PESTICIDE ASSESSMENT GUIDELINES

SUBDIVISION F

HAZARD EVALUATION: HUMAN AND DOMESTIC ANIMALS
ADDENDUM 8 ON DATA REPORTING

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OFFICE OF PESTICIDE PROGRAMS
US ENVIRONMENTAL PROTECTION AGENCY

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Robert P. Zendzian Ph.D., Orvill E. Paynter, Ph.D., Gardner

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For more information, refer to Pesticide Assessment Guidelines, Subdivision F, Health Effects Division: Human and Domestic Animals (EPA 540/09-84-014 and NTIS Order Number PB86-108958 dated February 1, 1985.

16. Abstract (Limit: 200 words)

The Data Reporting Guideline (DRG) for Acute Oral Toxicity, Series 81-1, Acute Dermal Toxicity Series 81-2, Subchronic and Chronic Dog Series 82-1, 83-1, Subchronic Oral Toxicity (90-day Study) Series 82-1, 83-1, 83-2 and 83-5 Subsections Chronic Toxicity Studies, Oncogenicity Study & Combined Chronic Toxicity/Oncogenicity Studies (Rodent Studies), Repeated Dose Dermal Toxicity: (21-day Study & Subchronic Toxicity Study: 90-day Study), Series 82-2, and 82-3, Reproductive and Fertility Effects, Series 83-4 also Mutagenicity Studies, Series 84, gives guidance to pesticide registrants on the format of their study report so that the Agency can review it efficiently. This guidance clarifies sections in the existing Pesticide Assessment Guidelines, Subdivision F, on data reporting. It provides an outline for the study report which data submitters can use in preparing their reports for submission to EPA to meet 40 CFR 158 data requirements for the registration of pesticides.

The DRG for these series are only one of a number of DRGs published by the National Technical Information Service as an addendum to Subdivision F of the Pesticide Assessment Guidelines.

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PESTICIDE ASSESSMENT GUIDELINES

SUBDIVISION F

HAZARD EVALUATION

HUMAN AND DOMESTIC ANIMALS

Series 81-1

Acute Oral Toxicity

ADDENDUM ON DATA REPORTING

Prepared by:

Robert P. Zendzian Ph.D.

for

Health Effects Division

Office of Pesticide Programs
US Environmental Protection Agency

Subdivision F - Acute Oral Toxicity Studies

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Acute Oral Toxicity

Guideline

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PESTICIDE ASSESSMENT GUIDELINES

HUMAN AND DOMESTIC ANIMALS

Acute Oral Toxicity

Subdivision F, Series 81-1

DATA REPORTING

INTRODUCTION

A. Purpose

The purpose of this addendum to the guideline is to provide a data reporting format for acute oral toxicity studies. Subpart F, Series 81-1 provides guidelines for carrying out the acute oral toxicity study.

B. Objective

The objective of the Data Reporting Guidelines (DRGs) is to provide an example of an acceptable general reporting format that can be reviewed effectively and expeditiously in accordance with the Agency's review process. The recommendations are intended to be consistant with the guidelines for data reporting as described in Sections 80-4 and 81-1 and those described in the Agency's Good Laboratory Practice Standards (40 CFR Part 160).

While following this Guideline is not mandatory, data submitters are encouraged to submit complete reports which can be effectively reviewed by the Agency. 40 CFR Part 158 pertains to the physical formatting of reports (which are referred to as "studies") and submitted packages. Some of its requirements are mandatory.

RESPONSE TO PUBLIC COMMENTS

The Agency received one response to its request for public comments on these documents published in the FEDERAL REGISTER of March 8, 1989 (54 FR 9886). These comments were considered in the final form of this DRG.

GUIDELINE

The Final Report should contain the following items.

COVER PAGE

The title page and additional documentation (i.e., requirements for data submission, Good Laboratory Practices statement and statement of data confidentiality claims), if relevant to the study report, must precede the content of the study format below. These requirements are described in 40 CFR Part 158.

TABLE OF CONTENTS

The table of contents should include a listing of the elements of the final report such as the Summary, an Introduction, the Materials and Methods, Results, Discussion Bibliography, Tables, Figures, Appendices and key subsections as appropriate.

BODY OF THE REPORT

This item shall include all information required in §80-4(b)(2), 80-4(c) and 81-1(h) of this subdivision and should be provided in such detail that the reviewer can assess the quality of the study and conformity to the acute ora toxicity Guideline. It should contain the following sections.

I. SUMMARY

As per §80-4(b)(1) of this subdivision, the test report shall contain a summary including a brief description of the study protocol, chemical used, the animals tested and the highlights of the results of the study relative to the positive findings. Any deviations from the intended protocols should be noted.

II. INTRODUCTION

Include the objectives of the study and the Guideline reference. The overall experimental design should be explained.

III. MATERIALS AND METHODS

A. Test substance

Test material (chemical name)
Form (technical, manufacturing-use product or formulation)
source
lot number
CAS No.
purity

state
Ionization constant (if applicable)
pH (if applicable)
octanol/water partition coefficient (if known)

vehicles used

B <u>Test Animals</u>

species and strain
sex
source
body weight
number of test animals
number of control animals

pre-test condition
housing conditions
test environment

C. Experimental Design

Doses used
Number and sex of animals per dose group
Observations, type and time
Termination

D. Evaluation Procedures

The final report should describe the types of observations of the animals for toxic signs, body weights, the frequency of observations, the gross pathological examination procedures and any other observations performed. The statistical methods used for calculation of the LD_{50}, the 95 percent confidence limits and the slope of the dose-response curve should be specified and referenced.

