for LLNA) and mortality. Necropsy results for LLNA **if significant**.

Results and discussion:

A. Reactions and duration:

B. Positive control:

C. Conclusions:

OBSERVATIONS FOR MAXIMIZATION TEST (GPMT) AND BUEHLER TEST:

a. **Justification for positive control other than mentioned in guideline:**

b. **Dose Range Finding Study (DRFS) result:**

c. **Treatment and control skin reaction observation**

Group		Skin reaction observation (dermal scoring)		
		21 hours of patch removal	Approx. 48 hours post challenge application	Approx. 72 hours post challenge application
Treatment group	Male			
Naïve control				
Treatment group	Female			
Naïve control				

0 = no visible change 1 = discrete or patchy erythema 2 = moderate and confluent erythema 3 = intense erythema and swelling

d. **Result of positive control for reliability check:**

e. **Clinical observations if any,**

histopathological examination	
skin fold thickness	

Observations for Local Lymph Node Assay (LLNA) Test:

Observations	Results
Dose Range Finding Study (DRFS) result:	
Clinical Observations	
Body weights changes	
Ear erythema measurements	
Ear thickness measurements	
Statistical tool used	
DPM of positive control (mean and associated error term)	
Stimulation index of positive control (concurrent/ historical)	
DPM of treatment group (mean and associated error term)	
Stimulation index of treatment group	
DPM of vehicle control group (mean and associated error term)	
Stimulation index of Vehicle control group (if any)	

DPM: Disintegration Per Minute

7. ACUTE AVIAN ORAL TOXICITY {Chicken, Pigeon, Quail, Duck etc.}

A. Executive Summary:

The acute oral toxicity of {test material} to X-d-old {common name and scientific name} was assessed over ....days. {Test material} was administered to the birds {enter the number of birds per treatment} by {method} at [Indicate doses used} mg ai/kg bw. The ...day-acute oral LD_{50} was ....mg a.i/kg bw. The ...day NOAEL of {test material} to the {species}, based on {endpoint} was ....mg a.i/kg bw. Describe toxicity briefly including mortality, behavioral abnormalities, and other signs of toxicity. If there was no toxicity, state that there was no compound related toxicity effect.

Results Synopsis

LD_{50}: {.....mg a..i./kg bw} 95% C.I.: {.... to ... mg a.i./kg bw} Probit Slope: {.....}

NOAEL: {.....mg a.i./kg bw}

Endpoint(s) Affected: {.....}

B. MATERIALS AND METHODS

1. Test Organism:

Species (common and scientific names): EPA recommends using either northern

Bobwhite [*Colinus virginianus*] or mallard [*Anas platrhynchos*]. Species that can be used in addition to northern bobwhite or mallard but are not preferred as an alternative include: pigeon [*Columba livia*], Japanese quail [*Coturnix coturnix japonica*], ring-necked pheasant [*Phasianus colchicus*], and red-legged partridge [*Alectoris rufa*], may be tested. If species other than the northern bobwhite or mallard are used,it is important that they are responsive to the conditions of the test and do not avoid exposure to the test material through fasting.

Age at study initiation: young adults of both sexes, not yet mated, and at least 16 weeks old at time of dosing.

Weight at study initiation: (mean and range): Birds are typically uniform in size and weight and phenotypically indistinguishable from *wild birds*

Source:

2. STUDY DESIGN:

1. Experimental Conditions

a) Range-finding study: If a range-finding study was conducted, briefly outline the test concentrations and other relevant conditions. Indicate the results from the preliminary study that were used to determine the conditions for the definitive study.

b) Definitive Study

Table X. Experimental Parameters

Parameter	Details	Remarks
Conditions (same as test or not): Feeding: Health (any mortality observed):		
Pen size and construction materials		
Test duration		
Dose preparation (Indicate method of confirmation of dose)		
Dose levels Nominal: Measured:		
Solvent/vehicle, if used Type: Amount/bw:		
Number of birds per groups/treatment Negative control: Solvent/vehicle control: Treated:		
Test conditions Temperature: Relative humidity: Photoperiod:		
Reference chemical, if used Name: Concentrations tested:		

2. Observations:

Table X: Observations

Criteria	Details	Remarks
Parameters measured (mortality/individual body weight at test initiation and termination/ mean feed consumption/ others)		
Indicate if the test material was regurgitated		
Groups on which necropsies were performed		
Observation intervals		
Were raw data included?		

3. Statistics:

List the parameters that were analyzed and the statistical tests that were performed. A copy of the statistical methods from the study may be attached.

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. MORTALITY:

Briefly summarize mortality; indicate if there was a dose-response effect; slope values, if provided. Compare with reference chemical toxicity test endpoints.

Table X: Effect of {Test Material} on Mortality of {Test Organism}

Treatment (mg a.i./kg bw)		No. of Birds	Cumulative Mortality				
			day 1	day 2	day 3	day 4	day n
Solvent/vehicle control							
Test dose 1							
Test dose 2							
Test dose 3							
Test dose n							
NOEL							
LD_{50}							
Reference chemical	Mortality						
	LD_{50}						
	NOAEL						

2. SUBLETHAL TOXICITY ENDPOINTS:

Briefly summarize behavioral abnormalities; other signs of toxicity (body weight loss, food consumption, organ effects, etc.). Indicate effects that were related to the chemical properties of the test material. Compare the sub-lethal effects with that of the reference chemical.

Table X: Sub-lethal Effect of {Test Material} on {Test Organism},

Treatment (mg a.i./kg bw)		**Observation**						
		body weight			**food consumption**			**other endpoint**
		day 0	**day x1**	**day x2**	**day 0**	**day x1**	**day x2**	**% affected**
Negative control								
Test dose 1								
Test dose 2								
Test dose 3								
Test dose n								
NOAEL								
EC_{50}								
Reference chemical	effect							
	NOAEL							
	LD_{50}							

D. CONCLUSIONS:

Indicate the acceptability classification. Provide the major conclusions, e.g., values for LD_{50} (95% confidence interval), probit slope (95% confidence interval), NOAEL, and sub-lethal effects.

8. ACUTE TOXICITY TO FISH

A. EXECUTIVE SUMMARY:

In a 96-hr acute toxicity study, {common name and scientific name} were exposed to {test chemical} at {nominal and/or measured} concentrations of {control, solvent control, x_1, x_2, x_3.....x_n mg a.i/L} under static/static renewal/flow-through conditions. The 96-hr LC_{50} was .....mg a.i/L. The NOAEC based on mortality/sub-lethal effects, was .... mg a.i/L (optional). Sublethal effects {list effects} were observed in the groups exposed to {list corresponding concentration(s)} of {test material}. Based on the results of this study, {test material} would be classified as {toxicity classification} to {test species} in accordance with U.S. EPA's classification system.

B. MATERIALS AND METHODS

1. Test organism:

Species

Age at test initiation: {mean and range in days}

Weight at study initiation: {mean and range}

Length at study initiation: {mean and range}

Source:

STUDY DESIGN:

Experimental Conditions

a) Range-finding Study: If a range-finding study was conducted, briefly outline the test concentrations and other relevant conditions. Indicate the results from the preliminary study that were used to determine the conditions for the definitive study.

b) Definitive Study:

Table X. Experimental Parameters

Parameter	Details	Remarks
Acclimation Period: Conditions: (same as test or not) Feeding: Health: (any mortality observed)		
Duration of the test		
Test condition static/static renewal/flow-through Type of dilution system for flow-through method. Renewal rate for static renewal		
Aeration, if any		
Test vessel Material: (glass/stainless steel) Size: Fill volume: Loading:		
Source of dilution water Quality:		
Water parameters Hardness (freshwater) pH Dissolved oxygen Total Organic Carbon Particulate matter Metals Pesticides Chlorine Alkalinity Conductivity COD (when testing cationic compounds) Temperature {Salinity for marine or estuarine species} Intervals of water quality measurement		

Parameter	Details	Remarks
Test concentrations: Nominal (corrected/uncorrected): Measured:		
Solvent (type and concentration if used)		
Number of replicates/group Negative control: Positive control: treatments:		
Number of organisms / replicate/group: Negative control: Positive control: Treatments:		
Biomass loading rate		
Lighting		
Feeding		
Recovery of chemical Level of Quantitation Level of Detection Method recoveries % of nominal		
Stability of chemical in the test system		
Variability of chemical in the test system		
Positive control {if used, indicate the chemical and concentrations}		
Other parameters, if any		

2. Observations:

Table X: Observations

Parameter	Details	Remarks
Parameters measured including the sub-lethal effects/toxicity symptoms		
Observation intervals		
Were raw data included?		

Other observations, if any		

Statistics:

List the parameters that were analyzed and the statistical tests that were performed. A copy of the statistical methods from the study may be attached.

C. RESULTS and DISCUSSIONS (OBSERVATIONS):

A. MORTALITY:

Briefly summarize mortality; indicate if there was a concentration-response effect; probit slope of concentration-response curve, if it can be calculated.

Table X: Effect of {Test Material} on Mortality of {Test Organism}.

Treatment (mg a.i./L) [record measured and nominal conc. used]	No. of fish at start of study	Observation period							
		24-hr		48-hr		72-hr		96-hr	
		No. Dead	% mortality	No. Dead	% mortality	No. Dead	% mortality	No. Dead	% mortality
Negative control (dilution water only)									
Positive control, if used (indicate carrier concentration)									
Test concentration 1									
Test concentration 2									
Test concentration 3									
Test concentration 4									
Test concentration 5									
Test concentration n									
NOAEC									
LC_{50}									
Probit slope, if applicable									

B. NON-LETHAL TOXICITY ENDPOINTS:

Briefly summarize behavioral abnormalities or other signs of toxicity. Indicate effects that were related to the chemical properties of the test material. Compare the sub-lethal effects with that of the reference chemical.

Table X: Sub-lethal Effect of {Test Material} on {Test Organism}.

Treatment (mg a.i./L) [record measured and nominal concentrations used]	Observation period											
	Endpoint 1 (% affected)				Endpoint 2 (% affected)				Endpoint 3 (% affected)			
	24 h	48 h	72 h	96 h	24 h	48 h	72 h	96 h	24 h	48 h	72 h	96 h
Negative control (dilution water only), if used												
Positive control, if used (indicate carrier concentration) % sub-lethal effect: EC_{50}												
Test concentration 1												
Test concentration 2												
Test concentration 3												
Test concentration n												
NOAEC												

D. CONCLUSIONS:

Provide the major conclusions, e.g., values for LC_{50} and NOAEC.

9. ACUTE HONEYBEES TOXICITY (Oral & Contact)

A. Executive Summary:

In a *[#]*-day *[oral or dietary]* toxicity and pathogenicity study, *[common name (scientific name)]* were exposed to a *[single OR #]* dose of *[dose amount]* of *[formulation, note its potency, biological activity or concentration per unit weight or volume]* (containing % *a.i. name*) by *[indicate exposure method]*. *[Include other pertinent details such as the controls used.*

The *[#]*-day LD50 was *[=, > or <] [insert LC50 in appropriate units]* (95% C.I. *-if applicable*). *[If the study included sublethal test endpoints and/or sublethal effects were observed and/or additional subchronic testing was triggered include the following text (otherwise-delete):* The EC50 based on sublethal effects, were *[insert EC50 in appropriate units.]* The NOEC value, based on mortality *[and sublethal effects]*, was *[=, > or <] [insert NOEC in appropriate units]*.

This study is classified as *[acceptable, unacceptable, and supplemental]*. This study was *[not]* conducted in accordance with the guideline recommendations for a *[oral or dietary]* toxicity and pathogenicity study for honey bees in the *[species]*.

B. MATERIALS AND METHODS:

1. Test Organism:

Species (common and scientific names): *[Indicate the species used.]*

Age at test initiation: *[Give the age of the test organisms.]*

Strain/Source: [Report the strain, supplier and/or source of the test organism.]

Date of collection: *[Insert the date of collection, if applicable.]*

2. STUDY DESIGN AND METHODS:

a. Experimental Methods and Conditions

Acclimation:

Duration:

Feeding:

Water:

Temperature:

Relative humidity:

b. Test chamber - description and size:

c. Route(s) of exposure:[Describe route of exposure and topical application apparatus, if applicable.]

d. Dose levels / test concentrations:

e. Preparation of dose or test concentration:

f. Confirmation of MPCA viability: [Describe methods used to confirm the concentration and/or viability of the MPCA in the dosing suspensions.]

g. Positive control / reference material: *[if used]* **[Insert a description of the reference material, with the number of arthropods treated and frequency of testing (if not concurrent).]**

h. Number of bees per chamber:

i. ***Control(s): Treatment(s):***

j. Number of replicates (chambers) per treatment:

k. Recovery of MPCA from bees: *[if applicable]* **[Describe methods used to recover the MPCA from collected samples.]**

l. **Feeding: [Describe the feeding regime used during the experiment.]**
m. **Test Conditions** Temperature: Humidity: Lighting:
n. **Duration of the study:**
o. **Other methods or conditions, if any:**

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. Parameters measured including sub-lethal effects/toxicity symptoms:

[List the parameters measured during the experiment, e.g., mortality, survival, abnormal behaviour or appearance, fecundity, growth inhibition, concentration of the MPCA in the test suspensions. Provide references to data summary tables, if used.]

Observation/measurement intervals:

[List time points for each parameter measurement and observation.]

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

TABLE *[#].* Viability of *[test substance]* in the *[dosing suspension/diet]* administered to honey bees (*Apis mellifera*) in a *[contact, acute oral or dietary]* test.

Dose Group	**Nominal Concentration *[units]***	**Measured Concentration *[units]***
Solvent/vehicle control		
Inactivated		
Sterile filtrate control		
Maximum hazard dose		
Negative control		

3. 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.]

TABLE *[#]*. Effect of *[test material]* on cumulative mortality of honey bees (*Apis mellifera*) in a *[contact, acute oral or dietary]* test.

Treatments *[indicate if nominal or measured (measured should be used, if provided)]*		**No. of Bees**	**Observation Period**					
			Day x1		***Day x2***		***Day n***	
			No. Dead	**% Mortality**	**No. Dead**	**% Mortality**	**No. Dead**	**% Mortality**
Negative control								
Solvent control, if used								
test concentration 1								
test concentration 2								
test concentration3								
test concentration 4								
test concentration n								
LD50/LC50 *[insert [>] if greater than]*								
NOEL/NOEC *[insert [>] if greater than]*								
Reference chemical	*Mortality (% or No.)*							
	LD50: LC50:	*[insert [>] if greater than]*						
	NOEL NOEC	*[insert [>] if greater than]*						

[a Use superscript and footnote to indicate values that are statistically significantly different from control.]

4. SUB-LETHAL TOXICITY EFFECTS:

[Include if any sub-lethal effects are observed- Briefly summarize behavioural abnormalities or other signs of toxicity. Indicate effects that were related to the t*est-material. Compare sub-lethal effects with control treatment and/or the reference chemical. 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 *[#]*. Effect of *[test material]* on *[endpoint]* of honey bees (*Apis mellifera*) in a *[contact, acute oral or dietary]* test.

Treatments *[indicate if nominal or measured (measured should be used, if provided)]*	**Observation Period**					
	Day x1		***Day x2***		***Day n***	
	endpoint 1	**% Affected**	***endpoint 2***	**% Affected**	***endpoint n***	**% Affected**
Negative control						
Solvent control, if used						
test concentration 1						
test concentration 2						
test concentration3						
test concentration 4						
test concentration n						
ED50/EC50 or other sublethal endpoint *[insert [>] if greater*						
NOEL/NOEC *[insert [>] if greater*						
Reference chemical	*LC50/ LC50*	*[insert [>] if greater than]*				
	NOEL/ NOEC	*[insert [>] if greater than]*				

D. CONCLUSIONS

Values for LD50, LC50, LT50, EC50, NOEL, NOEC, Probit slope, Endpoint(s) Affected: etc. were [=, > or <] insert final dose concentration/level (in appropriate units).]

10. ACUTE TOXICITY TO EARTHWORMS

A. Executive Summary:

In a..... day acute toxicity study, earthworms {species} were exposed to {test chemical} at {0, x1, x2, x3,...x_n mg a.i./kg dry weight of soil/artificial substrate}. The reference chemical used was..... (name) at x mg a.i/kg d w of the soil/substrate. The ..... day LC_{50} was..... mg a.i/kg dw of soil/substrate. The..... day EC_{50} was ..... mg a.i/kg dw of soil/substrate. The..... day NOAEC, based on [indicate parameter used] was x mg a.i./kg d.w. of soil/substrate. The LOAEC, based on [indicate parameter used] was x mg a.i./kg d.w. of soil/substrate. The {a.i.} is considered to be {non-toxic/toxic} to earthworms up to/above a concentration of {X} mg a.i./kg d.w of soil/substrate.

Briefly describe the mortality and other toxic effects that were observed. If toxicity or abnormalities were not observed, state that there were no compound related toxicity effects.

Results Synopsis

Test Organism Size/Age (mean weight or length):

Test Type (Flow-through, Static, Static Renewal):

LC_{50}: {.....mg a..i./kg dw soil} 95% C.I.: {.... to ... mg a.i./kg dw soil}

NOAEL: {.....mg a.i./kg dw soil}

Probit Slope: {.....} 95% C.I.: {.... to ... }

EC_{50}: {.....mg a.i./kg dw soil} 95% C.I.: {.... to ... mg a.i./kg dw soil}

Endpoint(s) Affected: {.....}

B. MATERIALS AND METHODS

1. Test organism:
Species: {common and scientific names} :OECD recommend *Eisenia fetida andrei* (Bouche). The earthworms should weigh 300-600 mg at the beginning of the test.
Age at test initiation: (mean and range)
Weight at study initiation: (mean and range)
Source:
2. STUDY DESIGN:
1. Experimental Conditions
a. Range-finding Study: If a range-finding study was conducted, briefly outline the test concentrations and other relevant conditions. Indicate the results from the preliminary study that were used to determine the conditions for the definitive study.
b. Definitive Study
1. Soil: Indicate if an artificial or natural soil was used. If an artificial soil is used, provide the composition, pH and moisture content. If a natural soil was used, complete the following table.

Table X: Physicochemical Properties of Natural Soil

Property	**Value**	**Remarks**
For natural soil: Texture: % sand % silt % clay Textural classification: For artificial substrate (provide composition):		
pH (__:__ soil:water)		
Organic carbon (%)		
Moisture (%)		

Table X . Experimental Design

Parameter	Value	Remarks
Acclimation: Duration: Conditions (state if same as the test conditions): Health:		
Soil [fresh or stored]		
Test Container Material Size Amount of soil/substrate		
No. of replicates: Per treatment group: Per control:		
No. of earthworms per treatment		
Solvents used or not (if yes report the name and concentration)		
Rates of application: Nominal: Measured:		
Reference chemical (if used) name: Concentration:		

Parameter	Value	Remarks
Test conditions: Temperature Lighting conditions Moisture		
Duration of the study		

2. Observations:

Table X: Observations

Parameters	**Details**	**Remarks**
Observation intervals		
Parameters measured including the sublethal effects/toxicity symptoms		
Were raw data included?		
Other observations, if any		

3. **Statistics:** List the parameters that were analyzed and the statistical tests that were performed. A copy of the statistical methods from the study may be attached.

C. RESULTS AND DISCUSSIONS (OBSERVATIONS):

1. MORTALITY: Briefly summarize mortality; dose response relationship and slope of dose-response curve, if provided; compare with reference toxicity end points.

Table X: Effect of {Test Material} on Mortality of {Species}

Treatment (mg a.i./kg soil) [record measured and nominal conc. used]	Observation period					
	Day x		Day x		Day x	
	No Dead	% mortality	No Dead	% mortality	No Dead	% mortality
Control						
Test concentration 1						
Test concentration 2						
Test concentration 3						
Test concentration n						
NOAEC						
LOAEC						
LC_{50}						
Reference chemical (% mortality; LC_{50})						

2. SUB-LETHAL TOXICITY ENDPOINTS:

Briefly summarize signs of sub-lethal toxicity. Indicate any results related to the chemical properties of the test material.

Table X: Sub-lethal Effect of {Test Material} on {Species}. [Indicate if average weight used]

Treatment (mg a.i./kg soil) [indicate if measured or nominal conc. used]	Observation period					
	Day x		Day x		Day x	
	weight	% loss	weight	% loss	weight	% loss
Control						
Test concentration 1						
Test concentration 2						
Test concentration 3						
Test concentration n						
NOAEC						
LOAEC						
EC_{50}						
Reference chemical (% mortality; LC_{50})						

D. CONCLUSIONS: Provide the major conclusions, e.g., values for EC_{50}, LC_{50}. NOAEC, and LOAEC.

TOXICOLOGY SCRTINY TEMPLATE

[9(3)TIM-Register Product)]

1. GENERAL INFORMATIONS:

1.	Application Details (category etc.)		
2.	Test Substance/Chemical Details (Common Name, IUPAC Name, CAS N. Batch N.)		
3.	Assay Purity/Active ingredient Content %		
4.	Type of Pesticides (Insecticide/ Fungicide/ Herbicide etc.)		
5.	Decoding Certificates details		
6.	Product Schedule Inclusion Details		
7.	Source of Technical Material [Information on registered source and its chemical composition. (Including RC decision or CR etc.)]		
8.	Source of manufacturer and supplier		

2. RTT PERMIT (If applicable)

RTT PERMIT DETAILS						
Permit Number	Name of The Insecticide/Chemical	Quantity Approved	Name of The Importer	Name of The Manufacturer	Source of Procurement	Purpose of Import

3. LABEL & LEAFLET

LABEL AND LEAFLET							
Chemical Composition	Precautions	Symptoms of Poisoning	Cautionary Statement	First Aid	Antidote	Toxicity Triangle	Pictogram Details

4. TEST SUBSTANCE & FORMULATION

1.	Physicochemical property		
2.	Adjuvants details		
3.	Compatibility		

1. STUDY DETAILS (Applicable for all studies)

S. No.	Parameters							
1.	Study Report No. & Type							
2.	Sponsor (Name and Address)							
3.	Test Facility (Name and Address)							
4.	Test Guideline (OECD/EPA etc.)							
5.	Study Initiation Date							
6.	Study Completion Date							
7.	CoA Attached (Yes/No)							
8.	IAEC No.							
9.	NGCMA GLP Certificate (Validity up to)							

2. **STUDY DESIGN/METHODOLOGY (Applicable for all studies)**

S. No.	Parameters						
1.	Species/Strain						
2.	No. and sex of animals per dose						
3.	Age and Body weight range at dosing						
4.	Doses/concentrations						
5.	Vehicle & positive control						
6.	Route of administration						
7.	Fasting Details (Duration)						
8.	Housing conditions (Temperature, Relative Humidity, Light cycle)						
9.	Diet and water report (source)						
10.	Feed analysis certificate						
11.	Acclimatization period and grouping						
12.	Dosing Schedule/ Single or repeated,						
13.	Rationale for dose selection						
14.	Homogeneity Analysis: *[range]*						

	Stability Analysis: *[range of values]* **Concentration Analysis:** *[range of values], if applicable*						
15.	**Any deviation from protocol or amendments**						

1. ACUTE ORAL TOXICITY RAT

Executive Summary:

In an acute oral toxicity study groups (#/sex) of strain, species (source), (age, weight) were given a single oral dose of (formulation/technical, note a.i. and %) in (vehicle or undiluted test article) at doses of??? or??mg/kg bw. Animals were then observed for (#) days.

Study Endpoints:

Oral LD_{50} = mg/kg bw

Toxicity based on the LD_{50} in males or females whichever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV.

Dose (mg/kg b.w)	Mortality/Number Tested Males/ Females	Morbidity/Number Tested Males/ Females	Survived/ Number Tested Males/ Females

Statistics/If any: The oral LD_{50} was calculated using the

Observations:

A. Morality: as noted in table.
B. Clinical observations including signs & symptoms:
C. Gross Necropsy/ pathological findings:
D. Weight changes:

Conclusions:

2. ACUTE DERMAL TOXICITY RAT

Executive Summary:

In an acute dermal toxicity study, groups (#/sex) of strain, species (source), (age, weight) were dermally exposed to (formulation/technical, note a.i. and %) in (vehicle or undiluted test article) to (% or amount of body surface area) at doses of, or mg/kg bw. Test sites were covered with a(n) occlusive/semi-occlusive dressing for (#) hours. Animals were then observed for (#) days.

Study Endpoints:

Dermal LD_{50} = mg/kg bw
Toxicity based on the LD_{50} in males or females whichever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV.

Dose (mg/kg b.w)	Mortality/Number Tested Males/ Females	Morbidity/Number Tested Males/ Females	Survived/ Number Tested Males/ Females

Statistics/If any: The Dermal LD_{50} was calculated using the
Observations:

A. **Morality:** as noted in table.
B. **Clinical observations including signs & symptoms:**
C. **Gross Necropsy/ pathological findings:**
D. **Weight changes:**

Conclusions:

3. ACUTE INHALATIONAL TOXICITY RAT

Executive Summary:

In an acute inhalation toxicity study, groups (#/sex) of strain, species (source), (age, weight) were exposed (nose only, head only or whole body) via the inhalation route to (formulation/technical, note a.i. and %) in (name of vehicle or undiluted test article) for [#] hours at concentrations of mg/L. Animals were then observed for [#] days.

Study Endpoints:

LC_{50} = mg/L

Toxicity: based on (males or females whichever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV.

Nominal Conc. (mg/L)	Actual Conc. (Gravimetric/ Analytical) (mg/L)	MMAD	GSD	Mortality/Number Tested	Morbidity/Number Tested	Survived/ Number Tested
				Males/ Females	Males/ Females	Males/ Females

Test Atmosphere /Chamber Description:

Chamber Volume:	
Airflow:	
Temperature:	
Relative Humidity:	
Time to Equilibrium:	

Test the atmosphere concentration:
Particle size determination:
Statistics/if any: The LC_{50} was calculated using the
Observations:

A. **Morality:** as noted in table.
B. **Clinical observations including signs & symptoms:**
C. **Gross Necropsy/ pathological findings:**
D. **Weight changes:**

Conclusions:

4. ACUTE EYE IRRITATION RABBIT

Executive Summary:

In an acute eye irritation study, (volume or weight of test material applied) of (formulation/technical, note a.i. and %) in (name of vehicle if appropriate, or undiluted test material) was instilled into the conjunctival sac of (which eye) of (#/sex), (strain), (species - rabbits) (source, age, weight) for [#] hours. (Note if eyes were washed) Animals were then observed for *[#]* days. Irritation was scored by the method as per guideline.
In this study, formulation/technical is not an eye irritant OR is minimally, mildly, moderately, severely, or extremely irritating to the eye based on GHS/EPA Toxicity Category I, II, III, IV.

	Number "positive"/number tested							
	Hours				**Days**			
Observations	1	**24**	**48**	**72**	**4**	**7**	**14**	**21**
Corneal Opacity								
Iritis								
Redness								
Chemosis								
Discharge								
Conjunctivae:								

Clinical observations including ocular signs & symptoms/ reactions:
Conclusion:

5. ACUTE DERMAL IRRITATION/PRIMARY SKIN IRRITATION RABBIT

Executive Summary:

In a primary skin irritation study, (#/sex) strain, species (source), (age, weight) were dermally exposed to (volume or weight of test material applied) of (formulation/technical, note a.i. and %) in (name of vehicle or undiluted test material) to (% or amount of body surface area - state location of test site). Test sites were covered with a(n) occlusive/semi-occlusive dressing for (#) hours. Animals were then observed for [#] days. Irritation was scored by the method of (cite method).

In this study, formulation/technical is not a dermal irritating OR is corrosive to the skin based on. GHS/EPA Toxicity Category I, II, III, IV.

	Number "positive"/number tested			
	Hours			
Observations	1	24	48	72
Erythema and Eschar Formation				
Oedema				

Observations:

Results:

Conclusions:

6. SKIN SENSITIZATION GUINEA PIG/LLNA

Executive Summary:

In a dermal sensitization study with (formulation/technical, note a.i. and %) in (name of vehicle if appropriate or undiluted test article), strain, species (source)(age, weight) were tested using the method of (cite study type). Identify positive control material. List clinical signs (systemic and local for LLNA) and mortality. Necropsy results for LLNA **if significant**.

Results and discussion:

A. Reactions and duration:

B. Positive control:

C. Conclusions:

OBSERVATIONS FOR MAXIMIZATION TEST (GPMT) AND BUEHLER TEST:

a. Justification for positive control other than mentioned in guideline:

b. Dose Range Finding Study (DRFS) result:

c. Treatment and control skin reaction observation

Group		Skin reaction observation (dermal scoring)		
		21 hours of patch removal	Approx. 48 hours post challenge application	Approx. 72 hours post challenge application
Treatment group	Male			
Naïve control				
Treatment group	Female			
Naïve control				

0 = no visible change 1 = discrete or patchy erythema 2 = moderate and confluent erythema 3 = intense erythema and swelling

d. **Result of positive control for reliability check:**
e. **Clinical observations if any,**

histopathological examination	
skin fold thickness	

OBSERVATIONS FOR LOCAL LYMPH NODE ASSAY (LLNA) TEST:

Observations	Results
Dose Range Finding Study (DRFS) result:	
Clinical Observations	
Body weights changes	
Ear erythema measurements	
Ear thickness measurements	
Statistical tool used	
DPM of positive control (mean and associated error term)	
Stimulation index of positive control (concurrent/ historical)	
DPM of treatment group (mean and associated error term)	
Stimulation index of treatment group	
DPM of vehicle control group (mean and associated error term)	
Stimulation index of Vehicle control group (if any)	

DPM: Disintegration Per Minute

7. *IN VITRO* BACTERIAL GENE MUTATION *(Bacterial system, Salmonella typhimurium; E. coli)*/ mammalian activation gene mutation assay

(Mutagenicity: AMES Test, 2 In Vitro, 1 In Vivo]

A. Executive Summary:

In a reverse gene mutation assay in bacteria (MRID *[number]*), strains *[specify]* of *S. typhimurium [or other acceptable bacterial strains, i.e., E. coli wp2 (pKM101) and WP2uvrA(pKM101)]* were exposed to *[Chemical name, (% a.i., batch/lot #), include solvent if appropriate]* at concentrations of in the presence and absence of mammalian metabolic activation *[specify] in the plate incorporation or pre-incubation procedure [specify]*.

(Chemical name) was tested *[up to cytotoxic (or insoluble) concentrations or limit concentration (5000 g/plate or 5 L/plate), include other details as appropriate]*. *(quantitate if positive for number of revertants e.g., a dose related increase to 782 revertants at the highest concentration vs. 110 revertants in control for strain TA 100)*. The positive controls induced *(did not induce)* the appropriate responses in the corresponding strains.

There was *(no) evidence (or a concentration related positive response)* of induced mutant colonies over background.

B. MATERIALS AND METHODS

1. Control Materials:		
	Negative:	*[e.g., culture medium]*
	Solvent (final conc=n):	
	Positive:	Nonactivation: Sodium azide _____ ?g/plate TA100, TA1535 2-Nitrofluorene _____ ?g/plate TA98, TA1538 9-Aminoacridine ___ ?g/plate TA97, TA1537 Other (list):
		Activation: 2-Aminoanthracene (2-anthramine) ?g/plate usually all strains Other (list):

2. Activation: S9 derived from *[mark those that apply with x]*								
		induced		Aroclor 1254		Rat		Liver
		non-induced		Phenobarbitol		Mouse		Lung
				None		Hamster		Other *[name]*
				Other *[name]*		Other *[name]*		

Describe S9 mix composition *[if purchased, give details]*:

3. Test organisms: *S. typhimurium* strains *[mark those that apply with x]*								
		TA97		TA98		TA100	TA102	TA104
		TA1535		TA1537		TA1538	list any others	
Properly maintained?							Yes	No
Checked for appropriate genetic markers (*rfa* mutation, R factor)?							Yes	No

4. Test compound concentrations used: *[preliminary cytotoxicity test, if performed and main assay]*

Nonactivated conditions:

Activated conditions:

[Note: list strains used and number of replicates per dose, per strain, per condition along with doses]

C. RESULTS & DISCUSSIONS (OBSERVATIONS) *[Report results of analytical determination if performed]*

A. PRELIMINARY CYTOTOXICITY ASSAY: *[include concentration ranges, activation and nonactivation; strain(s) used; reported results, e.g., cytotoxicity indices (effect on background lawn; reduction in revertant) and solubility]*

B. MUTAGENICITY ASSAY: *[reported results, e.g., induction of revertant - individual plate counts and/or summary given; appropriateness of positive and background (concurrent and/or historical) revertant levels; number of concentration levels used; number of replicate plates; include representative table(s), if appropriate]*

D. CONCLUSION:

8. *IN VITRO* MAMMALIAN CYTOGENETICS ASSAY

A. Executive Summary:

In a mammalian cell cytogenetics assay *[Chromosome aberration or SCE]*(MRID *[number]*), *[cell type, e.g., CHO/V79/L5178Y cell cultures/primary lymphocyte cultures]* were exposed to *[Chemical name, (% a.i.,*

batch/lot #), include solvent if appropriate] at concentrations of 0, x, x, x μg/mL with and/or without metabolic activation *[specify]* for *[give duration of exposure]*.

Chemical name was tested *(up to cytotoxic or precipitating concentrations, or limit concentration, 5000 μg/mL). [include other details as appropriate, quantitate if positive (e.g. a dose related increase to 80% cells with aberrations at the top concentration, or large increase in deletions, rearrangements, etc. vs controls]*. Positive controls induced (did *not* induce) the appropriate response.
There was *(no) evidence (or a concentration related positive response)* of *[Chromosome aberration or SCE]* **induced over background.**

B. MATERIALS AND METHODS

1. Control Materials:		
	Negative control:	*[e.g., culture medium]*
	Solvent control (final conc=n):	
	Positive control:	Nonactivation: (concentrations / solvent)
		Activation: (concentrations / solvent)

2. Activation: S9 derived from *[mark those with x that apply]*

		induced		Aroclor 1254		Rat	Liver
		non-induced		Phenobarbitol		Mouse	Lung
				None		Hamster	Other (name)
				Other (name)		Other (name)	

Describe S9 mix composition: *[if purchased, give details]*

3. Test cells: mammalian cells in culture *[identify cell line or primary cell culture (if human lymphocytes, describe subjects, e.g., donor's health, status, sex, smoker]*

	V79 cells (Chinese hamster lung fibroblasts)			
	Human lymphocytes			
	Chinese hamster ovary (CHO) cells			
Media: (identify)				
Properly maintained?		Yes		No
Periodically checked for *Mycoplasma* contamination?		Yes		No
Periodically checked for karyotype stability?		Yes		No

4. Test compound concentrations used: *[For preliminary cytotoxicity test, if performed, and main assay]*

	Nonactivated conditions:	
	Activated conditions:	

5. TEST PERFORMANCE

1. Preliminary Cytotoxicity Assay *[if performed, describe method; i.e., cell cycle kinetics, mitotic index, trypan blue, monolayer confluency, cloning efficience]*:

2. Cytogenetic Assay:

a.	**Cell exposure time:**	Test Material	Solvent Control	Positive Control
	Non-activated:	h	h	h
	Activated:	h	h	h

b.	**Spindle inhibition**	
	Inhibition used/concentration:	
	Administration time:	x hours (before cell harvest)

c.	**Cell harvest time after termination of treatment:**	Test Material	Solvent Control	Positive Control
	Non-activated:	h	h	h
	Activated:	h	h	h

d. Details of slide preparation: *[Describe briefly]*

e. Metaphase analysis

No. of cells examined per dose:				
Scored for structural?		Yes		No
Scored for numerical?		Yes If Y, list *[e.g., polyploid, endoreduplicated cells, etc.]*		No
Coded prior to analysis?		Yes		No

f. Statistical analysis: *[list parameters that were analyzed and the statistical methods]*

C. RESULTS & DISCUSSIONS (OBSERVATIONS) [*Report results of analytical determination if performed]*

1. PRELIMINARY CYTOTOXICITY ASSAY: *[reported results, e.g., include dose range, solubility, and evidence of cytotoxicity, rationale for exposure, harvest times and high dose with and without activation]*

2. *CYTOGENETIC or SCE* ASSAY:

[Reported results, e.g., include appropriateness of negative, solvent and positive control frequencies; appropriateness of dose levels; statistical evaluation; types of structural aberrations for significant dose levels; include representative table, if appropriate]

D. CONCLUSION

9. *IN VITRO* MAMMALIAN CELLS GENE MUTATION ASSAY *(name cell type used)*

Executive Summary:

In a mammalian cell gene mutation assay *[specify locus]* (MRID *[number]*), *[cell type]* cells cultured *in vitro* were exposed to *[Chemical name, (% a.i., batch/lot #), include solvent if appropriate]* at concentrations of x, x, x, x g/mL in the presence and absence of mammalian metabolic activation *[specify]* for *[give duration of exposure]*.
Chemical name was tested *[up to cytotoxic/insoluble/limit concentrations (i.e., 5000 g/mL, 5 L/mL, or 0.01 M), include other details as appropriate. Some quantitation here e.g., induced mutation frequency of $582x10^{-6}$ vs. $78x10^{-6}$ in controls at the top concentration]*. The positive controls *(did/did not)* induce the appropriate response. **There was *(no) evidence (or a concentration related positive response)* of induced mutant colonies over background.**

A. MATERIALS AND METHODS

1. Control Materials:		
	Negative control:	*[e.g., culture medium]*
	Solvent control (final conc=n):	
	Positive control:	Nonactivation:(concentrations / solvent)
		Activation: (concentrations / solvent)

2. Activation: S9 derived from *[mark those with x that apply]*							
	induced		Aroclor 1254		Rat		Liver
	non-induced		Phenobarbitol		Mouse		Lung
			None		Hamster		Other *[name]*
			Other *[name]*		Other *[name]*		

Describe S9 mix composition: *[if purchased, give details]*

3. Test cells: mammalian cells in culture *[mark those with x that apply]*			
	mouse lymphoma L5178Y cells		V79 cells (Chinese hamster lung fibroblasts)
	Chinese hamster ovary (CHO) cells		list any others
Media: *[Identify]*			
Properly maintained?		Yes	No
Periodically checked for Mycoplasma contamination?		Yes	No
Periodically checked for karyotype stability?		Yes	No
Periodically "cleansed" against high spontaneous background?		Yes	No

4.**Locus Examined:**		**Thymidine kinase (TK)**	**Hypoxanthine-guanine-phosphoribosyl transferase (HGPRT)**	**Na^+/K^+ ATPase**
	Selection agent:	bromodeoxyuridine (BrdU) *[give conc=n]*	8-azaguanine (8-AG) *[conc=n]*	ouabain*[conc=n]*
		fluorodeoxyuridine (FdU)	6-thioguanine (6-TG)	
		trifluorothymidine (TFT)		
	[Other? (details)]			

5. Test compound concentrations used: *[For preliminary cytotoxicity test, if performed, and main assay]*	
Nonactivated conditions:	
Activated conditions:	

6. Test performance

1. Cell treatment:

a. Cells were exposed to test compound, negative/solvent or positive controls for ___ hours (nonactivated) hours (activated).
b. After washing, cells were cultured for ___ days (expression period) before cell selection.
c. After expression, ____ cells/dish (__ dishes/ group) were cultured for ____ days in selection medium to determine numbers of mutants and __ cells/dish (_ dishes/group) were cultured for __ days without selective agent to determine cloning efficiency.
[If mouse lymphoma cells, include information regarding colony sizing]

7. Statistical Methods: *[list parameters that were analysed and the statistical methods used]*

C. RESULTS & DISCUSSIONS (OBSERVATIONS) *[Report results of analytical determination if performed]*

A. PRELIMINARY CYTOTOXICITY ASSAY

[include concentration ranges, activation and nonactivation; reported results, e.g., cytotoxicity and solubility, rationale for dose selection for main study]

B. MUTAGENICITY ASSAY *[reported results, e.g., induction of mutant colonies - individual colony counts and/or summary given; mutant frequencies per 10^6 survivors; positive and background mutant frequencies; inclusion of concentration levels used; number of cultures per concentration; levels of cytotoxicity obtained; appropriateness of cloning efficiencies; include representative table, if appropriate].*

D. CONCLUSION

10. *IN VIVO* MAMMALIAN BONE MARROW ERYTHROCYTES MICRONUCLEUS ASSAY

A. Executive Summary:

In a *(strain)* mouse *[or rats or other acceptable mammalian species]* bone marrow micronucleus assay (MRID *[number]*), *(number/sex/dose)* were treated *[route]* with *Chemical name (% a.i., batch/lot #)* at doses of 0, x, x, or x mg/kg bw. Bone marrow cells were harvested at *(list hours)* post-treatment. The vehicle was *(state vehicle)*. *(Note the route of exposure and if acute or multiple dosing)*
There were *(no)* signs of toxicity *(list if present)* during the study. *[Note, the signs of cytotoxicity, if present, and the quantitative evidence for a positive micronucleus response, if any]*. Chemical name was *(not)* tested at an adequate dose *(based on)*. The positive control induced the appropriate response.

B. MATERIALS AND METHODS

a. Test compound:										
	Dosing:		once		twice (24 hrs apart)			Other *(describe)*		
	Sampling (after last dose):*[mark all that are appropriate]*,		6 hr		12 hr		24 hr	48 hr		72 hr
	Other *[describe]*:									

b. Negative and/or vehicle control:										
	Dosing:		once		twice (24 hrs apart)			Other *(describe)*		
	Sampling (after last dose):*[mark all that are appropriate]*,		6 hr		12 hr		24 hr	48 hr		72 hr
	Other *[describe]*:									

c. Positive control:											
	Dosing:		once		twice (24 hrs apart)			Other *(describe)*			
	Sampling (after last dose):*[mark all that are appropriate]*,		6 hr		12 hr		24 hr		48 hr		72 hr
	Other *[describe]*:										

d. Tissues and Cells Examined:	
	Bone marrow OR other (identify):
	No. of polychromatic erythrocytes (PCE) examined per animal:
	No. of normochromatic erythrocytes (NCE; more mature RBCs) examined per animal:
	Other (if other cell types examined, describe):

e. Details of slide preparation: *[Describe briefly; were slides coded?]*

f. Evaluation Criteria: *[Describe]*

g. **Statistical methods:** *[list parameters that were analyzed and the statistical methods]*

C. RESULTS & DISCUSSIONS (OBSERVATIONS) *[Report results of analytical determination if performed]*

1. PRELIMINARY TOXICITY ASSAY: *[reported results, e.g., include dose range; signs of toxicity - e.g., MTD considerations; clinical signs; number of animals, rationale for dose selection for micronucleus assay]*

2. MICRONUCLEUS ASSAY: *[reported results, e.g., include in life animal observations, induction of micronuclei; appropriateness of negative, solvent and positive control micronucleus frequencies; ratio of PCE/NCE; sex differences (if any); appropriateness of dose levels and route; statistical evaluation; include representative table, if appropriate]*

D. DISCUSSION AND CONCLUSIONS:

11. UNSCHEDULED DNA SYNTHESIS IN MAMMALIAN LIVER CELL CULTURES;

A. Executive Summary:

In an unscheduled DNA synthesis, primary rat hepatocyte cultures were exposed to *[Chemical name, (% a.i., batch/lot #), include solvent if appropriate]* at concentrations of 0, x, x, or x □g/mL for *(duration of exposure)*.
Chemical name was tested *[up to cytotoxic or precipitating concentrations, or limit concentration, 5000 □g/mL. (Include other details as appropriate, quantitation if positive e.g. there was a significant increase in number of cells in repair (60% at top concentration vs 1% in controls))]*. The positive controls induced *(did not induce)* the appropriate response.
There was *(no)* evidence *(or a dose related positive response)* that unscheduled DNA synthesis, as determined by radioactive tracer procedures [nuclear silver grain counts] was induced.

B. MATERIALS AND METHODS

1. Cell Preparation:

a. Perfusion Technique:

b. Hepatocyte Harvest/Culture Preparation:

2. TEST PERFORMANCE *[(NOTE: If cells other than hepatocytes are tested, information regarding the S9 activated phase of testing must be included)]*

1. Cytotoxicity Assay: *[if conducted, briefly describe procedure]*

2. UDS Assay:

a. Treatment:

b. Preparation of Autoradiographs/Grain Development:

c. Grain Counting: *[include number of cells scored per dose, derivation of net nuclear grains, whether % cells in repair were scored]*

e. Statistical Analysis: *[list parameters that were analyzed and the statistical methods]*

C. RESULTS AND DISCUSSIONS (OBSERVATIONS): *[Report results of analytical determination if performed]*

1. PRELIMINARY CYTOTOXICITY ASSAY: *[include concentration ranges; reported results, e.g., cytotoxicity and solubility, rationale for dose selection for main study]*

2. UDS assay: *[reported results, e.g., net nuclear grain counts and/or summary; appropriateness of positive controls and background levels (concurrent and/or historical); number of concentration levels evaluated; number of replicates -- 100 cells/group (50 cells/slide); include representative table, if appropriate]*

D. CONCLUSIONS:

TOXICOLOGY SCRUTINY TEMPLATE
[9(3)BIO-PESTICIDES]

Sponsor:
Test Facility Name & GLP Validity:
GLP (Yes/No):
Test Material (% a. i.): (CAS#), Lot/ Batch No.#:

Study Type: Acute Oral Toxicity/Pathogenicity Rat
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:
In an acute oral toxicity study, groups of *[fasted], [age] [strain] [species] [#/sex]* were given a *[single OR #]* oral dose of *[dose amount]* of *[formulation, note its potency, biological activity or concentration per unit weight or volume]* (containing *% a.i. name*). The animals were then observed for a period of up to *[#]* days. *[Identify other control groups, if applicable.]* The oral LD50 of the test substance is ***[=, > or <] [#]*** *mg / kg bw]* **(95% C.I. if available)** *[note if limit test]* in *[male, female OR both sexes] species OR [both males and females] [species]. [NOTE: include sex-specific LD50 values if different values].*
Based on the results of this study, *[formulation, test material]* showed **[NO, LOW, SLIGHT, MODERATE, HIGH] Toxicity** on *[species]* after exposure to a single oral dose of *[dose level]* mg/kg *[note if limit test] [include EPA Toxicity Category I, II, III or IV]* in the *[species].*

I. MATERIALS AND METHODS

A. GUIDELINE FOLLOWED:
Deviations from guideline:

B. MATERIALS:

1. Test Material:
Description:
Microbiology:

2. Test Animals:
Species
Strain:
Number of animals/sex:
Age at test initiation:
Weight at test initiation:
Source:
Rationale:

C. STUDY DESIGN AND METHODS:
[Briefly describe the experimental design.]

1. Experimental Methods and Conditions:
Preliminary challenge assay: *[if applicable.]*

Acclimation
: Housing:
Diet: *[describe] ad libitum*
Water: *[describe] ad libitum*
Animal assignment and treatment:
Animals were assigned to the test groups noted in Table 1.
[Following an overnight fast], rats were given a single dose of *[test material name]* by gavage.

TABLE 1. Doses, mortality/animals treated.

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

Sample preparation: *[Describe all sample preparation procedures.]*
Controls: *[if applicable]*

Samples were prepared.]		
Environmental conditions:	Temperature Humidity Air changes Photoperiod	°C % /h h dark/ h light

Solvent/vehicle: *[if used]*
Duration of study:
Other methods or conditions, if any:

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

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

Were raw data included?

Other observations, if any:

II. RESULTS

A. **MORTALITY** is given in Table 1. The oral LD50 of the test substance is ***[=, > or <*** *mg / kg bw* (C.I. or standard deviation) *if conducted)] [note if limit test]* in *[species]*.

B. CLINICAL OBSERVATIONS:

C. BODY WEIGHT:

D. FEED CONSUMPTION:

E. NECROPSY:

F. REPORTED STATISTICS:

III. CONCLUSION

Results of the acute oral toxicity study showed *[no]* mortality after a *[single OR #]* oral dose of *[dose amount]* of *[formulation, test substance name]* (containing % *a.i. name*) in *[species]*. Based on the results of this study, the oral LD50 of *[test substance name]* is greater than # mg /kg in *[species]*.

IV. REFERENCES

Study Type: Acute Dermal Toxicity/Pathogenicity Rat
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:
In an acute dermal toxicity study, groups of *[fasted], [age] [strain] [species] [#/sex]* were dermally exposed to *[formulation, note its potency, biological activity or concentration per unit weight or volume]* for # hours to an area of approximately *[% or amount of body surface area]*. Following exposure, the animals were observed for a period of # days. The dermal LD50 of the test substance is ***[=, > or < mg test material / kg bw] [note if no mortality occurred, note if limit test]*** in *[species]*.
Based on the results of this study, *[formulation/test material]* showed **[NO, LOW, SLIGHT, MODERATE, HIGH] Toxicity** on *[species]* after exposure to a single dose of *[dose level]* mg/kg *[note if limit test]* by dermal route *[include EPA Toxicity Category I, II, III or IV]*.

V. MATERIALS AND METHODS

D. GUIDELINE FOLLOWED:

Deviations from guideline:

E. MATERIALS:

1. Test Material:

Description:

Microbiology:

2. Test Animals:

Species

Strain:

Number of animals/sex:

Age at test initiation:

Weight at test initiation:

Source:

Rationale:

F. STUDY DESIGN AND METHODS:

[Briefly describe the experimental design.]

1. Experimental Methods and Conditions:

Preliminary challenge assay: *[if applicable.]*

Acclimation

: Housing:

Diet: *[describe] ad libitum*

Water: *[describe] ad libitum*

Animal assignment and treatment: Animals were assigned to the test groups noted in Table 1. The test animals were given a single dose of [test material name mg/kg bw and note if limit test] by dermal route. [Describe how the product was applied.]

TABLE 1. Doses, mortality/animals treated.

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

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

Controls: *[if applicable]*

Samples were prepared.]		
Environmental conditions:	Temperature Humidity Air changes Photoperiod	°C % /h h dark/ h light

Solvent/vehicle: *[if used]*

Duration of study:

Other methods or conditions, if any:

2. **Observations:**

Clinical observations and body weights:

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

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

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

Were raw data included?

Other observations, if any:

VI. **RESULTS**

G. **MORTALITY** is given in Table 1. The oral LD50 of the test substance is *[=, > or < mg / kg bw* (C.I. or standard deviation) *if conducted)] [note if limit test]* in *[species]*.

H. **CLINICAL OBSERVATIONS:**

I. **BODY WEIGHT:**

J. **FEED CONSUMPTION:**

K. **NECROPSY:**

L. **REPORTED STATISTICS:**

VII. **CONCLUSION**

Results of the acute dermal toxicity study showed *[no]* mortality in *[species]* after dermally exposed to *[test substance name]* (containing % *a.i. name*) for # hours to a body surface area of approximately #%. Based on the results of this study, the dermal LD50 of *[test substance name]* is greater than # mg /kg in *[species]*.

VIII. **REFERENCES**

XI APPENDIX

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

Edema Formation

No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1.0 mm)	3
Severe edema (raised more than 1.0 mm beyond the area of exposure)	4

Note:

IRRITATION SCORE = Erythema Score + Edema Score

Source: 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.

Study Type: Acute Inhalation Toxicity/Pathogenicity Rat
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:
In an acute inhalation toxicity study (MRID *[number]*), groups of*[age] [strain] [species] [#/sex/group]* were exposed by the inhalation route to *[formulation, note its potency, biological activity or concentration per unit weight or volume]* in *[name of vehicle, if applicable]* for *[#]* hours to *[nose only, head only or whole body]* at concentration*(s)* of *[insert concentration range in appropriate units]*. Animals then were observed for *[#]* days. *[Identify other control groups, if applicable]* Based on the results of this study, the inhalation LC50 of *[formulation]* is greater than *[dose level]* mg/L *[note if limit test] [include EPA Toxicity Category I, II, III or IV]* in the *[species]*. *[Formulation]* is of **[LOW, SLIGHT, MODERATE, HIGH] Toxicity** This acute inhalation study is classified as *[acceptable, unacceptable (why)]*. This study was *[not]* conducted in accordance with the guideline recommendations for an acute inhalation study (OCSPP 870.1300; PMRA Data Code: M4.9; OECD 403 etc.) in the *[species]*.

IX. MATERIALS AND METHODS

G. GUIDELINE FOLLOWED:

Deviations from guideline:

H. MATERIALS:

1. Test Material:

Description:

Microbiology:

2. Test Animals:

Species

Strain:

Number of animals/sex:

Age at test initiation:

Weight at test initiation:

Source:

Rationale:

I. STUDY DESIGN AND METHODS:

[Briefly describe the experimental design.]

1. Experimental Methods and Conditions:

Preliminary challenge assay: *[if applicable.]*

Acclimatio

n: Housing:

Diet: *[describe] ad libitum*

Water: *[describe] ad libitum*

Animal assignment and treatment: Animals were assigned to the test groups noted in Table 1. [Species] were exposed to [Formulation] by [nose only or whole body] exposure for [duration in hours].

TABLE 1. Concentrations, exposure conditions, mortality/animals treated

Trials	Nominal Conc. (mg/L)	Analytical Conc. (mg/L)	MMAD µm	GSD	Mortality (# dead/total)		
					Males	Females	Combined

Exposure conditions:

Generation of the test atmosphere /chamber description:

Time to equilibrium was. Analytical chemistry

Test atmosphere concentration: [give method and results].

Results are in Table 1 above.

Particle size determination: [give method and results]. Results are in Table 1 above.

Sample preparation: [Describe all sample preparation procedures.]

Controls:

Samples were prepared.		
Environmental conditions:	Temperature Humidity Air changes Photoperiod	°C % /h h dark/ h light

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

Duration of study:

2. Observations:

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

Feed Consumption: Feed consumption was measured [frequency].

Necropsy: The necropsy included an examination of [the external surface of the body, all orifices, cranial cavity, and external surface of the brain, the thoracic, abdominal and pelvic cavities and the viscera].

I. RESULTS

A. **MORTALITY** is given in Table 1. *[Include approximate time of deaths, eg. ranged from 3-7 days]*. The acute inhalation LC50 of the test substance is greater than *[dose level]* mg/L in *[species]*, based on the gravimetric chamber concentration.

B. **CLINICAL OBSERVATIONS:**

C. **BODY WEIGHT:**

D. **FEED CONSUMPTION:**

E. **NECROPSY:**

F. **REPORTED STATISTICS:**

II. CONCLUSION

Results of the acute inhalation toxicity showed *[no]* mortality after a *[single OR #]* exposure to *[formulation, test substance name]* (containing % *a.i. name*) via the inhalation route *[nose only, head only or whole body]* exposure to *[species]* after *[#]* hours. Based on the results of this study, the acute inhalation LC50 of *[formulation, test substance name]* is greater than is greater than *[dose level]* mg/L in *[species]*.

References:

Study Type: Acute Pulmonary Toxicity/Pathogenicity Rat
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:

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

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

This acute pulmonary infectivity and toxicity study is classified as *[acceptable, unacceptable (why)]*. This study was *[not]* conducted in accordance with the guideline recommendations for an acute pulmonary infectivity and toxicity study (OPPTS 885.3150; PMRA: M4.2. OECD Data Code: IIM 5.3.3) in the *[species]*.

X. MATERIALS AND METHODS

J. GUIDELINE FOLLOWED:

Deviations from guideline:

K. MATERIALS:

1. Test Material:

Description:

Microbiology:

2. Test Animals:

Species

Strain:

Number of animals/sex:

Age at test initiation:

Weight at test initiation:

Source:

Rationale:

L. STUDY DESIGN AND METHODS:

[Briefly describe the experimental design.]

1. Experimental Methods and Conditions:

Preliminary challenge assay: *[if applicable.]*

Acclimatio

n: Housing:

Diet: *[describe] ad libitum*

Water: *[describe] ad libitum*

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

TABLE 1. Doses, mortality/animals treated

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

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

Controls:

Samples were prepared		
Environmental conditions:	Temperature Humidity Air changes Photoperio	*[#]* °C *[#]*% *[#]*/h *[#]*h dark/ *[#]* h light

Solvent/vehicle:
Microbial enumeration:
Sensitivity of detection:
Duration of study:

1. **Observations:**

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

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

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

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

I. RESULTS

A. **MORTALITY** is given in Table 1. The pulmonary LD50 of the test substance is *[=, > or < mg / kg bw* (C.I. or standard deviation) *(if conducted)] [note if limit test]* in *[speoies]*.

B. **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.)]*

C. **BODY WEIGHT:** *[Indicate if the animals gained or lost weight.]*

D. **FEED CONSUMPTION:** *[Indicate if there were any treatment related effects.]*

E. **NECROPSY:** *[single sentence or two as to whether there were any treatment related effects, do not stress effects due to agonal death.]*

F. **ORGAN WEIGHTS:** *[If applicable]*

G. **MICROBIAL ENUMERATION:** *[Summarize the enumeration data and note if a pattern of clearance was achieved.]*

H. **REPORTED STATISTICS:**

II. CONCLUSION

Results of the acute pulmonary toxicity and pathogenicity study showed *[no]* mortality after a single dose of *[test substance name]* (containing % *a.i. name*) by the intratracheal route and *[is or is not]* pathogenic in *[species]*. Based on the results of this study, the pulmonary LD50 of *[Formulation]* is greater than # mg /kg in *[species]*.

REFERENCES

Study Type: Acute Injection Toxicity and Pathogenicity-Rat
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:

In an acute injection toxicity and pathogenicity study, groups of *[age] [strain] [species] [#/sex/group]* were administered by *[intravenous or Intraperitoneal]* injection with *[test substance or TGAI, note its potency, biological activity or concentration per unit weight or volume]* in *[name of vehicle, if applicable]* at a dose of *[in units of potency, biological activity or concentration per kg bw or animal]*. Animals were then observed for up to *[#]* days. *[Identify other control groups, if applicable]*

Based on the results of this study, *[test substance or TGAI]* showed **[NO, LOW, SLIGHT, MODERATE, HIGH] Toxicity** on *[species]* after exposure to a single dose of *[dose level]* mg/kg *[include EPA Toxicity Category I, II, III or IV]* by *[intravenous or Intraperitoneal]* injection and *[test substance name OR TGAI] [is or is not]* pathogenic in the *[species]*.

This acute injection toxicity and pathogenicity study is classified as *[acceptable, unacceptable (why)]*. This study was *[not]* conducted in accordance with the guideline recommendations for an acute injection toxicity and pathogenicity study (OCSPP 885.3200; PMRA Data code: *[M4.3.3 (if Intraperitoneal) OR M4.3.2 (if intravenous)]*; OECD Data Code: IIM 5.3.4) in the *[species]*.

XI. MATERIALS AND METHODS

M. GUIDELINE FOLLOWED:

Deviations from guideline:

N. MATERIALS:

1. Test Material:

Description:

Microbiology:

2. Test Animals:

Species

Strain:

Number of animals/sex:

Age at test initiation:

Weight at test initiation:

Source:

Rationale:

O. STUDY DESIGN AND METHODS:

[Briefly describe the experimental design.]

1. Experimental Methods and Conditions:

Preliminary challenge assay: *[if applicable.]*

Acclimatio

n: Housing:

Diet: *[describe] ad libitum*

Water: *[describe] ad libitum*

Animal assignment and treatment:

Animals were assigned to the test groups noted in Table 1. [Briefly describe treatment] [Following an overnight fast (if applicable)], a single high dose of [test material name OR TGAI] was administered by [intravenous OR Intraperitoneal] injection to [species].

TABLE 1. Doses, mortality/animals treated

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

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

Controls: *[if applicable]*

Samples were prepared.]		
Environmental conditions:	Temperature Humidity Air changes Photoperiod	°C % /h h dark/ h light

Solvent/vehicle: *[if used]*

Duration of study:

2. **Observations:**

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

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

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

of the body, all orifices, cranial cavity, and external surface of the brain, the thoracic, abdominal and pelvic cavities and the viscera].

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

III. RESULTS

I. **MORTALITY** is given in Table 1. The pulmonary LD50 of the test substance is ***[=, > or < mg / kg*** *bw*
(C.I. or standard deviation) *(if conducted)] [note if limit test]* in *[species].*

J. **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. 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.)]*

K. **BODY WEIGHT:** *[Indicate if the animals gained or lost weight.]*

L. **FEED CONSUMPTION:** *[Indicate if there were any treatment related effects.]*

M. **NECROPSY:** *[single sentence or two as to whether there were any treatment related effects, do not stress effects due to agonal death.]*

N. **ORGAN WEIGHTS:** *[If applicable]*

O. **MICROBIAL ENUMERATION:** *[Summarize the enumeration data and note if any]*

P. **REPORTED STATISTICS:** if any

IV. CONCLUSION

Results of the acute injection toxicity and pathogenicity study showed *[no]* mortality after *[test substance name OR TGAI]* (containing % *a.i. name*) was administered by *[intravenous OR Intraperitoneal]* injection and *[is or is not]* pathogenic in *[species]*. Based on the results of this study, the *[intravenous OR Intraperitoneal]* LD50 of *[test substance name OR TGAI]* is greater than # mg /kg in *[species]*.

REFERENCES

Study Type: Acute Dermal Irritation-Rabbit
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

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 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.]*

XII. MATERIALS AND METHODS
P. GUIDELINE FOLLOWED:
Deviations from guideline:
Q. MATERIALS:
1. Test Material:
Description:
Microbiology:
2. Test Animals:
Species
Strain:
Number of animals/sex:
Age at test initiation:
Weight at test initiation:
Source:
Rationale:
R. STUDY DESIGN AND METHODS:
[Briefly describe the experimental design.]
1. Experimental Methods and Conditions:
Preliminary challenge assay: *[if applicable.]*
Acclimatio
n: 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 Photoperiod	°C % /h H dark/h light

Solvent/vehicle: *[if used]*

Duration of study:

2. **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].*

XIII. RESULTS

M. MORTALITY

A. 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		TOTAL PDI Score
	Erythe	Edema	
30-60 mins	# (#/#)	# (#/#)	#
24 hrs			
48 hrs			
72 hrs			
Day 7			

B. **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.)]*

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

I. CONCLUSION

A. *[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 cm^2]* 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]*.

REFERENCES

Appendix

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 eschar formation (injuries in depth)	4

Edema Formation

No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1.0 mm)	3
Severe edema (raised more than 1.0 mm beyond the area of exposure)	4

Note:
IRRITATION SCORE = Erythema Score + Edema Score

Source: 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.

Study Type: Acute Eye Irritation-Rabbit
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

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].

XIV. MATERIALS AND METHODS

S. GUIDELINE FOLLOWED:

Deviations from guideline:

T. MATERIALS:

1. Test Material:

Description:

Microbiology:

2. Test Animals:

Species

Strain:

Number of animals/sex:

Age at test initiation:

Weight at test initiation:

Source:

Rationale:

U. STUDY DESIGN AND METHODS:

[Briefly describe the experimental design.]

1. Experimental Methods and Conditions:

Preliminary challenge assay: *[if applicable.]*

Acclimatio

n: 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]*
Duration of study:

2. **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].*

XV. **RESULTS**

B. **MORTALITY**

C. **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].*
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

D. **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.)]*

E. **REPORTED STATISTICS:**

II. **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]*.

REFERENCES

Appendix I: Description of Ocular Reactions

Evaluation of Ocular Reactions

		Score
Cornea		
A.	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
B.	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
Score =	A × B × 5	
Iris		
A.	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		
A.	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
B.	Chemosis	
	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
C.	Discharge	
	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.

Source: 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.

Study Type: Avian Acute Oral Toxicity
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:
In a [#]-day acute oral toxicity and pathogenicity study of [test material] to [#]-day-old [common name of species (scientific name), enter the number of birds per treatment] were exposed to a [single OR #] [indicate exposure method] dose of [indicate doses used, e.g., mg a.i./kg bw and/or CFU/kg bw] of [formulation, note its potency, biological activity or concentration per unit weight or volume] (containing % a.i. name). [Include other pertinent details such as the controls used.]
[Describe toxicity and/or pathogenicity briefly including mortality, behavioral abnormalities, and other clinical signs. If there was no toxicity, state that there was no test material-related toxic or pathogenic effect. Describe microbial clearance, if assessed]
The [#]-day acute oral LD50 was [=, > or <] [insert LD50 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 in mg a.i./kg bw and/or CFU/kg bw]. This toxicity [or] infectivity/pathogenicity study is classified as [acceptable / unacceptable / supplemental.] This study was [not] conducted in accordance with the guideline recommendations for an acute oral toxicity and pathogenicity study for birds (OCSPP 885.4050; PMRA: M9.2.1 and OECD: IIM 8.1, IIIM 10.1) in the [species]. [If it does not satisfy the requirement, concisely list only major deficiencies or refer to deficiency section.]

XVI. MATERIALS AND METHODS

V. GUIDELINE FOLLOWED:

Deviations from guideline:

W. MATERIALS:

1. Test Material:

Description:

Microbiology:

2. Test Animals:

3. Test Organism:

Species (common and scientific names): *[Insert names of species used in test.]*

Number of animals/sex:

Age at test initiation:

Weight at test initiation:

Source:

Rationale:

X. STUDY DESIGN AND METHODS:

[Briefly describe the experimental design.]

Experimental Methods and Conditions:

Acclimation:

Duration:

Conditions:

Feeding:

Water:

Temperature:

Health:

Pen size and construction materials:

Method of administration:
Dose levels:
Nominal:
Measured:
Dose preparation:
Solvent/vehicle:
Confirmation of MPCA viability:
[Describe methods used to confirm the concentration and/or viability of the MPCA in the dosing suspensions.]
Number of feed withholding days before dosing:
Positive control / reference material: *[if used]*
Number of birds per group/treatment:
For negative control:
For solvent/vehicle control:
For non-infective control:
For sterile filtrate control:
For treated birds:
Recovery of MPCA from tissues:
Feeding:
Test conditions: *[Describe the test conditions.]*
Temperature:
Ventilation:
Relative humidity:
Lighting:
Photoperiod:
Duration of study:

1. **Observations:**

Parameters measured including sub-lethal effects/toxicity symptoms:
Observation/measurement intervals:
Indicate if the test material was regurgitated:
Testing for infectivity:
Necropsy:

RESULTS

VIABILITY OF DOSING SUSPENSIONS:

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		

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 (MHD) testing. Modify as appropriate to accommodate differences in experimental design.]

MORTALITY:

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

Treatment		**Cumulative Mortality/Total Number of Birds**		
		Negative Control	**Killed *[test substance]* Control**	***[Test substance]***
Cumulative mortality	*Day 0*			
	Day x1			
	Day x2			
	Day n			
LD_{50} [insert [>] if greater than]				
NOEL [insert [>] if greater than]				

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

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

Treatment (mg a.i./kg bw)	No. of Birds	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						
LD_{50}	*[insert [>] if greater than]*					
NOEL	*[insert [>] if greater than]*					

[Table suitable for chemical acute toxicity (multiple-dose) testing (e.g., U.S. EPA guideline OCSPP 850.2100). Modify as appropriate to accommodate differences in experimental design, or delete if infectivity/pathogenicity and toxicity test used.]

SUBLETHAL TOXICITY ENDPOINTS:

TABLE *[#]*. Mean body weight for control and *[test material]*-treated *[test organism]* measured *[frequency of weighing]*.

Day	Negative Control		Killed *[test substance]* Control		*[Test substance]*	
	Mean Body Weight (g)	**Mortality** *(% or No.)*	**Mean Body Weight (g)**	**Mortality** *(% or No.)*	**Mean Body Weight (g)**	**Mortality** *(% or No.)*
Initiation						
Day 7						
Day 14						
Day 21						
Day 28						
Termination						
LD_{50} *[insert [>] if greater than]*						
NOEL *[insert [>] if greater than]*						

[Table suitable for microbial infectivity/pathogenicity and toxicity (maximum hazard dose) testing. Modify as

appropriate to accommodate differences in experimental design or delete if acute toxicity test is used.]
[[a] Use superscript and footnote to indicate values that are statistically significantly different from control.]

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

Day	Food Consumption (g/duck/day)		
	Negative Control	**Killed *[test substance]* Control**	***[test substance]***
Initiation			
Day 7			
Day 14			
Day	**Food Consumption (g/duck/day)**		
	Negative Control	**Killed *[test substance]* Control**	***[test substance]***
Day 21			
Day 28			
Termination			

[Table suitable for microbial infectivity/pathogenicity and toxicity (MHD) 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						
Brain						
Lung						
Liver						
Spleen						
Kidney						
GI tract						
[other tissues]						

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

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

Treatment (mg a.i./kg bw)	**Percent Affected by *[sublethal effect observed, (e.g., lethargy)]***						
	Day 0	***Day x1***	***Day x2***	***Day x3***	***Day x4***	***Day x5***	***Day n***
Negative control							
Test dose 1							
Test dose 2							
Test dose 3							
Test dose n							

Treatment (mg a.i./kg bw)	**Percent Affected by *[sublethal effect observed, (e.g., lethargy)]***						
	Day 0	***Day x1***	***Day x2***	***Day x3***	***Day x4***	***Day x5***	***Day n***
ED_{50}	*[insert [>] if greater than]*						
NOEL	*[insert [>] if greater than]*						

[Table suitable for chemical acute toxicity (multiple-dose) testing (e.g., U.S. EPA guideline OCSPP 850.2100). Modify as appropriate to accommodate differences in experimental design, or delete if infectivity/pathogenicity test used.]

REPORTED STATISTICS: if any

Statistical Method:

	LD_{50}: NOEL:	95% C.I.:
	Probit Slope:	95% C.I.:
III.	**CONCLUSION:**	
A		*[Summarize the study author's conclusions- Provide the major Conclusions e.g., values for LD_{50}, ID_{50} LC_{50}, NOEL, NOEC]*

REFERENCES:

Study Type: Acute Toxicity to fresh Water Fish
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:

In a *[#]*-day *toxicity [or] [infectivity/pathogenicity]* study, *[#] [common name (scientific name)]* were exposed to a *[single OR #] [indicate exposure method]* dose of *[dose amount]* of *[formulation, note its potency, biological activity or concentration per unit weight or volume]* (containing % *a.i. name*) under *[static/flow through]* conditions. *[Include other pertinent details such as the controls used.]*

[Describe findings briefly including mortality, behavioral abnormalities, and other signs of toxicity. If there were no effects, state that there was no test material-related toxic or pathogenic effect.]

The *[#]*-day LC_{50} was *[=, > or <] [insert LC_{50} in appropriate units]. [If the study included sub-lethal test endpoints and/or sub-lethal effects were observed and/or additional sub-chronic testing was triggered include the following text:* The EC_{50} based on sub-lethal effects was *[=, > or <] [insert EC_{50} in appropriate units]*. The NOEC value, based on mortality *[and sub-lethal effects (if applicable)]*, was *[=, > or <] [insert NOEC in appropriate units]*.

This study is classified as *[acceptable, unacceptable, and supplemental]*. This study was *[not]* conducted in accordance with the guideline recommendations for a toxicity/pathogenicity study for freshwater fish (OCSPP 885.4200; PMRA: M9.4.1 and OECD: IIM 8.2, IIIM 10.2) in the *[species]*.

XVII. MATERIALS AND METHODS

Y. GUIDELINE FOLLOWED:

Deviations from guideline:

Z. MATERIALS:

1. **Test Material:**

Description:

2. **Test Organism:**
3. **Species (common and scientific names):**
4. **Age at test initiation:**
5. **Weight at test initiation (mean and range):**
6. **Length at test initiation (mean and range):**
7. **Number of test species:**
8. **Strain/Source:**
9. **Rationale:**

STUDY DESIGN AND METHODS:

10. **Acclimation:**

Duration:
Feeding:
Water:
Temperature:

11. **Health**

Test vessel:
Material:
Size:
Fill volume:
Test system:
Source of dilution water:

Water parameters:
Dissolved oxygen
pH
Temperature
Hardness
Particulate matter
Total organic carbon (TOD) or chemical oxygen demand (COD)
Metals
Pesticides
Chlorine
Aeration:
Route(s) of exposure:
Test concentrations:
Nominal:
Measured:
Preparation of test concentrations:
Solvent/vehicle:
Confirmation of MPCA viability:
Positive control / reference material: *[if used]*
Number of replicates/groups:
Control(s): Treatments:
Number of organisms per replicate /groups:
Control(s): Treatments:
Biomass loading rate:
Recovery of MPCA from tissues:
Feeding:
Lighting:
Duration of study:

1. **Observations:**
Parameters measured including sublethal effects/toxicity symptoms:
Observation/measurement intervals:
Testing for infectivity:
RESULTS:

WATER QUALITY PARAMETERS:

[Summarize water quality measurements and discuss the acceptability]

TABLE *[#].* Dissolved oxygen, temperature and pH in test suspensions during the *[X]*-day exposure of *[test organism]* to *[concentration]* of *[test substance]* under *[static renewal/flow-through]* conditions.

Parameter	Replicate	Day 0	Day 2		Day 4		*Day –2*		*Day n*
		New	Old	New	Old	New	Old	New	Old
Dissolved oxygen (% saturation or mg/L)	1								
	2								
	n								
	Mean								

Temperature (℃)	1									
	2									
	n									
	Mean									
pH	1									
	2									
	n									
	Mean									

[Table suitable for microbial infectivity/pathogenicity and toxicity testing of the maximum hazard concentration. Modify as appropriate to accommodate differences in experimental design or delete if acute toxicity test or multiple concentrations are used.]

TABLE *[#].* *[Dissolved oxygen concentration/Temperature/pH]* in *[units]* in test suspensions during the *[X]*- day exposure of *[test organism]* to *[test substance]* under *[static renewal/flow-through]* conditions.

Day	**Suspension**	***[Parameter (units)]***					
		Nominal Concentration of Test Suspension (CFU/L)					
		$X \times 10^X$	$X \times 10^X$	$X \times 10^X$	$X \times 10^X$	$X \times 10^X$	Control
0	new						
2	old						
	new						
–2	old						
	new						
n	old						

[Table suitable for microbial infectivity/pathogenicity and toxicity testing of multiple concentrations. Modify as appropriate to accommodate differences in experimental design or delete if acute toxicity test or maximum hazard concentration is used.]

TABLE *[#].* Water quality parameters in test suspensions during the *[X]*-hour exposure of *[test organism]* to [test substance].

Parameter	**Replicate**	***Treatment 1***		***Treatment 2***		***Treatment 3***		***Treatment n***		***Control***	
		0 h	**48 h**	**0 h**	**48 h**	**0 h**	**48 h**	**0 h**	**48 h**	**0 h**	**48 h**
Dissolved oxygen (% saturation or mg/L)	1										
	n										
	Mean										

Temperature (℃)	1											
	n											
	Mean											
pH	1											
	n											
	Mean											

[Table suitable for chemical acute toxicity (multiple-dose) testing (e.g., U.S. EPA guideline OCSPP 850.1010). Modify as appropriate to accommodate differences in experimental design, or delete if infectivity/pathogenicity and toxicity test used.]

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

B. **TABLE *[#].*** *[Method (e.g., Viable count)]* verification of test and control suspension concentrations during an *[X]*-day exposure of *[test organism]* to *[test substance]*.

Day	**Suspension**	**Measured Concentration of Test Suspension (CFU/L)**					
		Nominal Concentration of Test Suspension (CFU/L)					
		$X \times 10^X$	$X \times 10^X$	$X \times 10^X$	$X \times 10^X$	$X \times 10^X$	Control
0	new						
2	old						
	new						
–2	old						
	new						
n	old						

MORTALITY:

TABLE *[#].* Cumulative mortality *[OR number of immobilized] [test organism]* exposed to *[test substance]* for *[test duration]* under *[static-renewal/flow-through]* conditions.

Day	**Cumulative Mortality *[OR Number of Immobilized] [test organism]***											
	Measured Concentration of Test Suspension (CFU/L)											
	$X \times 10^X$		$X \times 10^X$		$X \times 10^X$		$X \times 10^X$		$X \times 10^X$		**Control**	
	A	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**
1	*X/Y*											

2												
3												
N												
Total % Mortality ***[OR Immobility]***												

TABLE *[#].* Mean percent survival in *[test organism]* exposed to *[test substance]* for *[test duration]* under *[static-renewal/flow-through]* conditions.

Treatments (CFU/L)	**Mean Percent Survival (%)**
Mean measured concentration 1	
Mean measured concentration 2	
Mean measured concentration 3	
Mean measured concentration 4	
Mean measured concentration n	
Control	
LC_{50} *[insert [>] if greater than]*	
NOEC *[insert [>] if greater than]*	
Positive control, if used *[insert [>] if greater than]*	

[[a] Use superscript and footnote to indicate values significantly different from control.]

SUBLETHAL TOXICITY ENDPOINTS:

TABLE *[#].* *[Sublethal effect, (e.g., growth)]* in *[test organism]* during [test duration] *[acute/chronic]* exposure to *[test substance]* under *[static-renewal/flow-through]* conditions.

Day	***[Sublethal effect]* in *[test organism]***					
	Mean Measured Concentration (CFU/L)					
	$X.XX \times 10^{X}$	$X.XX \times 10^{X}$	$X.XX \times 10^{X}$	$X.XX \times 10^{X}$	$X.XX \times 10^{X}$	Control
1						
2						

3						
4						
5						
n						
EC_{50} *[insert [>] if greater than]*						
Day	***[Sublethal effect]* in *[test organism]***					
	Mean Measured Concentration (CFU/L)					
	X.XX × 10^X	*X.XX* × 10^X	*X.XX* × 10^X	*X.XX* × 10^X	*X.XX* × 10^X	Control
NOEC *[insert [>] if greater than]*						

[Table suitable for testing at multiple concentrations. Modify as appropriate to accommodate differences in experimental design, otherwise delete if maximum hazard concentration was used.]

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

Day	**Mean Body Weight at Beginning and End of Test**		
	Negative Control	**Inactivated *[test substance]***	***[test substance]***
Initiation			
Termination			

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

TABLE *[#].* *[Sublethal effects (e.g., growth,, etc.)]* in *[test organism]* during [test duration] *[acute/chronic]* exposure to *[test substance]* under *[static-renewal/flow-through]* conditions.

Mean Measured Concentration	**Observation Period**		
	endpoint 1* at *Day x	***endpoint 2* at *Day x***	***endpoint 3* at *Day x***
	% Affected	**% Affected**	**% Affected**
Test concentration 1			
Test concentration 2			
Test concentration 3			

Test concentration n			
Control			
EC_{50} *[insert [>] if greater than]*			
NOEC *[insert [>] if greater than]*			
LOEC *[insert [>] if greater than]*			
Positive control, if used % sublethal effect: EC_{50}: *[insert [>] if greater than]*			

[Modify table as appropriate to accommodate differences in experimental design. Alternatively generate one table per endpoint/sublethal effect, if appropriate.]

REPORTED STATISTICS:

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 LC_{50}, LT_{50}, NOEC are greater than the MHC level, use <symbol.]*

Statistical Method:

LC_{50}:
NOEL: 95% C.I.:
Probit Slope:
95% C.I.:

CONCLUSION:
[Summarize the study author's conclusions- Provide the major conclusions e.g., values for LC_{50}, EC_{50}, NOEC were [=, > or <] in appropriate units]

REFERENCES:

Study Type: Acute Honeybees Toxicity (Oral & Contact)
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:
In a *[#]*-day *[oral or dietary]* toxicity and pathogenicity study, *[common name (scientific name)]* were exposed to a *[single OR #]* dose of *[dose amount]* of *[formulation, note its potency, biological activity or concentration per unit weight or volume]* (containing % *a.i. name*) by *[indicate exposure method]*. *[Include other pertinent details such as the controls used.]*
The *[#]*-day LD50 was *[=, > or <] [insert LC50 in appropriate units]* (95% C.I. *-if applicable*). *[If the study included sublethal test endpoints and/or sublethal effects were observed and/or additional subchronic testing was triggered include the following text (otherwise-delete):* The EC50 based on sublethal effects, were *[insert EC50 in appropriate units.]* The NOEC value, based on mortality *[and sublethal effects]*, was *[=, > or <] [insert NOEC in appropriate units]*.
This study is classified as *[acceptable, unacceptable, and supplemental]*. This study was *[not]* conducted in accordance with the guideline recommendations for a *[oral or dietary]* toxicity and pathogenicity study for honey bees (OCSPP 885.4380; PMRA: M9.5.1 and OECD: IIM 8.7, IIIM 10.3) in the *[species]*.

I. MATERIALS AND METHODS:

A. GUIDELINE FOLLOWED:

B. MATERIALS:

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

2. Test Organism:
Species (common and scientific names): *[Indicate the species used.]*
Age at test initiation: *[Give the age of the test organisms.]*
Strain/Source: [Report the strain, supplier and/or source of the test organism.]
Date of collection: *[Insert the date of collection, if applicable.]*

C. STUDY DESIGN AND METHODS:

[Briefly describe the experimental design.]

1. Experimental Methods and Conditions:

Acclimation:
Duration:
Feeding:
Water:
Temperature:
Relative humidity:
Test chamber - description and size:
Route(s) of exposure:
Dose levels / test concentrations:
Nominal:
Measured: *(from confirmation of dose viability)*
Preparation of dose or test concentration:
[Briefly describe methods for dose preparation.]
Solvent/vehicle: *[if used]*
[Describe the type and percentage, if used]

Confirmation of MPCA viability:

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

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

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

Number of bees per chamber:

Control(s): Treatment(s):
Ten bees per replicate (chamber) are preferred.

Number of replicates (chambers) per treatment:

Control(s): Treatment(s):
A minimum of 3 replicate test groups should be dosed with each test concentration, and three replicate controls are required.

Recovery of MPCA from bees: *[if applicable]*

[Describe methods used to recover the MPCA from collected samples.]

No specific recommendations (guidelines developed for chemical toxicity testing).

Feeding:

[Describe the feeding regime used during the experiment.]

Test Conditions

Temperature:
Humidity:
Lighting:

Bees should be held in the dark in an experimental room at a temperature of 25 ± 2°C with a relative humidity of 50% to 70%.

Duration of the study:

The duration of the test is 48h after the test solution has been replaced with sucrose solution alone. If mortality continues to rise by >10% after the first 24h, the test duration should be extended to a maximum of 96h, provided that the control mortality does not exceed 10%.

The duration of the test is 48h. If mortality increases by more than 10% between 24h and 48h, the test duration should be extended up to a maximum of 96h provided that control mortality does not exceed 10%.

2. Observations:

Parameters measured including sub-lethal effects/toxicity symptoms:

[List the parameters measured during the experiment, e.g., mortality, survival, abnormal behavior or appearance, fecundity, growth inhibition, concentration of the MPCA in the test suspensions. Provide references to data summary tables, if used.]

Observation/measurement intervals:

[List time points for each parameter measurement and observation.]

No recommendations are given for environmental parameters such as temperature or humidity. The amount of diet consumed should be determined following treatment (OECD 213 only). Mortality is recorded 4 h after dosing and thereafter at 24 h and 48 h. If a prolonged observation period is required, further assessments should be made at 24 h intervals, up to a maximum of 96h, provided that control mortality does not exceed 10%.

II. RESULTS

A. VIABILITY OF DOSING SUSPENSIONS:

[Summarize the dose verification data and indicate if the tested sample was still viable.]

TABLE *[#].* Viability of *[test substance]* in the *[dosing suspension/diet]* administered to honey bees (*Apis mellifera*) in a *[contact, acute oral or dietary]* test.

Dose Group	Nominal Concentration	Measured Concentration *[units]*
Solvent/vehicle		
Inactivated		
Sterile filtrate		
Maximum hazard		
Negative		

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.]

TABLE *[#].* Effect of *[test material]* on cumulative mortality of honey bees (*Apis mellifera*) in a *[contact, acute oral or dietary]* test.

Treatments *[indicate if nominal or measured (measured*	No. of Bees	Observation					
		Day		*Day*		*Day n*	
		No. Dea	% Mortalit	No. Dea	% Mortali	No. Dea	% Mortalit
Negative control							
Solvent control, if							
test concentration 1							
test concentration 2							
test concentration3							
test concentration 4							
test concentration n							

LD50/LC50 *[insert [>] if greater than]*								
NOEL/NOEC *[insert [>] if greater than]*								
Reference chemical	*Mortality (% or No.)*							
	LD50 : / LC50	*[insert [>] if greater than]*						
	NOEL /	*[insert [>] if greater than]*						

[a Use superscript and footnote to indicate values that are statistically significantly different from control.]

B. SUB-LETHAL TOXICITY EFFECTS:

[Include if any sub-lethal effects are observed- Briefly summarize behavioral abnormalities or other signs of toxicity. Indicate effects that were related to the *test-material. Compare sub-lethal effects with control treatment and/or the reference chemical. 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 *[#].* Effect of *[test material]* on *[endpoint]* of honey bees (*Apis mellifera*) in a *[contact, acute oral or dietary]* test.

Treatments *[indicate if nominal or measured (measured*	**Observation**					
	Day		***Day***		***Day***	
	endpoint 1	**% Affect**	***endpoint 2***	**% Affecte**	***endpoint n***	**% Affected**
Negative control						
Solvent control, if used						
test concentration 1						
test concentration 2						
test concentration3						
test concentration 4						
test concentration n						

ED50/EC50 or other sublethal endpoint *[insert [>]*							
NOEL/NOEC *[insert [>] if greater*							
Reference chemical	*LC50/*	*[insert [>] if greater than]*					
	NOEL/	*[insert [>] if greater than]*					

C. REPORTED STATISTICS:

[If applicable- List the parameters that were analyzed and the statistical tests that were performed.]

D. **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.]

	LD50:	95% C.I.:
	LC50:	95% C.I.:
	NOEL:	
	NOEC:	
	Probit Slope:	95% C.I.:
	Endpoint(s) Affected:	
III.	**CONCLUSION**	
A.	**CONCLUSION:**	*[Summarize the study author's conclusions- Provide the*

Conclusions e.g., values for LD50, LC50, LT50, EC50, NOEL, NOEC, etc. were [=, > or <] insert final dose concentration/level (in appropriate units).]

III. REFERENCES

TOXICOLOGY SCRUTINY TEMPLATE
[PHEROMONESSEMIO-CHEMICALS]

Sponsor:
Test Facility Name & GLP Validity:
GLP (Yes/No):
Test Material (% a. i.): (CAS#), Lot/ Batch No.#:

Study Type: Acute Oral Toxicity Rat
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:
Executive Summary:
In an acute oral toxicity study groups (#/sex) of strain, species (source), (age, weight) were given a single oral dose of (formulation/technical, note a.i. and %) in (vehicle or undiluted test article) at doses of??? or??mg/kg bw. Animals were then observed for (#) days.
Study Endpoints:
Oral LD_{50} Males = mg/kg bw
Oral LD_{50} Females = mg/kg bw
Oral LD_{50}Combined = mg/kg bw
Toxicity based on the LD_{50} in males or females which ever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV. Label comment if applicable.
This acute oral study is classified as acceptable. It does satisfy the guideline requirement for an acute oral study (OECD 423/425 etc.) in the rat.
Compliance:
Signed and dated GLP Compliance Statement, Quality Assurance Statement and Data Confidentiality statements will be provided.
RESULTS and DISCUSSION:

Dose (mg/kg b.w)	**Mortality/Number Tested**		
	Males	**Females**	**Combined**

Statistics/If any: The oral LD_{50} was calculated using the

A. **Morality:** as noted in table.
B. **Clinical sings & symptoms:**
C. **Gross Necropsy:**
D. **Conclusions:**

Study Type: Acute Dermal Toxicity Rat
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:
In an acute dermal toxicity study, groups (#/sex) of strain, species (source), (age, weight) were dermally exposed to (formulation/technical, note a.i. and %) in (vehicle or undiluted test article) to (% or amount of body surface area) at doses of, or mg/kg bw. Test sites were covered with a(n) occlusive/semi-occlusive dressing for (#) hours. Animals were then observed for (#) days.
Study End Points:
Dermal LD_{50} Males = mg/kg bw
Females = mg/kg bw
Combined = mg/kg bw
Toxicity: based on the LD_{50} in (males or females which ever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV. Label comment if applicable.
This acute dermal study is classified acceptable. It does satisfy the guideline requirement for an acute dermal study (OECD 402 etc.) in the rat.
Compliance:
Signed and dated GLP Compliance Statement, Quality Assurance Statement and Data Confidentiality statements will be provided.

RESULTS and DISCUSSION:

Dose (mg/kg bw)	Mortality/Number Tested		
	Males	Females	Combined

Statistics/If any: The dermal LD_{50} was calculated using the
A. Mortality: as noted in table:
B. Clinical signs & symptoms:
C. Gross Necropsy:
D. Conclusions:

Study Type: Acute Inhalation Toxicity Rat
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:
Executive Summary:
In an acute inhalation toxicity study, groups (#/sex) of strain, species (source), (age, weight) were exposed (nose only, head only or whole body) via the inhalation route to (formulation/technical, note a.i. and %) in (name of vehicle or undiluted test article) for [#] hours at concentrations of mg/L. Animals were then observed for [#] days.
Study Endpoints:
LC_{50} Males = mg/L
LC_{50} Females = mg/L
LC_{50} Combined = mg/L
Toxicity: based on (males or females which ever is lower, or lack of deaths at the limit dose) GHS/EPA Toxicity Category I, II, III, IV. Label comment if applicable.
This acute inhalation study is classified as acceptable. It does satisfy the guideline requirement for an acute inhalation study (OECD 403 etc.) in the rat.
Compliance:
Signed and dated GLP Compliance Statement, Quality Assurance Statement and Data Confidentiality Statements will be provided.
RESULTS and DISCUSSION:

Nominal Conc. (mg/L)	Actual Conc. (mg/L)	MMAD Φm	GSD Φm	Mortality/Number Tested		
				Males	Females	Combined

Test Atmosphere /Chamber Description:

Chamber Volume:	**L**
Airflow:	**LPM**
Temperature:	**EC or EF**
Relative Humidity:	**%**
Time to Equilibrium:	**min.**

Test atmosphere concentration
Particle size determination
Statistics/if any: The LC_{50} was calculated using the
A. Mortality: as noted in table.
B. Clinical signs & symptoms:
C. Gross Necropsy:
D. Conclusions:

Study Type: Acute Eye Irritation Rabbit.
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:
In an acute eye irritation study, (volume or weight of test material applied) of (formulation/technical, note a.i. and %) in (name of vehicle if appropriate, or undiluted test material) was instilled into the conjunctival sac of (which eye) of (#/sex), (strain), (species - rabbits) (source, age, weight) for [#] hours. (Note if eyes were washed) Animals were then observed for *[#]* days. Irritation was scored by the method as per guideline.
In this study, formulation/technical is not an eye irritant OR is minimally, mildly, moderately, severely, extremely irritating to the eye based on [(indicate basis - list MAS (of 24, 48 and 72 hrs) and MIS (state time recorded)] GHS/EPA Toxicity Category I, II, III, IV if joint review. Label comment if applicable.
This study is classified as acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OECD 405 etc.) in the rabbit.
Compliance:
Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.
RESULTS AND DISCUSSION:

	Number "positive"/number tested							
	Hours				**Days**			
Observations	1	24	48	72	4	7	14	21
Corneal Opacity								
Iritis								
Conjunctivae:								
Redness								
Chemosis								
Discharge								

A. Observations:

B. Conclusions:

Study Type: Acute Dermal Irritation/primary Skin Irritation Rabbit
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:

In a primary skin irritation study, (#/sex) strain, species (source), (age, weight) were dermally exposed to (volume or weight of test material applied) of (formulation/technical, note a.i. and %) in (name of vehicle or undiluted test material) to (% or amount of body surface area - state location of test site). Test sites were covered with a(n) occlusive/semi-occlusive dressing for (#) hours. Animals were then observed for [#] days. Irritation was scored by the method of (cite method).

In this study, formulation/technical is not a dermal irritating OR is corrosive to the skin based on... [Indicate basis - list MAS (of 24, 48 and 72 h) and MIS (state time recorded) GHS/EPA Toxicity Category I, II, III, IV. Label comment if applicable.

This study is classified as acceptable. It does satisfy the guideline requirement for a primary dermal irritation study (OECD 404 etc.) in the rabbit.

Compliance:

Signed and dated GLP Compliance Statement, Quality Assurance Statement and Data Confidentiality statements will be provided.

RESULTS and DISCUSSION:

A. Observations:

B. Results:

C. Conclusions:

Study Type: Skin Sensitization Guinea Pig/LLNA
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:
In a dermal sensitization study with (formulation/technical, note a.i. and %) in (name of vehicle if appropriate or undiluted test article), strain, species (source)(age, weight) were tested using the method of (cite study type). Identify positive control material. List clinical signs (systemic and local for LLNA) and mortality. Necropsy results for LLNA **if significant**.
In this study, **Formulation/technical is not a dermal sensitizer or...** Label comment if applicable. This study is classified as acceptable. It does satisfy the guideline requirement for a dermal sensitization study (OECD 406, 429) in the Guinea pig .
Compliance:
Signed and dated GLP Compliance Statement, Quality Assurance Statement and Data Confidentiality statements will be provided.
(For traditional sensitization tests, otherwise delete; for LLNA, see below)
I. PROCEDURE
A. Induction:
B. Challenge -
C. Naive Controls -
II. RESULTS and DISCUSSION:
A. Reactions and duration:
B. Positive control:
C. Conclusions:
(For LLNA, otherwise delete)

I. MATERIALS and METHODS

1.	**Radio Isotope**	(as named in study)
	Description:	(e.g. technical, nature, color, stability)
	Lot/Batch #:	
	Radio-Purity:	(purity and radio-purity)
	CAS #:	
	Date of Isotope Activity Assay:	
	Date of use in bio-Assay:	

2. Vehicle and/or positive control:
(4:1 acetone/olive oil, N,N-dimethylformamide, methyl ethyl ketone, propylene glycol or dimethyl sulfoxide - If the vehicle used is not from the preceding list a rationale must be provided)./ Positive control should be hexyl cinnamic aldehyde or mercaptobenzothiazole dissolved in 4:1 AOO unless a rationale is provided.

3. Animal assignment and treatment:

4. Dose selection rationale:

5. Treatment preparation and administration:

25 µl of compound x was applied to the entire dorsal surface of each ear of each mouse. The application was repeated on days 2 and 3. On day 6 an injection of 250 µl phosphate buffered saline (PBS) containing 20 µCi of ^{3}H-methyl thymidine (^{3}H-TdR) or 250 µl PBS containing 2 µCi of ^{125} I-iododeoxy-uridine (^{125}IU) and 10^{-5} M fluorodeoxy-uridine was made into the tail vein of each experimental mouse. Five hours later, the draining Auricular lymph node of each ear was excised into PBS. A single cell suspension of lymph node cells was prepared from each mouse. (Describe method of cell suspension). Cells were precipitated with 5% trichloroacetic acid at 4 ^{B}C for 18 hours.

6. Statistics:

The following statistical procedures were employed (e.g., linear regression analysis to assess dose-response trends; Dunnett =s test to make pairwise comparisons).

7. Range finding study (if conducted):

II. RESULTS and DISCUSSION:

A. Disintegrations per Minute/Mouse (group means):

Sample Description Test or Control Group	Animal #	Individual Animal DPM [a]	Group Mean DPM ∀ (SE)	Stimulation Index (SI)*
Vehicle	1			
	2			
	3			
	4			
	5			
Low	1			
	2			
	3			
	4			
	5			
Medium	1			
	2			
	3			
	4			
	5			
High	1			
	2			
	3			
	4			
	5			
Positive control	1			
	2			
	3			
	4			
	5			

a) PMRA: Pooled animal data is also acceptable (minimum of 4 animals/group)

*** SI = Group mean DPM) Vehicle control mean DPM**

B. Stimulation Index:

Sample Description Test or Control Group	**Vehicle**	**Low**	**Medium**	**High**	**Positive Control**
Stimulation Index (SI)					
EC3[b]					

b) EC3 is the minimum concentration required to elicit a sensitization reaction (interpolated)
SI = Group Mean DPM) Vehicle control mean DPM
EC3 = C + [(3-D) / (B-D)] * (A-C)
Where (C, D) fall below SI of 3 (C = concentration, D = SI)
(A, B) fall above SI of 3 (A = concentration, B = SI)

C. Conclusions:

Study Type: Sub-acute Oral Toxicity Rat (90-days)
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:
Executive Summary:
In a 90-day oral toxicity study test substance (technical/formulation was administered to *[(# of animals) species, strain]*/sex/dose in *[diet, water, by gavage]* at dose levels of 0, x, x, or x ppm (equivalent to 0, x, x, x mg/kg bw/day).
[Describe toxicity briefly following instructions for exec summary paragraph 2. If there is no toxicity, state that there were no compound related effects on mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology. ***Note:*** *if there was a NOAEL for clinical findings and when they occurred (for acute reference dose consideration during subsequent risk assessment.)]*.
The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material:		*[as named in study]*
	Description:	*[e.g., technical, nature, color, stability]*
	Lot/Batch #:	
	Purity:	% a.i.
	Compound Stability:	
	CAS # of TGAI:	
		[Structure]

2. Vehicle and/or positive control: *[when appropriate]*, Lot/Batch #; Purity

3. Test animals:			
	Species:		
	Strain:		
	Age/weight at study initiation:		
	Source:		
	Housing:		
	Diet:	*[describe] ad libitum*	
	Water:	*[describe] ad libitum*	
	Environmental conditions:	**Temperature:**	EC
		Humidity:	%
		Air changes:	/hr
		Photoperiod:	hrs dark/ hrs light

	Acclimation period:	

B. STUDY DESIGN:

1. Animal assignment: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design *[change heading and units as appropriate for method of administration]*

Test Group	Conc. in Diet *(units)*	Dose to Animal *(units)*	# Male	# Female
Control				
Low				
Mid				
High				

2. Dose selection rationale:

The dose levels were selected based on the results from *[state study type(s)]* where *[route]*-administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available.]*

3. Diet preparation and analysis:

Diet was prepared *[how often]* by mixing appropriate amounts of test substance with *[type of food eg. Purina Certified Rodent Diet #5001]* and was stored at ___ temperature. Homogeneity and stability were tested at *[how often]*. During the study, samples of treated food were analyzed *[when and at what dose levels]* for stability and concentration.

Results: Homogeneity Analysis: *[range]*

Stability Analysis: *[range of values]*

Concentration Analysis: *[range of values]*

4. Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. METHODS:

1. Observations:

1a. Cage side Observations

Animals were inspected *[frequency]* for signs of toxicity and mortality.

1b. Clinical Examinations

Clinical examinations were conducted [*frequency*].

1c. Neurological Evaluations

The following evaluations (measurements) were performed on day *[insert treatment day: [list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*

2. Body weight:

Animals were weighed *[frequency]*.

3. Food consumption and compound intake: *[if feeding study]*

Food consumption for each animal was determined and mean daily diet consumption was calculated as g food/kg body weight/day. Food efficiency *[if given] [body weight gain in kg/food consumption*

in kg per unit time X 100] and compound intake (mg/kg bw/day) values were calculated as time-weighted averages from the consumption and body weight gain data.

4. Ophthalmoscopic examination:

Eyes were examined [*when - before test and at termination?, which dose groups - control and high dose or all groups?]*

5. Hematology & Clinical Chemistry:

Blood was collected *[were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.

a. Hematology

	Hematocrit (HCT)*	Leukocyte differential count*
	Hemoglobin (HGB)*	Mean corpuscular HGB (MCH)*
	Leukocyte count (WBC)*	Mean corpusc. HGB conc.(MCHC)*
	Erythrocyte count (RBC)*	Mean corpusc. volume (MCV)*
	Platelet count*	Reticulocyte count
	Blood clotting measurements*	
	(Thromboplastin time)	
	(Clotting time)	
	(Prothrombin time)	

* Recommended for 90-day oral rodent studies based on Guideline 870.3100

Clinical Chemistry

	ELECTROLYTES	**OTHER**
	Calcium	Albumin*
	Chloride	Creatinine*
	Magnesium	Urea nitrogen*
	Phosphorus	Total Cholesterol*
	Potassium*	Globulins
	Sodium*	Glucose*
	ENZYMES	Total bilirubin
	Alkaline phosphatase (ALK)*	Total protein (TP)*
	Cholinesterase (ChE)	Triglycerides
	Creatine phosphokinase	Serum protein electrophoresis
	Lactic acid dehydrogenase (LDH)	
	Alanine aminotransferase (ALT/also SGPT)*	
	Aspartate aminotransferase (AST/also SGOT)*	
	Sorbitol dehydrogenase*	
	Gamma glutamyl transferase (GGT)*	
	Glutamate dehydrogenase	

* Recommended for 90-day oral rodent studies based on Guideline 870.3100

6. Urinalysis

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

	Appearance*	Glucose
	Volume*	Ketones
	Specific gravity/osmolality*	Bilirubin
	pH*	Blood/blood cells*
	Sediment (microscopic)	Nitrate
	Protein*	Urobilinogen

1 Optional for 90-day oral rodent studies

* Recommended for 90-day oral rodent studies

7. Sacrifice and Pathology

All animals that died and those sacrificed on schedule were subjected to gross pathological examination and the CHECKED (X) tissues were collected for histological examination *[note if not all collected tissues were examined]*. The (XX) organs, in addition, were weighed.

	DIGESTIVE SYSTEM	**CARDIOVASC./HEMAT.**	**NEUROLOGIC**
	Tongue	Aorta*	Brain*+
	Salivary glands*	Heart*+	Peripheral nerve*
	Esophagus*	Bone marrow*	Spinal cord (3 levels)*
	Stomach*	Lymph nodes*	Pituitary*
	Duodenum*	Spleen*+	Eyes (optic nerve)*
	Jejunum*	Thymus*+	**GLANDULAR**
	Ileum*		Adrenal gland*+
	Cecum*	**UROGENITAL**	Lacrimal gland
	Colon*	Kidneys*+	Parathyroid*
	Rectum*	Urinary bladder*	Thyroid*
	Liver*+	Testes*+	**OTHER**
	Gall bladder (not rat)*	Epididymides*+	Bone (sternum and/or femur)
	Bile duct (rat)	Prostate*	Skeletal muscle
	Pancreas*	Seminal vesicles*	Skin*
	RESPIRATORY	Ovaries*+	All gross lesions and
	Trachea*	Uterus*+	
	Lung*	Mammary gland*	
	Nose*		
	Pharynx*		
	Larynx*		

* Recommended for 90-day oral rodent studies based on Guideline 870.3100

+ Organ weights required for rodent studies.

II. RESULTS: *[describe findings, include tables if needed; tables are recommended to depict any treatment-related findings, thus limiting use of text to highlight specific points]*:

A. OBSERVATIONS:

1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*

2. Mortality:

3. Neurological Evaluations -

B. BODY WEIGHT AND WEIGHT GAIN: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment-related effect]*

TABLE 2. Average body weights and body weight gains during 90 days of treatment

Dose rate [insert units]	Body Weights (g∀SD)				Total Weight Gain	
	Week -1	Week 1	Week 7	Week 13	g	% of control
Male						
0						
Low						
Mid						
High						
Female						
0						
Low						
Mid						
High						

[a] Data obtained from pages *(insert page #s)* in the study report.

* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

C. FOOD CONSUMPTION AND COMPOUND INTAKE *[if feeding study]*:

1. Food consumption:

2. Compound consumption: *[time-weighted average] [include compound intake in table 1]* -

3. Food efficiency: *[if relevant] - [relate to any changes in body weight]*

D. OPHTHALMOSCOPIC EXAMINATION:

E. BLOOD ANALYSES: *[Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]*:

1. Hematology: *[relate to any histological findings]*
2. Clinical Chemistry: *[relate to any histological findings]*
F. Urinalysis:
G. SACRIFICE AND PATHOLOGY: [*Tables are recommended for treatment-related findings; limit text to integration of findings, highlights]*
1. Organ weight - *[absolute and relative as appropriate, relate to any histological changes]*
2. Gross pathology -
3. Microscopic pathology - *[relate with other findings, as appropriate]*
III. INVESTIGATORS' DISCUSSION AND CONCLUSIONS:
[Note any deficiencies and how they impact on the study results and interpretation, if at all. Include the following points in your discussion/conclusions section.]
[Describe the significant findings and provide justification for the conclusions.

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.]

Study Type: Sub-acute Dermal Toxicity-Rat
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:
In a 28-day dermal toxicity study test substance was applied to the shaved skin of *[(# of animals) species, strain]*/sex/dose at dose levels of 0, x, x, x mg/kg bw/day, 6 hours/day for 5 days/week during a 28-day period.
[Describe toxicity briefly. If there is no toxicity, state that there were no compound related effects in mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology. Note if there was a LOAEL/NOAEL for clinical findings (for acute reference dose consideration during subsequent risk assessment)].

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material:		*[as named in study]*
	Description:	*[e.g., technical, nature, color, stability]*
	Lot/Batch #:	
	Purity:	% a.i.
	Compound Stability:	
	CAS #:	
		[Structure]

2. Vehicle and/or positive control: *[when appropriate]*, Lot/Batch #; Purity

3. Test animals:			
	Species:		
	Strain:		
	Age/weight at study initiation:		
	Source:		
	Housing:		
	Diet:	*[describe] ad libitum*	
	Water:	*[describe] ad libitum*	
	Environmental conditions:	**Temperature:**	EC
		Humidity:	%
		Air changes:	/hr
		Photoperiod	hrs dark/ hrs light

		:	
	Acclimation period:		

B. STUDY DESIGN:

1. In life dates - Start: End:

2. Animal assignment: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design: *[change heading and units as appropriate]*

Test Group **Control**	**Dose (mg/kg bw/d)**	**# Male**	**# Female**
Low **Mid** **High**			

3. Dose selection rationale

The dose levels were selected based on the results from *[state study type(s)]* where *[route]*-administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available.]*

4. Preparation and treatment of animal skin

Shortly before the first application and weekly thereafter, the fur of each test animal was clipped from the dorsal area of the trunk over an area of at least 10% of the body surface *[include any other relevant details regarding preparation of the test area]*. The applied quantities of the test substance were adjusted weekly to individual animal body weight. The test substance/vehicle suspension was evenly dispersed on gauze patches that were then applied to the clipped skin, loosely covered with aluminum foil, and fastened to the body with non-irritating, adhesive tape. The dressings were removed after 6 hours and the application areas were cleaned with lukewarm water.

Rats in the control group were exposed to the vehicle using the same procedure as described for the treated rats.

5. Statistics: *[list parameters that were analyzed and the statistical methods used]*

C. METHODS:

1. Observations: *[Example below]*

1a. Cage side Observations

Animals were observed daily for signs of mortality, toxicity, and the presence of dermal irritation. The animals were examined for signs of local skin irritation approximately 17 hours after removing the gauze patches and were evaluated using the Draize method.

1b. Clinical Examinations: Clinical examinations were conducted [*frequency*].

1c. Neurological Evaluations:

The following evaluations (measurements) were performed on day *[insert treatment day]*: *[list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*

2. Body weight: *[Example below]*
Animals were weighed prior to initiation of the study and at the beginning of each study week.
3. Food consumption: *[Example below]*
Food consumption was determined weekly *[individually or by cage]* from the weight of the offered diet at the beginning of a specific week and its difference to the re-weight amount after several days. Mean food consumption was reported as g food/animal/*[day or week]*. Food consumption ratios were calculated [frequency e.g., weekly].
4. Ophthalmoscopic examination: Eyes were examined [*when - before test and at termination?, which dose groups - control and high dose or all groups?]*
5. Hematology & Clinical Chemistry: Blood was collected *[from where? were animals fasted? time of collection and how many animals]* for hematology and clinical chemistry from all surviving animals. The CHECKED (X) parameters were examined.
a. Hematology

	Hematocrit (HCT)*	Leukocyte differential count*
	Hemoglobin (HGB)*	Mean corpuscular HGB (MCH)*
	Leukocyte count (WBC)*	Mean corpusc. HGB conc.(MCHC)*
	Erythrocyte count (RBC)*	Mean corpusc. volume (MCV)*
	Platelet count*	Reticulocyte count
	Blood clotting measurements*	
	(Thromboplastin time)	
	(Clotting time)	
	(Prothrombin time)	

* Recommended for 28-day dermal toxicity studies based on Guideline 870.3200

b. Clinical Chemistry

	ELECTROLYTES	OTHER
	Calcium	Albumin*
	Chloride	Creatinine*
	Magnesium	Urea nitrogen*
	Phosphorus	Total Cholesterol*
	Potassium* (K)	Globulins
	Sodium* (NA)	Glucose*
	ENZYMES (more than 2 hepatic enzymes, eg., *)	Total bilirubin
	Alkaline phosphatase (AP)*	Total protein*
	Cholinesterase (ChE)	Triglycerides
	Creatine phosphokinase	Serum protein electrophoresis
	Lactic acid dehydrogenase (LDH)	
	Alanine aminotransferase (ALT/also SGPT)*	
	Aspartate aminotransferase (AST/also SGOT)*	
	Gamma glutamyl transferase (GGT)*	
	Glutamate dehydrogenase	
	Sorbitol dehydrogenase*	

* Recommended for 28-day dermal toxicity studies based on Guideline 870.3200

6. Urinalysis*

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

	Appearance*	Glucose*
	Volume*	Ketones
	Specific gravity / osmolality*	Bilirubin
	pH*	Blood / blood cells*
	Sediment (microscopic)	Nitrate
	Protein*	Urobilinogen

* Optional for 28-day dermal toxicity studies

7. Sacrifice and Pathology

All animals were sacrificed on schedule and subjected to gross pathological examination. The CHECKED (X) tissues were collected for histological examination. The (XX) organs, in addition, were weighed.

	DIGESTIVE SYSTEM	CARDIOVASC./HEMAT.	NEUROLOGIC
	Tongue	Aorta, thoracic*	Brain*+
	Salivary glands*	Heart*+	Peripheral nerve*
	Esophagus*	Bone marrow*	Spinal cord (3 levels)*

	Stomach* Duodenum* Jejunum* Ileum* Cecum* Colon* Rectum* Liver*+ Gall bladder* (not rat) Bile duct* (rat) Pancreas* **RESPIRATORY** Trachea* Lung* Nose* Pharynx* Larynx*	Lymph nodes* Spleen*+ Thymus*+ **UROGENITAL** Kidneys*+ Urinary bladder* Testes*+ Epididymides*+ Prostate* Seminal vesicles* Ovaries*+ Uterus*+ Mammary gland*	Pituitary* Eyes (optic nerve)* **GLANDULAR** Adrenal gland*+ Lacrimal gland Parathyroid* Thyroid* **OTHER** Bone (sternum and/or femur) Skeletal muscle Skin* (treated & untreated areas) All gross lesions and

* Recommended for 28-day dermal toxicity studies based on Guideline 870.3200
\+ Organ weights required.

II. RESULTS [*describe findings, include tables if needed]*

A. OBSERVATIONs:

1. Clinical signs of toxicity: *[include cage side observations and clinical examinations; note when signs were first observed]*

2. Mortality: *[indicate if any animals died]*

3. Neurological Evaluations:

4. Dermal Irritation: *[Describe any dermal effects]*

B. BODY WEIGHT AND WEIGHT GAIN: *[include a table of body weight gain when there is a treatment related effect]*

TABLE 2. Average body weights and body weight gains during XX days of treatment

Dose rate [insert units]	**Body Weights (g∀SD)**				**Total Weight Gain**	
	Week -1	**Week 1**	**Week X**	**Week X**	**g**	**% of control**
Male						
0						

Low						
Mid						
High						
Female						
0						
Low						
Mid						
High						

[a] Data obtained from pages *(insert page #s)* in the study report.
* Statistically different ($p < 0.05$) from the control.
** Statistically different ($p < 0.01$) from the control.

C. FOOD CONSUMPTION AND EFFICIENCY:

1. Food consumption:

2. Food efficiency: *[if relevant] - [relate to any changes in body weight]*

D. OPHTHALMOSCOPIC EXAMINATION:

E. BLOOD ANALYSES: *[Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]*

1. Hematology: *[relate to any histological findings]*

2. Clinical Chemistry: *[relate to any histological findings]*

F. URINALYSIS (if done)

G. Sacrifice and Pathology: *[Tables are OPTIONAL, but recommended for treatment-related findings; limit text to integration of findings, highlights]*

1. Organ weight - *[absolute and relative as appropriate, relate to any histological changes]*

2. Gross pathology -

3. Microscopic pathology - *[relate with other findings, as appropriate]*

III. INVESTIGATORS' DISCUSSION AND CONCLUSIONS:

[Note any deficiencies and how they impact on the study results and interpretation, if at all. Include the following points in your discussion/conclusion section.]

[Describe the significant findings and provide justification for the conclusions.]

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

Study Type: Sub-acute Inhalation Toxicity (28-day)-Rat
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Investigators' Executive Summary:
In a sub-chronic inhalation toxicity study test substance was administered to *[(# of animals) species, strain]*/sex/concentration by dynamic *[nose only, head only or whole body]* exposure at concentrations of 0, x, x, x mg/L for x hours per day, x days/week for a total of x days *(include concentrations in units reported in the study as well as mg/L conversion).*
[Describe toxicity briefly. If there is no toxicity, state that there were no compound related effects in mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology. Note if there was a LOAEL/NOAEL for clinical findings (for acute reference dose consideration during subsequent risk assessment)].
The LOAEL is mg/L/day, based on the NOAEL is mg/L/day.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material:		*[as named in study]*
	Description:	*[e.g., technical, nature, color, stability]*
	Lot/Batch #:	
	Purity:	% a.i.
	Compound Stability:	
	CAS # of TGAI:	
		[Structure]

2. Vehicle and/or positive control: *[when appropriate]*, Lot/Batch #; Purity

3. Test animals:			
	Species:		
	Strain:		
	Age/weight at study initiation:		
	Source:		
	Housing:		
	Diet:	*[describe]* *ad libitum* (except during exposure)	
	Water:	*[describe]* *ad libitum*	
	Environmental conditions:	**Temperature:**	EC
		Humidity:	%
		Air	/hr
			hrs dark/ hrs light

		changes: Photoperiod:	
	Acclimation period:		

B. STUDY DESIGN:

1. In life dates Start: End:

2. Animal assignment

Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: Study design

Test group	Nominal Conc. (mg/L)	Analytical Conc. (mg/L)	MMAD Φm	GSD	Rats/sex
Control					
Low (LCT)					
Mid (MCT)					
High (HCT)					

3. Dose selection rationale

The dose levels were selected based on the results from *[state study type(s)]* where *[route-*administration of up to *[dose]* resulted in *[state effects]. [Use data from range-finding study if available.]*

4. Generation of the test atmosphere / chamber description:

Time to equilibrium was .

Analytical Chemistry .

Test atmosphere concentration *[give method and results]*. Results are in table 1 above.

Particle size determination [*give method and results]*. Results are in table 1 above.

5. Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. METHODS:

1. Observations:

1a. Cage side Observations

Animals were inspected *[frequency]* for signs of toxicity and mortality.

1b. Clinical Examinations

Clinical examinations were conducted [*frequency*].

1c. Neurological Evaluations

The following evaluations (measurements) were performed on day *[insert treatment day]*: *[list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*.

2. Body weight:

Animals were weighed *[frequency]*.

3. Food consumption:

Food consumption for each animal was determined and mean daily diet consumption was calculated as g food/kg body weight/day. Food efficiency *[if given] [body weight gain in kg/food consumption in kg per unit time X 100]* and compound intake (mg/kg bw/day) values were calculated as time-weighted averages from the consumption and body weight gain data.

4. Ophthalmoscopic examination:

Eyes were examined *[when - before test and at termination?, which exposure groups - control and high concentration or all groups?]*

5. Hematology & Clinical Chemistry:

Blood was collected *[were animals fasted? time and site of collection and how many animals]* for hematology and clinical analysis from all surviving animals. The CHECKED (X) parameters were examined.

a. Hematology

	Hematocrit (HCT)*	Leukocyte differential count*
	Hemoglobin (HGB)*	Mean corpuscular HGB (MCH)*
	Leukocyte count (WBC)*	Mean corpusc. HGB conc.(MCHC)*
	Erythrocyte count (RBC)*	Mean corpusc. volume (MCV)*
	Platelet count*	Reticulocyte count
	Blood clotting measurements*	
	(Thromboplastin time)	
	(Clotting time)	
	(Prothrombin time)	

* Recommended for subchronic inhalation studies based on Guideline 870.3465

b. Clinical Chemistry

	ELECTROLYTES	**OTHER**
	Calcium	Albumin*
	Chloride	Creatinine*
	Magnesium	Urea nitrogen*
	Phosphorus	Total Cholesterol*
	Potassium*	Globulins
	Sodium*	Glucose*
	ENZYMES (more than 2 hepatic enzymes eg., *)	Total bilirubin
	Alkaline phosphatase*	Total serum protein (TP)*
	Cholinesterase (ChE)	Triglycerides
	Creatine phosphokinase	Serum protein electrophoresis
	Lactic acid dehydrogenase (LDH)	
	Alanine aminotransferase (ALT/also SGPT)*	
	Aspartate aminotransferase (AST/also	

	SGOT)* Sorbitol dehydrogenase* Gamma glutamyl transferase (GGT)* Glutamate dehydrogenase	

* Recommended for subchronic inhalation studies based on Guideline 870.3465

6. Urinalysis*

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

	Appearance* Volume* Specific gravity / osmolality* pH* Sediment (microscopic) Protein*	Glucose* Ketones Bilirubin Blood / blood cells* Nitrate Urobilinogen

* Optional for inhalation toxicity studies

7. Sacrifice and Pathology

All animals that died and those sacrificed on schedule were subjected to gross pathological examination and the CHECKED (X) tissues were collected for histological examination *[note if not all collected tissues were examined]*. The (XX) organs, in addition, were weighed.

	DIGESTIVE SYSTEM Tongue Salivary glands* Esophagus* Stomach* Duodenum* Jejunum* Ileum* Cecum* Colon* Rectum* Liver*+ Gall bladder* (not rat) Bile duct* (rat) Pancreas* **RESPIRATORY** Trachea*	**CARDIOVASC./HEMAT.** Aorta, thoracic* Heart*+ Bone marrow* Lymph nodes* Spleen*+ Thymus*+ **UROGENITAL** Kidneys*+ Urinary bladder* Testes*+ Epididymides*+ Prostate* Seminal vesicles* Ovaries*+ Uterus*+	**NEUROLOGIC** Brain*+ Peripheral nerve* Spinal cord (3 levels)* Pituitary* Eyes (optic nerve)* **GLANDULAR** Adrenal gland*+ Lacrimal gland Parathyroid* Thyroid* **OTHER** Bone (sternum and/or femur) Skeletal muscle Skin All gross lesions and

	Lung* Nose* Pharynx* Larynx*	Mammary gland*	

* Recommended for subchronic rodent studies based on Guideline 870.3465
\+ Organ weights required

II. RESULTS [*describe findings, include tables if needed]*

A. OBSERVATIONS:

1. Clinical signs of toxicity - *[include cage side observations and clinical examinations; note when signs were first observed]*

2. Mortality

3. Neurological Evaluations

B. BODY WEIGHT AND WEIGHT GAIN: *[include a table of body weight gain, especially 0-30, 30-60, 60-90 days, only when there is a treatment related effect.*

TABLE 2. Average body weights and body weight gains during 90 days of treatment *[SAMPLE - some form of this table is required when there is a treatment-related effect].*

Analytical Concentration (mg/L)	Body Weights (g∀SD)				Total Weight Gain	
	Week -1	Week 1	Week 7	Week 13	g	% of control
Male						
0						
LCT						
MCT						
HCT						
Female						
0						
LCT						
MCT						
HCT						

[a] Data obtained from pages *(insert page #s)* in the study report.
* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

C. FOOD CONSUMPTION:

1. Food consumption

2. Food efficiency *[if relevant] - [relate to any changes in body weight]*

D. OPHTHALMOSCOPIC EXAMINATION -

E. BLOOD ANALYSES: *[Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]*

1. Hematology: *[relate to any histological findings]*

2. Clinical Chemistry: *[relate to any histological findings]*

F. URINALYSIS - *[if done - relate to any histological findings]*

G. SACRIFICE AND PATHOLOGY: *[Tables are OPTIONAL, but recommended for treatment-related findings; limit text to integration of findings, highlights]*

1. Organ weight - *[absolute and relative as appropriate, relate to any histological changes]*

2. Gross pathology -

3. Microscopic pathology - *[relate with other findings, as appropriate]*

III. INVESTIGATORS' DISCUSSION AND CONCLUSIONS: *[Note any deficiencies and how they impact on the study results and interpretation, if at all. Include the following points in your discussion/conclusions section.]*

[Describe the significant findings and provide justification for the conclusion.]

Study Type: Neuro-behavioral Toxicity /Acute Neurotoxicity Rodent
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:
In an acute neurotoxicity study, grups of *(fasted)*, *(age) (strain) (species) (#/sex)* were given a single oral dose of *(chemical name (% a.i., batch/lot #)* in *(name of vehicle)* at doses of x, x, or x mg/kg bw and observed for *(#)* days. Neurobehavioral assessment (functional observational battery and motor activity testing) was performed in *[number]* animals/sex/group *[at what time points]*. *[If applicable]* Cholinesterase activity was determined by the *[?]* method in *X* rats/sex/dose in plasma and erythrocytes *[at what time points]*, and in *[# of regions or whole]* brain *[at what time points]*. At study termination, *[how many?]* animals/sex/group were euthanized and perfused [*in situ*] for neuropathological examination. Of the perfused animals, *[how many from which groups?]* were subjected to histopathological evaluation of brain and peripheral nervous system tissues.
[Any additional measures should be included in procedures section above.]
Discuss findings at low, mid- and high doses. Include only major treatment related clinical signs, FOB findings, motor activity changes, body weight or brain weight changes or gross and histopathology or neuropathology, including onset and/or duration if any, or the following statement: There were no treatment related effects on mortality, clinical signs, body weight, brain weight or gross and histologic pathology or neuropathology. FOB and motor activity testing revealed no treatment-related effects. Note if there was a NOAEL for acute neurotoxicity (for acute reference dose consideration during subsequent risk assessment.)
Based on the effects seen in this study, the LOAEL was *xxx mg/kg bw/day (based on xxx)*, with a NOAEL *of xxx mg/kg bw/day.*
[If applicable]
The LOAEL for plasma cholinesterase inhibition was *xxx mg/kg bw/day*, with a NOAEL of *xxx mg/kg bw/day*.
The LOAEL for erythrocyte cholinesterase inhibition was *xxx mg/kg bw/day*, with a NOAEL of *xxx mg/kg bw/day*.
The LOAEL for brain cholinesterase inhibition was *xxx mg/kg, bw/day* with a NOAEL of *xxx mg/kg bw/day*.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material:		*[as named in study]*
	Description:	*[e.g. technical, nature, color, stability]*
	Lot/Batch #:	
	Purity:	% a.i.
	CAS # of TGAI:	
		[Verification of concentration/homogeneity as necessary]

2. Vehicle and/or positive control: *[note how dosage form was prepared if unusual]*

3. Test animals:			
	Species:		
	Strain:		
	Age/weight at dosing:		
	Source:		
	Housing:		
	Diet:	*[describe]* *ad libitum*	
	Water:	*[describe]* *ad libitum*	
	Environmental conditions:	**Temperature:** **Humidity:** **Air changes:** **Photoperiod:**	EC % /hr hrs dark/ hrs light
	Acclimation period:		

B. STUDY DESIGN:

1. Animal assignment and treatment: Animals were assigned to the test groups noted in Table 1 *[e.g., by a computerized random sort program to the test groups so that body weight means for each group were comparable. Following an overnight fast]*, rats were given a single dose *[how, in what vehicle/volume]* then observed *[frequency]* and weighed *[frequency]* for 14 days. Dose levels were chosen based on *[what]*. *[Dose selection rationale should be discussed; rationale for selection of time of peak effect should also be discussed. Use data from range-finding study if available.]* Survivors were sacrificed and a necropsy *[was/was not]* performed.

[Include additional description of study design, e.g. use of replicates, as needed, to supplement the information in the table.]

Table 1. Study Design *[change headings and units as appropriate, add or delete rows as needed]*

Experimental Parameter	**Dose Group (mg/kg bw)**			
	Control	**Low Dose**	**Mid Dose**	**High Dose**
Total number of Animals/sex/group				
Behavioral Testing (FOB, Motor Activity)	10/sex	10/sex	10/sex	10/sex
Neuropathology	6/sex	6/sex	6/sex	6/sex
Blood cholinesterase determination	5/sex	5/sex	5/sex	5/sex

Brain cholinesterase determination	5/sex	5/sex	5/sex	5/sex

2. Test Substance Preparation and Analysis: *[Indicate how test substance was prepared for administration, how it was stored, and how stability, concentration, and homogeneity were verified.]*
Results - Homogeneity Analysis: *[range of values]*
Stability Analysis: *[range of values]*
Concentration Analysis: *[range of values]*
3. Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. METHODS / OBSERVATIONS:

1. Mortality and Clinical Observations:
Animals were observed *[how frequently]* for mortality and morbidity. Detailed clinical observations were recorded *[when?]*.
[e.g., Animals were inspected twice daily during the week and once a day on the weekends and holidays for signs of toxicity and mortality. Detailed physical examinations were performed daily].

2. Body weight:
Animals were weighed *[frequency]*.

3. Food consumption: *[indicate when and whether food consumption was recorded, and how test substance intake was calculated (if feeding study)]*

4. Cholinesterase Determination: *[If applicable]* Cholinesterase activity was determined in *[how many animals, how often?]*. *[How were samples collected and processed, what tissues were used (e.g. plasma, whole blood, RBCs, brain (whole brain or regions)), were animals fasted, what methodology was used for cholinesterase determination? Is there information indicating that samples were analyzed in a way that would minimize dissociation of the chemical from the enzyme?]*

5. Neurobehavioral Assessment:

a. Functional Observational Battery (FOB): *[Describe the procedures used. Were the same technicians used throughout testing? Were they blind to treatment status of animals? Where was the testing done? When was testing done, with respect to time of test substance administration? What were the environmental conditions (e.g., noise level, etc.)? We're scoring criteria given for the measured parameters? For open field observations, include the duration of the observation period (e.g., 2 minutes); for any test requiring equipment (e.g. strain gauges used for grip strength), describe the equipment used.]*

The CHECKED (X) parameters were examined. *[Add and delete parameters from the following table, as needed.]*

X	**HOME CAGE OBSERVATIONS**	X	**HANDLING OBSERVATIONS**	X	**OPEN FIELD OBSERVATIONS**
	Posture*		Reactivity*		Mobility
	Biting		Lacrimation* / chromodacryorrhea		Rearing+
	Convulsions*		Salivation*		Arousal/ gereral activity level*
	Tremors*		Piloerection*		Convulsions*
	Abnormal Movements*		Fur appearance		Tremors*
	Palpebral closure*		Palpebral closure*		Abnormal movements*

Faeces consistency	Respiratory rate+	Urination / defecation*
	Red/crusty deposits*	Grooming
SENSORY OBSERVATIONS	Mucous membranes /eye /skin colour	Gait abnormalities / posture*
Approach response+	Eye prominence*	Gait score*
Touch response+	Muscle tone*	Bizarre / stereotypic behaviour*
Startle response*		Backing
Pain response*		Time to first step
Pupil response*		
Eyeblink response	**PHYSIOLOGICAL OBSERVATIONS**	**NEUROMUSCULAR OBSERVATIONS**
Forelimb extension	Body weight*	Hindlimb extensor strength
Hindlimb extension	Body temperature+	Forelimb grip strength*
Air righting reflex+		Hindlimb grip strength*
Olfactory orientation		Landing foot splay*
	OTHER OBSERVATIONS	Rotarod performance

*Required parameters; +Recommended parameters

b. Locomotors Activity: Locomotors Activity was evaluated *[when in relation to FOB performance]. [Include information on whether replicates were used, what type of equipment was used, length of session, number and length of subsessions, what parameters were measured (e.g., total activity, ambulatory activity, large movements, small movements, etc.)]*

6. Sacrifice and Pathology:

[When and how were animals sacrificed, how many were perfused, what parameters were measured (e.g. brain weight, length and width), what were the procedures for perfusion, what tissues were evaluated, what type of staining was used, how were sections prepared (thickness, embedding media, number of sections). How many animals from each sex and treatment group were evaluated?]

The CHECKED (X) tissues were evaluated. *[add or delete tissues as needed].*

	CENTRAL NERVOUS SYSTEM	X **PERIPHERAL NERVOUS SYSTEM**
	BRAIN	**SCIATIC NERVE**
	Forebrain	Mid-thigh
	Center of cerebrum	Sciatic Notch
	Midbrain	
	Cerebellum	**OTHER**
	Pons	Sural Nerve
	Medulla oblongata	Tibial Nerve
	SPINAL CORD	Peroneal Nerve

Cervical swelling	Lumbar dorsal root ganglion
Lumbar swelling	Lumbar dorsal root fibers
Thoracic swelling	Lumbar ventral root fibers
OTHER	Cervical dorsal root ganglion
Gasserian Ganglion	Cervical dorsal root fibers
Trigeminal nerves	Cervical ventral root fibers
Optic nerve	
Eyes	
Gastrocnemius muscle	

7. Positive Controls: *[Briefly describe the positive control data cited, and its acceptability for use with the current study].*

For Positive control data to be acceptable, it must demonstrate the sensitivity of the test method to detect changes in the measured parameters. For observational measures, the data should demonstrate the ability to detect major neurotoxic endpoints, including limb weakness, paralysis, tremor, and autonomic signs; motor activity positive control data should demonstrate the ability to detect both increases and decreases in motor activity; pathology positive control data should demonstrate the ability to detect central and peripheral nervous system pathology (separate groups may be used to demonstrate each type of pathology, for example, acrylamide for peripheral nervous system pathology and trimethyl tin for central nervous system pathology).

The methods should be completely described, and must be the same as those used in the study being evaluated (for example, the same equipment should be used, motor activity sessions should be of the same duration, the observation arena should be the same, the same sections should be evaluated for neuropathology, using the same types of stains, etc.), and preferably the same personnel should have conducted the testing. The data presentation should be complete enough to evaluate the sensitivity of the method, including individual data and measures of variability. Statistical evaluations used to demonstrate sensitivity should also be the same as those used in the study being evaluated. The number of animals per test group should not be greater than that used in the study under evaluation.

Positive control data should also demonstrate inter-observer reliability for the FOB (i.e., the same results should be seen regardless of who is doing the observations). The positive control data should have been collected within a reasonable time frame before the current study, e.g., the last few years. New data should also be collected when observational personnel or other critical laboratory elements change.

Historical control data are not required and should be used with care. Behavioral baselines can vary considerably based on current testing conditions, time of testing, environmental conditions, etc., so use of concurrent control data and pre-test data is strongly preferred over historical control data. If historical control data are provided, and if they are used in evaluation of results, these data should be required and evaluated as discussed above for positive control data.

II. RESULTS

A. OBSERVATIONS:

1. Clinical signs- *[Describe results] [include table only if treatment-related effects were seen]*

Table 2. Clinical observations

Observation	Dose Level (mg/kg bw/day)			
	Control	**Low dose**	**Mid dose**	**High dose**
Males				
[observation type]				
	x/x			
Females				
[observation type]				

Data were extracted from *[cite report page nos.]*

Numbers represent the total number of observations/number of animals with at least one instance of the observation

N = *[give number of animals in each group]*

2. Mortality:

B. BODY WEIGHT AND BODY WEIGHT GAIN: *[include only that data needed to document any effects seen, or lack thereof; include standard deviations in table]*

Table 3. Body weight and body weight gain (g)

Observation (g ± s.d.)	Dose Level (mg/kg bw)			
	Control	**Low dose**	**Mid dose**	**High dose**
Body weight-Males				
-Day #				
Body weight-Females				
-Day #				
Body weight gain-Males				
-Day #				
Body weight gain-Females				

Observation (g ± s.d.)	Dose Level (mg/kg bw)			
	Control	Low dose	Mid dose	High dose
-Day #				

Data were extracted from *[cite report page nos.]*.
Values represent mean ± s.d.
n=[give number of animals in each group]
*=p<.05, **=p<.01, when compared to control means.

C. FOOD CONSUMPTION: *[Include if measured. - Include only enough food consumption information to document any effects, or as necessary to explain effects on body weight.]*

Table 4. Food consumption (g/kg/day)

Week No.	Dose Level (mg/kg bw)			
	Control	Low dose	Mid dose	High dose
Males				
-Days #-#				
Females				
-Days #-#				

Data were extracted from *[cite study report page nos.]*
Values represent mean ± s.d.
n=*[give number of animals for each group]*
*=p<.05, **=p<.01, when compared to control means

D. CHOLINESTERASE ACTIVITIES: *[Describe results - if applicable]*

Table 5. Blood cholinesterase activity

Observation	Dose Level (mg/kg bw)			
	Control	Low dose	Mid dose	High dose
Plasma ChE (U/L)				
Males				
Day 0				

Observation	Dose Level (mg/kg bw)			
	Control	**Low dose**	**Mid dose**	**High dose**
Day 7				
Day 14				
Females				
Day 0				
Day 7				
Day 14				
RBC ChE (U/L)				
Males				
Day 0				
Day 7				
Day 14				
Females				
Day 0				
Day 7				
Day 14				

Data were extracted from *[cite study report page nos.]*
Values represent mean ± s.d. *[% difference from control mean]*

**=p<.01, *=p<.05, when compared to control mean.
n=[give *number of animals in each group]*
[Include all data for whole brain (if brain regions were evaluated, also include all data from cortex and hippocampus; for other regions include data from all time points if statistically significant changes were found for a particular region or if changes from baseline of 20% or greater were seen) - add extra lines to table as needed].

Table 6. Brain cholinesterase activity (U/g)

Brain Region	Dose Level (Mg/kg Bw)			
	Control	Low Dose	Mid Dose	High Dose
Tissue 1				
Male				
Day 0				
Day 7				
Day 14				
Female				
Day 0				
Day 7				
Day 14				
Tissue 2				
Male				
Day 0				
Day 7				
Day 14				
Female				
Day 0				
Day 7				
Day 14				

Data were extracted from *[cite study report page nos.]*
Values represent mean ± s.d. *[% difference from control mean]*
**=p<.01, *=p<.05, when compared to control mean.

n=[give *number of animals in each group]*

E. NEUROBEHAVIORAL RESULTS

Data should be included for all statistically significant findings, and for any findings the reviewer feels are toxicologically relevant (even if not statistically significant [in our view, an incidence of 3/10 for a parameter where controls are 0/10 would warrant inclusion]). If significant effects are found, data from all groups, time points, and both sexes should be included for that parameter (so that the reader of the DER can see what happened to the effect across time and groups). [However, note that if a given parameter is (e.g.) 0 for all groups at all-time points except for day 0, that can be stated in the text and such data need not be included in the table.] Include severity information if there are changes in severity. Duplicate the table as necessary to include different types of findings (e.g., activity levels, landing foot splay, etc.).

1. FOB Findings:

Table 7. Functional observation battery results

	Dose Level (mg/kg bw)			
Observation	**Control**	**Low dose**	**Mid dose**	**High dose**
Males				
Type of Observation -1 -Pretest -Day 0 -Day 7 -Day 14				
Type of Observation -2 -Pretest -Day 0 -Day 7 -Day 14				
Females				
Type of Observation -1 -Pretest -Day 0 -Day 7 -Day 14				
Type of Observation				

Observation	Dose Level (mg/kg bw)			
	Control	Low dose	Mid dose	High dose
-2 -Pretest -Day 0 -Day 7 -Day 14				

Data were extracted from *[cite study report page nos.] [include units for measurements, as needed]*
Values represent incidence (or other appropriate measure)
n=*[include number of animals for all groups]*
*=p<.05,** p<.01 compared with controls

2. Motor activity:

Include data for total motor activity in all DERs, regardless of statistical significance. Include data for subsessions if it is statistically or toxicologically significant. Even if data for subsessions is not included in a table, it should be discussed, especially with regard to whether or not habituation was demonstrated. Table can be duplicated as necessary to include additional types of motor activity data or subsession data.

Table 8. Motor activity (total activity counts for session)

Test Day	Dose Level (mg/kg bw)			
	Control	Low Dose	Mid Dose	High Dose
Males				
Pre-test				
Day 0				
Day 7				
Day 14				
Females				
Pre-test				
Day 0				
Day 7				
Day 14				

Data were extracted from *[cite study report page nos.] [include units for measurements, as needed]*
Values represent mean ±s.d.
n=*[give number of animals for all groups]*
*=p<.05,** p<.01 compared with controls

F. SACRIFICE AND PATHOLOGY: *[Tables are OPTIONAL, but recommended for treatment-related findings; limit text to integration of findings, highlights]*:

1. Gross pathology: *[describe results, including whether there were any changes in brain weights (if measured - provide table)]*

2. Brain weight - *[absolute and relative as appropriate, relate to any histological changes]*

Table 9: Absolute and relative brain weights (n=6/sex)

Weights (mg)	Dose Level (mg/kg bw)			
	Control	Low Dose	Mid Dose	High Dose
Males				
Body wt				
Brain wt				
Brain/body wt				
Female				
Body wt				
Brain wt				
Brain/body wt				

Data were extracted from *[cite study report page nos.]*
* Statistically different ($p < 0.05$) from the control.

3. Neuropathology:

Include information as to what types of lesions were found. If neuropathological alterations were observed in the high dose group, were lower dose groups sequentially examined? If evidence of neuropathological alterations was seen, was a subjective diagnosis (dose-blind coded re-reading) conducted? If treatment-related lesions were found, include information in a table, including information regarding lesion severity; if no treatment-related lesions were found, include some information in text regarding reported incidence of lesions unrelated to treatment and in control groups. A sample table (with sample data) is included below.

Table 10. Incidence of neuropathological findings *[Tissues listed are examples, change as needed.]*

	Treatment Group	
	Male	Female

Lesion	Control	High Dose	Control	High Dose
Sciatic Nerve -mid-thigh -notch (mid-thigh or notch)				
Sural Nerve				
Tibial Nerve				
Lumbar Roots -dorsal -ventral -(dorsal or ventral)				
Axonal degeneration -some peripheral nerve				

n=5 for all groups
All lesions were graded minimal except for sciatic nerve degeneration in one control female (graded mild) MF=multifocal; all other lesions were focal.
Numbers in parentheses represent combined incidence.
Data were extracted from individual animal pathology data tables, *[cite study report page nos.]*

III. INVESTIGATORS' DISCUSSION AND CONCLUSIONS: *[Note any deficiencies and how they impact on the study results and interpretation, if at all. Include the following points in your discussion/conclusions section.]*

[Discuss findings at low, mid- and high doses. Include only major treatment related clinical signs, FOB findings, motor activity changes, body weight or brain weight changes or gross and histopathology or neuropathology, including onset and/or duration if any, or the following statement: There were no treatment related effects on mortality, clinical signs, body weight, brain weight or gross and histologic pathology or neuropathology. FOB and motor activity testing revealed no treatment-related effects. Note if there was a NOAEL for acute neurotoxicity (for acute reference dose consideration during subsequent risk assessment.)]

Based on the effects seen in this study, the LOAEL was *xxx mg/kg bw/day (based on xxx)*, with a NOAEL *of xxx mg/kg bw/day.*

[If applicable]

The LOAEL for plasma cholinesterase inhibition was *xxx mg/kg bw/day*, with a NOAEL of *xxx mg/kg bw/day*.

The LOAEL for erythrocyte cholinesterase inhibition was *xxx mg/kg bw/day*, with a NOAEL of *xxx mg/kg bw/day*.

The LOAEL for brain cholinesterase inhibition was *xxx mg/kg, bw/day* with a NOAEL of *xxx mg/kg bw/day*.

Study Type: Combined chronic toxicity/carcinogenicity-Rat/Mice
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:
Executive Summary:

In a combined chronic /carcinogenicity study test substance was administered to *[(# of animals) species, strain]*/sex/dose in *[dietary, gavage, drinking water, dermal or inhalation]* at dose levels of 0, x, x, or x ppm (equivalent to 0, x, x, x mg/kg bw/day) for *(duration)*.

[Describe toxicity briefly following instructions for exec summary paragraph 2. If there is no toxicity, state that there were no compound related effects on mortality, clinical signs, body weight, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic (including tumors) pathology. Note if there was a NOAEL for clinical findings and when they occurred (for acute reference dose consideration during subsequent risk assessment.)].

The LOAEL is , based on The NOAEL is

At the doses tested, there was *(not)* a treatment related increase in tumor incidence *[specify tumor type]* when compared to controls. ***(Brief** description)*. Dosing was *(not)* considered adequate based on *(mention critical endpoint noted above)*.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material:		*[as named in study]*
	Description:	*[e.g., technical, nature, color, stability]*
	Lot/Batch #:	
	Purity:	% a.i.
	Compound Stability:	
	CAS # for TGAI:	
		[Structure]

2. Vehicle and/or positive control: *[when appropriate]*, Lot/Batch #

3. Test animals:			
	Species:		
	Strain:		
	Age/weight at study initiation:		
	Source:		
	Housing:		
	Diet:	*[describe] ad libitum*	
	Water:	*[describe] ad libitum*	
	Environmental conditions:	**Temperature:**	EC %

		Humidity: **Air changes:** **Photoperiod :**	/hr hrs dark/ hrs light
	Acclimation period:		

B. STUDY DESIGN:

1. Animal Assignment/Dose Levels: Animals were assigned [*note how assigned, e.g., random]* to the test groups noted in Table 1.

TABLE 1: STUDY DESIGN *[change heading and units as appropriate for method of administration]*

Test Group	**Conc. in Diet** ***(units)***	**Dose to animal** ***(units)***	**Main Study # months**		**Interim Sac. # months**	
			Male	**Female**	**Male**	**Female**
Control						
Low (LDT)						
Mid (MDT)						
High (HDT)						

2. Dose Selection: The dose levels were selected based on the results from *[state study type(s)]* where *[route]* - administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available. Put more detail when available in a 1-2 page summary following the Discussions and Conclusions section of this Study Profile]*

3. Diet preparation and analysis: *[if diet is route of administration]*

Diet was prepared *[frequency]* by mixing appropriate amounts of test substance with *[type of food eg., Purina Certified Rodent Diet #5001]* and was stored at temperature. Homogeneity and stability were tested at . During the study, samples of treated food were analyzed *[when and at what dose levels]* for stability and concentration.

Results - Homogeneity Analysis: *[range of values]*

Stability Analysis: *[range of values]*

Concentration Analysis: *[range of values]*

4. Statistics - *[list parameters that were analyzed and the statistical methods used]*

C. METHODS:

1. Observations:

1a. Cage side Observations

Animals were inspected *[frequency]* for signs of toxicity and mortality.

1b. Clinical Examinations

Clinical examinations were conducted *[frequency]*.

1c. Neurological Evaluations

The following evaluations (measurements) were performed on day *[insert treatment day]*: *[list parameters measured] [If neurological evaluations were omitted, give explanation for why, such as available from other studies]*

2. Body weight:

Animals were weighed *[frequency]*.

3. Food consumption and compound intake: *[if feeding study]*

Food consumption for each animal was determined and mean daily diet consumption was calculated as g food/kg body weight/day. Food efficiency *[if given] [body weight gain in kg/food consumption in kg per unit time X 100]* and compound intake (mg/kg bw/day) values were calculated as time-weighted averages from the consumption and body weight gain data.

4. Ophthalmoscopic examination:

Eyes were examined *[when]*

5. Hematology & Clinical Chemistry:

Blood was collected *[fasted? method and time of collection and how many animals]* for hematology and clinical chemistry analysis from all surviving animals. The CHECKED (X) parameters were examined.

a. Hematology

	Hematocrit (HCT)*	Leukocyte differential count*
	Hemoglobin (HGB)*	Mean corpuscular HGB (MCH)*
	Leukocyte count (WBC)*	Mean corpusc. HGB conc.(MCHC)*
	Erythrocyte count (RBC)*	Mean corpusc. volume (MCV)*
	Platelet count*	Reticulocyte count
	Blood clotting measurements*	
	(Thromboplastin time)	
	(Clotting time)	
	(Prothrombin time)	

* Recommended for combined chronic/carcinogenicity studies based on Guideline 870.4300.

b. Clinical Chemistry

	ELECTROLYTES	**OTHER**
	Calcium*	Albumin*
	Chloride*	Creatinine*
	Magnesium*	Urea nitrogen*
	Phosphorus*	Total Cholesterol*
	Potassium*	Globulins*
	Sodium*	Glucose (fasting)*

	ENZYMES (more than 2 hepatic enzymes)* Alkaline phosphatase (ALK)* Cholinesterase (ChE) Creatine phosphokinase Lactic acid dehydrogenase (LDH) Alanine aminotransferase (ALT/ SGPT)* Aspartate aminotransferase (AST/ SGOT)* Gamma glutamyl transferase (GGT)* Sorbitol Glutamate dehydrogenase*	Total bilirubin Total protein (TP)* Triglycerides Serum protein electrophoresis

* Recommended for combined chronic and carcinogenicity studies based on Guideline 870.4300.

6. Urinalysis:

Urine was collected from *[fasted?]* animals at *[times]*. The CHECKED (X) parameters were examined.

	Appearance* Volume* Specific gravity / osmolality* pH* Sediment (microscopic) Protein*	Glucose* Ketones* Bilirubin* Blood/ red blood cells* Nitrate Urobilinogen

* Recommended for combined chronic and carcinogenicity studies based on Guideline 870.4300.

7. Sacrifice and Pathology

All animals that died and those sacrificed on schedule were subjected to gross pathological examination and the CHECKED (X) tissues were collected for histological examination *[note if not all collected tissues were examined]*. The (XX) organs, in addition, were weighed.

	DIGESTIVE SYSTEM Tongue Salivary glands* Esophagus* Stomach* Duodenum* Jejunum* Ileum* Cecum* Colon* Rectum* Liver*+ Gall bladder* (not rat) Bile duct (rat) Pancreas* **RESPIRATORY** Trachea* Lung*++ Nose* Pharynx* Larynx*	**CARDIOVASC./HEMAT.** Aorta, thoracic* Heart*+ Bone marrow* Lymph nodes* Spleen*+ Thymus **UROGENITAL** Kidneys*+ Urinary bladder* Testes*+ Epididymides*+ Prostate* Seminal vesicle* Ovaries*+ Uterus*+ Mammary gland*	**NEUROLOGIC** Brain (multiple sections)*+ Periph.nerve* Spinal cord (3 levels)* Pituitary* Eyes (retina, optic nerve)* **GLANDULAR** Adrenal gland*+ Lacrimal gland Parathyroids* Thyroids* **OTHER** Bone (sternum and/or femur) Skeletal muscle Skin* All gross lesions and masses*

* Required for combined chronic/carcinogenicity studies based on Guideline 870.4300.
+Organ weight required in combined chronic/carcinogenicity studies.
++Organ weight required if inhalation route.

II. RESULTS *[describe findings, include tables if needed; tables are recommended to depict any treatment-related findings, thus limiting use of text to highlight specific points]*:

A. OBSERVATIONS:

1. Clinical signs of toxicity - *[include cage side observations and clinical examinations; note when signs were first observed]*

2. Mortality -

3. Neurological Evaluations -

B. BODY WEIGHT *[Include a table of body weight gain, especially 0-3, 3-13, (0-13), 13-26, 26-52, 52-75, 75-104 weeks, rather than cumulative weight gain alone, especially if there is a treatment related effect. Other time points should be included as appropriate to get the point across]*

TABLE 2: Mean body weights (BW) and body weight gains (BWG) [a] *[SAMPLE - some form of this table is required when there is a treatment-related effect]*

g∀SD	0	LDT	MDT	HDT
MALES Initial BW				

Final BW				
BWG Wk 1 (% C)				
BWG Wk 1-13 (%C)				
BWG Wk 13-26 (% C)				
BWG Wk 26-52 (% C)				
BWG Wk 52-75 (% C)				
Overall BWG Wk -1-104				
FEMALES Initial BW				
Final BW				
BWG Wk 1 (% C)				
BWG Wk 1-13 (%C)				
BWG Wk 13-26 (% C)				
BWG Wk 26-52 (% C)				
BWG Wk 52-75 (% C)				
Overall BWG Wk -1-104				

C = control

[a] Data obtained from pages *(insert page #s)* in the study report.

* Statistically different ($p < 0.05$) from the control.

** Statistically different ($p < 0.01$) from the control.

C. FOOD CONSUMPTION AND COMPOUND INTAKE *[if feeding study]*

1. Food consumption -

2. Compound consumption (time-weighted average) *[include compound intake in table 1]* -

3. Food efficiency *[if relevant, - relate to effects on body weight gain]*

D. OPHTHALMOSCOPIC EXAMINATION -

E. BLOOD ANALYSES ***[Tables to show treatment-related findings are OPTIONAL, but recommended for treatment-related findings]*:**

1. Hematology - *[relate to any histological findings]*

2. Clinical Chemistry - *[relate to any histological findings]*

F. URINALYSIS -

G. SACRIFICE AND PATHOLOGY [*Tables are OPTIONAL, but recommended for treatment-related findings; limit text to integration of findings, highlights]*:

1. Organ weight - *[absolute and relative as appropriate, relate to any histological changes]*

2. Gross pathology -

3. Microscopic pathology - *[relate with other findings, as appropriate]*

a) Non-neoplastic -

b) Neoplastic -

III. INVESTIGATORS' DISCUSSION AND CONCLUSIONS: *[Note any deficiencies and how they impact on the study results and interpretation, if at all. Include the following points in your discussion/conclusions section]*

[Describe the significant findings and provide justification for the conclusions.]

The LOAEL is mg/kg/day, based on the NOAEL is mg/kg/day.

[At the doses tested, there was *(not)* a treatment related increase in tumor incidence *[specify tumor type]* when compared to controls. ***(Brief** description)*. Dosing was *(not)* considered adequate based on *(mention critical endpoint noted above).*]

Study Type: Prenatal Developmental Toxicity Study - *[Rodent species]*

Guidelines:

Study No.:

Study Initiation Date:

Study Completion Date:

Executive Summary:

In a developmental toxicity study test substance *(% a.i., batch/lot #)]* was administered to *[(# of females) strain]* rats/dose in *[diet, water, by capsule, by gavage]* at dose levels of 0, x, x, or x mg/kg bw/day from days *[#]* through *[#]* of gestation.

[Describe maternal toxicity briefly. If none, state that there were no treatment-related effects in survival, clinical signs, body weight, food consumption, or cesarean parameters. Include effects at doses >LOAEL.]

The maternal LOAEL is mg/kg bw/day, based on *[endpoints]*.

The maternal NOAEL is mg/kg bw/day.

[Describe developmental toxicity briefly. If none, state that there were no treatment-related effects in developmental parameters. Include effects at doses > LOAEL.

The developmental LOAEL is mg/kg bw/day, based on *[endpoints].*

The developmental NOAEL is mg/kg bw/day.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material:		*[as named in study]*
	Description:	*[e.g., technical, nature, color, stability]*
	Lot/Batch #:	
	Purity:	% a.i.
	Compound Stability:	
	CAS #of TGAI:	
		[Structure]

2. Vehicle and/or positive control: *[when appropriate]*, Lot/Batch #; Purity

3. Test animals:		*[include information for females and males]*	
	Species:		
	Strain:		
	Age/weight at study initiation:		
	Source:		
	Housing:		
	Diet:	*[describe]* *ad libitum*	
	Water:	*[describe]* *ad libitum*	
	Environmental conditions:	**Temperature:** **Humidity:** **Air changes:** **Photoperiod:**	EC % /hr hrs dark/ hrs light
	Acclimation period:		

B. PROCEDURES AND STUDY DESIGN

1. Mating: *[describe technique used, e.g.,* sexually mature females were mated with sexually mature males *(verify males were same strain, source as female).]* Confirmation of mating was determined by *[describe, e.g., the presence of sperm in the vaginal washing; or the presence of a copulatory plug]* and was designated as day [0] of gestation.

2. Animal Assignment: Animals were assigned [*randomly?, how?]* to dose groups as indicated in Table 1 *[The information in this table is **MANDATORY**]*.

TABLE 1. Animal Assignment *[change heading / units as appropriate for method of administration]*

Dose (mg/kg bw/day)	**0**	**LDT**	**MDT**	**HDT**
# Females				

3. Dose selection rationale: The dose levels were selected based on the results from *[state study type(s)]* where *[route-* administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available.]*

5. Dosage preparation and analysis *[include frequency]*

Test material-vehicle mixture was prepared *[frequency]* by mixing appropriate amounts of test substance with *[vehicle]* with storage at *[describe]* temperature. Prior to the start of the study, stability of the test substance in *[vehicle]* was evaluated for a period of *[number]* days at *[temperature]*. Concentration and homogeneity (top, middle, and bottom) of the test mixture were evaluated *[frequency]*.

Results - Homogeneity Analysis: *[Range of values]*
Stability Analysis: *[Range of values]*
Concentration Analysis: *[Range of values]*
6. Dosage administration: All doses were administered once daily by *[route]*, on gestation days *[#]* through *[#]*, in a volume of *[#]* mL/kg of body weight/day. Dosing was based on the body weight on the most recent body weight determination *[or on gestation day #]*.

C. OBSERVATIONS

1. Maternal Observations and Evaluations - The animals were checked for mortality or clinical signs *[frequency]*. Body weight and food consumption data were recorded on gestation days *[description]*. Dams were sacrificed on day *[#]* of gestation. Examinations at sacrifice consisted of: *[describe]*

2. Fetal Evaluations - The fetuses were examined in the following manner: *[describe in detail i.e., external, soft tissue and skeletal examination, including assignment of fetuses and standard/non-standard methodologies used]*

D. DATA ANALYSIS

1. Statistical analyses: *[Statistical procedures should be described in detail for each endpoint evaluated. The litter should be considered the unit of statistical analysis. Differentiate between parametric and non-parametric analysis Describe any data transformations used. General statistical assumptions need not be stated unless there are deviations from generally applied techniques. Animals excluded from analyses should be in table footnotes.]*

2. Indices: The following indices were calculated from cesarean section records of animals in the study: *[Formulas or descriptions of pre- and post-implantation loss indices and any other indices as provided in the study report.]*

3. Historical control data: Historical control data were *(not)* provided to allow comparison with concurrent controls. *[Briefly describe source of data and what data were included.]*

II. RESULTS

A. MATERNAL TOXICITY

1. Mortality and Clinical Observations: The following observations were reported: *[Describe findings along with incidences or #animals affected/# animals examined]. [Tables are OPTIONAL]*

2. Body Weight - Body weight data are summarized in Table 2 and as follows: *[Some form of this table is **MANDATORY**. Also include, body weight gain, corrected for gravid uterine weight, as necessary.]*

TABLE 2. Mean (∀SD) Maternal Body Weight Gain (g) [a]

	Dose in mg/kg bw/day (# of Dams)			
Interval	**Control (N)**	**LDT (N)**	**MDT (N)**	**HDT (N)**
Pretreatment: **Days # -#**				
Treatment: **Days # -#**				
Posttreatment: **Days # -#**				

Corrected BW Gain				

a Data obtained from pages *(insert page #s)* in the study report.
* Statistically different ($p < 0.05$) from the control.
** Statistically different ($p < 0.01$) from the control.

3. Food Consumption - Food consumption data are summarized as follows: *[Describe findings]*. *(Include table only if needed).*

4. Gross Pathology - Gross pathology data are summarized as follows: *[Describe findings]*.

5. Cesarean Section Data - Data are as follows: *[Describe findings]*; as summarized in Table 3. *[Some form of this table is **MANDATORY**; data should be presented as both fetal and litter incidences]*

TABLE 3 Cesarean Section Observations [a] *[Include ∀SD with mean values, as appropriate.]*

Observation	Dose (mg/kg bw/day)			
	0	LDT	MDT	HDT
# Animals Assigned (Mated)				
# Animals Pregnant Pregnancy Rate (%)				
# Nonpregnant				
Maternal Wastage # Died # Died Pregnant # Died Nonpregnant # Aborted # Premature Delivery				
Total # Corpora Lutea Corpora Lutea/Dam				
Total # Implantations (Implantations/Dam)				
Total # Litters				
Total # Live Fetuses (Live Fetuses/Dam)				
Total # Dead Fetuses (Dead Fetuses/Dam)				
Total # Resorptions Early Late Resorptions/Dam Early Late				

Litters with Total Resorptions				
Mean Fetal Weight (g) **Males** **Females**				
Sex Ratio (% Male)				
Preimplantation Loss (%)				
Postimplantation Loss (%)				

a Data obtained from pages *(insert page #s)* in the study report.
* Statistically different ($p < 0.05$) from the control.
** Statistically different ($p < 0.01$) from the control.

B. DEVELOPMENTAL TOXICITY *[Special instructions for Tables 4a, b, c: generally present variations and malformations (or other classifications of anomalies) separately; if there are no treatment-related findings include only a few of the most common findings; give the total visceral, skeletal and visceral alterations when applicable. Some form of these tables are **MANDATORY**.]*

1. External Examination - *[Describe noteworthy findings]*.
2. Visceral Examination - *[Describe noteworthy findings]*.
3. Skeletal Examination - *[Describe noteworthy findings]*.

TABLE 4a. External Examinations [a]

Observations [b]	**Dose (mg/kg bw/day)**			
	0	**LDT**	**MDT**	**HDT**
#Fetuses(litters) examined				
#Fetuses(litters) affected				
[Finding]	( ) [c]	( )	( )	( )

a Data obtained from pages *(insert page #s)* in the study report.
b Some observations may be grouped together.
c Fetal (litter) incidence
* Statistically different ($p < 0.05$) from the control.
** Statistically different ($p < 0.01$) from the control.

TABLE 4b. Visceral Examinations a

Observations [b]	Dose (mg/kg bw/day)			
	0	LDT	MDT	HDT
#Fetuses(litters) examined				
#Fetuses(litters) affected				
[Finding]	( ) [c]	( )	( )	( )

a Data obtained from pages *(insert page #s)* in the study report.
b Some observations may be grouped together., c Fetal (litter) incidence
* Statistically different ($p < 0.05$) from the control.

TABLE 4c. Skeletal Examinations [a]

Observations [b]	Dose (mg/kg bw/day)			
	0	LDT	MDT	HDT
#Fetuses(litters) examined				
#Fetuses(litters) affected				
[Finding]	( ) [c]	( )	( )	( )

a Data obtained from pages *(insert page #s)* in the study report.
b Some observations may be grouped together., c Fetal (litter) incidence
* Statistically different ($p < 0.05$) from the control., ** Statistically different ($p < 0.01$)

III. INVESTIGATORS' DISCUSSION and CONCLUSIONS: *[Note any deficiencies and how they impact on the study results and interpretation, if at all. Include the following points in your discussion/conclusions section.]*

[Describe the significant maternal findings and provide justification for the conclusions.]

The maternal LOAEL is mg/kg bw/day, based on *[endpoints]*.
The maternal NOAEL is mg/kg bw/day.

[Describe developmental toxicity briefly.]

a. Deaths/Resorptions:
b. Altered Growth:
c. Developmental Variations:
d. Malformations:

[If none, state that there were no treatment-related effects in developmental parameters. Include effects at doses >LOAEL.]

The developmental LOAEL is mg/kg bw/day, based on *[endpoints]*.
The developmental NOAEL is mg/kg bw/day.

Study Type: Two Generation Reproduction and Fertility Effects Study - *[Rodent species]*
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:
In a *[#]*-generation reproduction study (MRID *[number]) [Chemical name (% a.i., batch/lot #)]* was administered to *[(# of animals) strain, species]*/sex/dose in *[diet, water, by capsule, by gavage]* at dose levels of 0, x, x, x ppm (equivalent to 0, x, x, or x mg/kg bw/day). *(Mention number of litters per generation and other critical or unusual procedures)*
[Describe parental toxicity briefly for both males and females, including treatment-related effects at doses >LOAEL if applicable.
The parental systemic LOAEL is ppm (mg/kg bw/day in males, mg/kg bw/day in females), based on *[endpoint]*.

The parental systemic NOAEL is ppm (mg/kg bw/day in males, mg/kg bw/day in females).

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material:		*[as named in study]*
	Description:	*[e.g., technical, nature, color, stability]*
	Lot/Batch #:	
	Purity:	% a.i.
	Compound Stability:	
	CAS # of TGAI:	
		[Structure]

2. Vehicle and/or positive control: *[when appropriate]*, Lot/Batch # , Purity

3. Test animals:			
	Species:		
	Strain:		
	Age at study initiation:	(P) x wks; (F_1) x wks	
	Wt. at study initiation:	(P) Males: x-x g; Females: x-x g (F_1) Males: x-x g; Females: x-x g	
	Source:		
	Housing:		
	Diet:	*[describe[ad libitum*	
	Water:	*[describe] ad libitum*	
	Environmental conditions:	**Temperature:** **Humidity:** **Air changes:** **Photoperiod:**	EC % /hr hrs dark/ hrs light
	Acclimation period:		

B. PROCEDURES AND STUDY DESIGN

1. Mating procedure: *[SAMPLE - [#] male was caged with [#] females from the same test group until sperm cells were observed in vaginal smears taken daily during the mating period. If sperm were not found after [#] days' observation, the first male was removed and [#] days later was replaced by another male with proven fertility in the same test group. (If two attempts at mating were unsuccessful the report should state that no further matings were tried. Sibling matings should also be avoided for F_1.)*

After successful mating, each pregnant female was individually placed into a cage with a solid bottom and bedding where it was kept through gestation and lactation.]

2. Study schedule: *[SAMPLE - The P parental animals were given test diets for [#] weeks before they were mated, and the F_1 parental animals were not mated until [#] weeks after they were selected from the F_1 litters. Selection of parents for the F_1 generation was made when the pups were [#] days of age, and the mated animals in the study were approximately [#] weeks of age at mating.]*

3. Animal assignment: P animals were randomly *[how]* assigned to test groups as seen in Table 1. ***[The information in this table is MANDATORY]***

TABLE 1. Animal Assignment *[**MANDATORY**, include data from both generations in the table as needed]*

Test Group	Dose in Diet [a] *(units)*	Animals/group			
		P Males	P Females	F_1 Males	F_1 Females
Control					
Low (LDT)					
Mid (MDT)					
High (HDT)					

a Diets were administered from *[beginning of the study until sacrifice]*

4. Dose selection rationale: The dose levels were selected based on the results from *[state study type(s)]* where *[route]*- administration of up to *[dose]* resulted in *[state effects]*. *[Use data from range-finding study if available.]*

5. Dosage preparation and analysis:

Formulations were prepared *[frequency]* by mixing appropriate amounts of test substance with *[vehicle, e.g., type of food]* and were stored at *[describe]* temperature. Prior to the start of the study, stability of the test substance in *[vehicle]* was evaluated for a period of *[number]* days at *[temperature]*. Homogeneity (top, middle, and bottom) was evaluated at *[frequency]*. During the study, samples of *[treated food or test substance formulations]* were analyzed *[when and at what dose levels]* for concentration.

Results - Homogeneity Analysis: *[Range of values]*

Stability Analysis: *[Range of values]*

Concentration Analysis: *[Range of values]*

C. OBSERVATIONS

1. Parental animals: Observations and the schedule for those observations are summarized from the report. *[Description of endpoints in text or table format is **MANDATORY**; including: mortality and clinical signs, detailed examinations, body weight and food consumption, estrous cyclicity, sperm parameters, etc.]*

2. Litter observations: According to the report, the following litter observations (X) were made (see Table 2). *[Some form of this table is **MANDATORY** for both generations; include anogenital distance, if measured, sexual maturation, etc.]*

TABLE 2. F_1 / F_2 Litter Observations [a] *[MANDATORY]*

Observation	Time of observation (lactation day)					
	Day 0	Day 4 [b]	Day 4 [c]	Day 7	Day 14	Day 21
Number of live pups						
Pup weight						
External alterations						
Number of dead pups						
Sex of each pup (M/F)						

a Data obtained from pages *(insert page #s)* in the study report.
b Before standardization (culling)
c After standardization (culling)
On day 4 postpartum, litters were/were not standardized to a maximum of *[#]* pups/litter (*[#]*/sex/litter, as nearly as possible); excess pups were killed and discarded.
Dead pups were examined grossly for external and internal abnormalities, and a possible cause of death was/was not determined for pups born or found dead.

3. Postmortem observations:

1) Parental animals: All surviving parental males were sacrificed [*SAMPLE - as soon as possible after the last litters in each generation were produced.]* Maternal animals were sacrificed [*SAMPLE - after the last litter of each generation was weaned.]* These animals were subjected to postmortem examinations as follows.
Gross necropsy consisted of external and internal examinations including the cervical, thoracic, and abdominal viscera.
The following tissues (X) were prepared for microscopic examination and weighed (XX): *[Table is OPTIONAL; add other organs to the list if necessary.]*

	Ovaries		Testes
	Uterus		Epididymides
	Vagina/cervix		Prostate
	Lesions		Seminal vesicles

2) Offspring: The F_1 offspring not selected as parental animals and all F_2 offspring were sacrificed at *[number]* days of age. These animals were subjected to postmortem examinations (macroscopic and/or microscopic examination) as follows. *[Table is OPTIONAL]*

D. DATA ANALYSIS

1. Statistical analyses: *[list parameters that were analyzed and the statistical methods used]*

2. Indices:

Reproductive indices: The following reproductive indices were calculated from breeding and parturition records of animals in the study: *[Formulas or descriptions as provided in the study report.]*

Offspring viability indices: The following viability indices were calculated from lactation records of litters in the study: *[Formulas or descriptions as provided in the study report.]*

3. Historical control data: *[If provided, describe sample set.]*

II. RESULTS

A. PARENTAL ANIMALS

1. Mortality and clinical signs: *[Discuss treatment-related mortality including cause of death and time of occurrence.]*

The following clinical signs were observed: *[Describe findings]*. These results are summarized in Table 3. *[Table is OPTIONAL; findings should be presented for each generation and sex]*

TABLE 3. Mortality and Clinical Signs a

Observation	Dose Group			
	Control	LDT	MDT	HDT
***[P or F_1]* Generation - Males**				
***[P or F_1]* Generation - Females**				

a Data obtained from pages *(insert page #s)* in the study report.

2. Body weight and food consumption:

Body weight was *[Describe findings]*.

Food consumption was *[Describe findings]*.

Reported body weight and selected food consumption results are summarized in Table 4. *[The data contained in this table are **MANDATORY**; findings should be presented for each generation and sex; data can be split into more than one table.]*

TABLE 4. Mean (∀SD) Body Weight and Food Consumption - Pre-mating [a]

Observations/study week	Dose Group			
	Control	LDT	MDT	HDT
***[P or F_1]* Generation Males - Pre-mating**				
Mean body weight (g) Week *[#]*				
Mean weight gain (g) Weeks *[# - #]*				
Mean food consumption (g/animal/day)				

Weeks *[# - #]*				
***[P or F_1]* Generation Females - Pre-mating**				
Mean body weight (g) Week *[#]*				
Mean weight gain (g) Weeks *[# - #]*				
Mean food consumption (g/animal/day) Week *[# - #]*				

a Data obtained from pages *(insert page #s)* in the study report.
* Statistically different from control, $p<0.05$.
** Statistically different from control, $p<0.01$.
Selected group mean body weights and food consumption values for pregnant or nursing dams were summarized in the report as follows. *[Table presentation is OPTIONAL; findings during gestation and lactation should be presented or discussed for each generation.]*

3. Test Substance Intake: Based on food consumption, body weight, *[and dietary analyses results]*, the doses expressed as mean daily mg test substance/kg body weight during the *[duration in weeks]* pre-mating period are presented in Table 5. ***[MANDATORY]*** The values for the *[P or F_1]* generation are considered to be representative of the test substance intake for the entire study.

TABLE 5. Mean test substance intake during premating (mg/kg body weight/day) [a]

	Male			**Female**		
	LDT	**MDT**	**HDT**	**LDT**	**MDT**	**HDT**
P						
F1						

a Data obtained from pages *(insert page #s)* in the study report.

4. Reproductive function:

a. Estrous cycle length and periodicity: *[Summarize any biologically relevant effects on the estrous cycle]* Results from the evaluation of vaginal smears indicated *[Describe findings]*. *[Table is OPTIONAL; findings should be presented for each generation.]*

b. Sperm measures: *[Summarize any biologically relevant effects on sperm parameters (epididymis sperm counts, motility, morphology; and testicular spermatid counts).]* Results from the evaluation of sperm parameters revealed *[Describe findings]*. *[Tables are OPTIONAL; findings should be presented for each generation.]*

5. Reproductive performance: *[Summarize any biologically relevant effects on reproductive performance]* Results for the parental animals are summarized from the report in Table 6. *[**MANDATORY**; findings should be presented for each generation and each litter; the table should be based on report content and include any calculated reproductive indices.]*

TABLE 6. Reproductive Performance [a] *[Example:]*

Observation	Dose Group (ppm)			
	Control	LDT	MDT	HDT
P Generation - Litter A				
Mean (∀SD) precoital interval (days)				
MALES				
Number mated				
Number fertile				
Fertility not determined				
Intercurrent deaths				
FEMALES				
Number mated				
Number fertile				
Fertility not determined				
Intercurrent deaths				
Mean (∀SD) gestation interval (days)				
Number of litters				

a Data obtained from pages *(insert page #s)* in the study report.
* Statistically different from control, $p<0.05$.
** Statistically different from control, $p<0.01$.

6. Parental postmortem results:

a) Organ weights: The report noted *[Describe findings, relate to histological observations]*. Selected absolute and relative (to body weight *[brain weight])* organ weight values are presented in the following table. *[Table is OPTIONAL, but recommended]*

b) Pathology

1) Macroscopic examination: The report noted the following observations to be related to the administration of the test substance. *[Describe findings] [Table is OPTIONAL, but recommended for treatment-related findings]*

2) Microscopic examination: The report noted the following observations to be related to the administration of the test substance. *[Describe findings, relate with other findings as appropriate] [Table is OPTIONAL, but recommended for treatment-related findings]*

B. OFFSPRING

1. Viability and clinical signs: The following findings were reported: *[Discuss results; describe anogenital distance results, if measured.]*

Mean litter size and viability (survival) results from pups during lactation are summarized from the report in Table 7. *[MANDATORY]*

TABLE 7. Litter parameters for F_1 and F_2 generations [a] *[Example; data should be presented for each generation (F_1 and F_2 pups); include ∀SD with mean values, as appropriate.]*

Observation	Dose Group (ppm)			
	Control	50	250	1250
F_1 Generation				
Mean implantation sites				
Number born live				
Number born dead				
Sex Ratio Day 0 (% %)				
# Deaths Days 0-4 (%)				
# Deaths Days 4-21 (%)				
Mean litter size Day 0				
Day 4 [b]				
Day 4 [c]				
Day 7				
Day 14				
Day 21				
Birth index				
Live birth index				
Viability index				
Lactation index				
F_2 Generation				
Mean implantation sites				
Number born live				
Number born dead				
Sex Ratio Day 0 (%				

Observation	Dose Group (ppm)			
	Control	50	250	1250
%)				
# Deaths Days 0-4 (%)				
# Deaths Days 4-21 (%)				
Mean litter size Day				
Day 4 [b]				
Day 4 [c]				
Day 7				
Day 14				
Day 21				
Birth index				
Live birth index				
Viability index				
Lactation index				

a Data obtained from pages *(insert page #s)* in the study report.
b Before standardization (culling)
c After standardization (culling)
* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$

The report stated that the clinical observations of offspring during lactation included *[Describe findings]*. The results of these observations are as follows. *[Table is OPTIONAL]*.

2. Body weight: Offspring body weights were *[Describe findings]*. Selected mean pup body weight data are presented in Table 8. *[Table is **MANDATORY**]*

TABLE 8. Mean (∀SD) Litter and Pup Weights (g) [a] *[Example; data should be presented for each generation (F_1 and F_2 pups)]*

Dose Group (ppm)								
Lactation Day	0	50	250	1250	0	50	250	1250
	F_1 Litters				F_2 Litters			
1								

4 b								
4 c								
7								
14								
21								
	F_1 Pups - male				**F_2 Pups - male**			
1								
4 b								
4 c								
7								
21								
	F_1 Pups - female				**F_2 Pups - female**			
1								
4 b								
4 c								
7								
21								

a Data obtained from pages *(insert page #s)* in the study report.
b Before standardization (culling)
c After standardization (culling)
* Statistically different from control, $p<0.05$
** Statistically different from control, $p<0.01$

3. Sexual maturation (F_1): *[Summarize any biologically relevant effects on vaginal opening and preputial separation.]* Sexual maturation was *[Describe findings]*. *[Table is OPTIONAL]*

4. Offspring postmortem results:

a) Organ weights: The report noted *[Describe findings]*. Selected absolute and relative (to body weight *[brain weight])* organ weight values are presented in the following table. *[Table is OPTIONAL, but recommended for treatment-related findings]*

b) Pathology

1) Macroscopic examination: The following findings were reported: *[Describe findings] [Table is OPTIONAL, but recommended for treatment-related findings]*

2) Microscopic examination: The report noted the following: *[Describe findings] [Table is OPTIONAL, but recommended for treatment-related findings]*

III. INVESTIGATORS' DISCUSSION AND CONCLUSIONS: *[Note any deficiencies and how they impact on the study results and interpretation, if at all.] [Describe the significant findings for and provide justification for the conclusions parental systemic, offspring, and reproductive toxicity.]*

The parental systemic LOAEL is ppm (mg/kg bw/day in males, mg/kg bw/day in females), based on *[endpoint]*.
The parental systemic NOAEL is ppm (mg/kg bw/day in males, mg/kg bw/day in females).

The offspring LOAEL is ppm (mg/kg bw/day), based on *[endpoint]*. The offspring NOAEL is ppm (mg/kg bw/day).

[Note: If unequivocal evidence of reproductive toxicity was observed, then describe and determine a separate LOAEL and NOAEL for reproductive toxicity. Include treatment-related effects at doses >LOAEL if applicable.], i.e.,
The reproductive LOAEL is ppm (mg/kg bw/day in males, mg/kg bw/day in females), based on *[endpoint]*.
The reproductive NOAEL is ppm (mg/kg bw/day in males, mg/kg bw/day in females).

Study Type: Metabolism Rat- *[rodent species]*;
Guidelines:
Study No.:
Study Initiation Date:
Study Completion Date:

Executive Summary:
In a metabolism study test substance *[Chemical name (% a.i., batch/lot #), include location of radioactive label]* was administered to *[(# of animals) species, strain]*/sex/dose in *[method of exposure: eg. by gavage]* at dose levels of 0, x, x [mg/kg or other pertinent units].
Be brief (one or two paragraphs) [Describe, as appropriate: recoveries and routes of elimination of radioactivity and time frame as they relate to absorption and excretion of the compound; radioactivity in organs of concern, especially as it relates to bioaccumulation; sex and treatment group differences; and expired air radioactivity; major metabolites; other major factors.]
This metabolism study in the *(species)* is classified *[acceptable, unacceptable (guideline, non-guideline)]* and satisfies *(does not satisfy)* the guideline requirement for a metabolism study [OPPTS 870.7485, OECD 417] in *[species] [If unacceptable, why and is it upgradable. If it does not satisfy the requirement, concisely list only major deficiencies or refer to deficiency section.]*

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Compound:

Radiolabelled Test Material:		*[indicate position of radiolabel, eg.,* **[Phenyl-U-^{14}C] XX***]*
	Radiochemical purity	% *[determined by HPLC, GC or TLC]*
	Specific Activity	ΦCi/mg
	Lot/Batch #:	
Non-Radiolabelled Test Material:		*[as named in study]*
	Description:	*[e.g., technical, nature, color, stability]*
	Lot/Batch #:	
	Purity:	% a.i. *[determined by HPLC, GC or TLC]*
	Contaminants:	
	CAS # of TGAI:	
		[Structure, include location of label]

2. Vehicle and/or positive control: *[when appropriate]*, Lot/Batch #; Purity

3. Test animals:		
	Species:	
	Strain:	
	Age/weight at study initiation:	
	Source:	

	Housing:		
	Diet:	*[describe]* *ad libitum*	
	Water:	*[describe]* *ad libitum*	
	Environmental conditions:	**Temperature:** **Humidity:** **Air changes:** **Photoperiod:**	EC % /hr hrs dark/ hrs light
	Acclimation period:		

4. Preparation of dosing solutions:

B. STUDY DESIGN AND METHODS:

1. Group Arrangements

Animals were assigned *[note how assigned, e.g., random, briefly describe groups as needed]* to the test groups noted in Table 1.

TABLE 1: Dosing groups for pharmacokinetic studies for *(chemical) [some form of this data presentation is **RECOMMENDED**. If additional test groups are used (e.g., pilot study, dermal exposure, inhalation exposure or biliary cannulation etc.) include them in the table]*

Test Group	Dose of labeled material (mg/kg)	Number/sex	Remarks (eg. time of sacrifice)
Oral Dose			
Treatment 2 *[if applicable]*			
Treatment 3 *[if applicable]* : :			

2. Dosing and sample collection:

[Briefly describe dosing methods and sample collection]

a. Pharmacokinetic studies

[give details of experiments including what was sampled (urine, feces, tissues, cage washes, bile, if appropriate) and when and how often.]

b. Metabolite characterization studies

[What was collected for identification, when and from how many animals (samples pooled or not), method type for identification (e.g. GCMS or TLC)].

3. Statistics: *[list parameters that were analyzed and the statistical methods used]*

II. RESULTS

A. PHARMACOKINETIC STUDIES:

1. Preliminary experiment *[if applicable]*

[Briefly describe results]

2. Absorption

[Briefly describe absorption, may include an optional table relating excretion of radioactivity (in urine, feces, etc.) to sampling time]