E. Deviation from protocol

Deviations from the protocol recommended in § 81-1 should be described along with the rational for the changes.

IV. RESULTS

This sections should provide a summary of the toxic signs, mortality, body weight changes, gross pathology and other observations performed associated with the doses tested. Typically, these results are summarized in tabular form.

V. DISCUSSION

This section should provide an assessment of the results of the study, an interpretation of the toxicity observed, the consistancy of the dose-response effects and should try to explain unexpected findings. The impact of any deviation from the Guideline protocol should be discussed.

VI. BIBLIOGRAPHY

This item should contain a list of references cited in the body of the report.

VII. VERIFICATION

This item shall contain information required by §80-4(b)(2). Each test report shall be:

A. Signed by each of the senior scientific personnel, including the laboratory director responsible for performing and supervising the testing, preparing, reviewing and approving the test report and

B. Certified by the applicant or an authorized agent of the applicant as a complete and unaltered copy of the report provided by the testing laboratory whether independent or owned, operated or controlled by the applicant.

VII. ARCHIVES

This section of the final report shall contain all information required in 40 CFR 160.185.

IX. TABLES/FIGURES

X. APPENDIX(ES)

These should include individual animal data, historical control data, pathology report, analytical methods and results of analysis of the test substance, details of statistical analysis, protocol and other information as appropriate.

PESTICIDE ASSESSMENT GUIDELINES

SUBDIVISION F

HAZARD EVALUATION

HUMAN AND DOMESTIC ANIMALS

Series 81-2

Acute Dermal Toxicity

ADDENDUM ON DATA REPORTING

Prepared by:

Robert P. Zendzian Ph.D.

for

Health Effects Division

Office of Pesticide Programs
US Environmental Protection Agency

Subdivision F - Acute Dermal Toxicity Studies

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PESTICIDE ASSESSMENT GUIDELINES

HUMAN AND DOMESTIC ANIMALS

Acute Dermal Toxicity

Subdivision F, Series 81-2

DATA REPORTING

INTRODUCTION

A. Purpose

The purpose of this addendum to the guideline is to provide a data reporting format for acute dermal toxicity studies. Subpart F, Series 81-2 provides guidelines for carrying out the acute dermal toxicity study.

B. Objective

The objective of the Data Reporting Guidelines (DRGs) is to provide an example of an acceptable general reporting format that can be reviewed effectively and expeditiously in accordance with the Agency's review process. The recommendations are intended to be consistant with the guidelines for data reporting as described in Sections 80-4 and 81-2 and those described in the Agency's Good Laboratory Practice Standards (40 CFR Part 160).

While following this Guideline is not mandatory, data submitters are encouraged to submit complete reports which can be effectively reviewed by the Agency. 40 CFR Part 158 pertains to the physical formatting of reports (which are referred to as "studies") and submitted packages. Some of its requirements are mandatory.

RESPONSE TO PUBLIC COMMENTS

The Agency received one response to its request for public comments on these documents published in the FEDERAL REGISTER of March 8, 1989 (54 FR 9886). These comments were considered in the final form of this DRG.

GUIDELINE

The Final Report should contain the following items.

COVER PAGE

The title page and additional documentation (i.e., requirements for data submission, Good Laboratory Practices statement and statement of data confidentiality claims), if relevant to the study report, must precede the content of the study format below. These requirements are described in 40 CFR Part 158.

TABLE OF CONTENTS

The table of contents should include a listing of the elements of the final report such as the Summary, an Introduction, the Materials and

Methods, Results, Discussion Bibliography, Tables, Figures, Appendices and key subsections as appropriate.

BODY OF THE REPORT

This item shall include all information required in §80-4(b)(2), 80-4(c) and 81-2(h) of this subdivision and should be provided in such detail that the reviewer can assess the quality of the study and conformity to the acute dermal toxicity Guideline. It should contain the following sections.

I. SUMMARY

As per §80-4(b)(1) of this subdivision, the test report shall contain a summary including a brief description of the study protocol, chemical used, the animals tested and the highlights of the results of the study relative to the positive findings. Any deviations from the intended protocols should be noted.

II. INTRODUCTION

Include the objectives of the study and the Guideline reference. The overall experimental design should be explained.

III. MATERIALS AND METHODS

A. Test substance

Test material (chemical name)
Form (technical, manufacturing-use product or formulation)
source
lot number
CAS No.
purity

state
Ionization constant (if applicable)
pH (if applicable)
octanol/water partition coefficient (if known)
vapor pressure at 20° C (if known)

vehicles used

B <u>Test Animals</u>

species and strain
source
sex
body weight
number of test animals

number of control animals
pre-test condition
housing conditions
test environment

C. Experimental Design

Doses and duration of exposure
Number and sex of animals per dose group
Application site, preparation and method(s) of protection
Observations, type and time
Termination

D. Evaluation Procedures

The final report should describe the types of observations of the animals for toxic signs, body weights, the frequency of observations, the gross pathological examination procedures and any other observations performed. The statistical methods used for calculation of the LD_{50}, the 95 percent confidence limits and the slope of the dose-response curve should be specified and referenced.

E. Deviation from protocol

Deviations from the protocol recommended in § 81-2 should be described along with the rational for the changes.

IV. RESULTS

This sections should provide a summary of the toxic signs, mortality, body weight changes, gross pathology and other observations performed associated with the doses tested. Typically, these results are summarized in tabular form.

V. DISCUSSION

This section should provide an assessment of the results of the study, an interpretation of the toxicity observed, the consistancy of the dose-response effects and should try to explain unexpected findings. The impact of any deviation from the Guideline protocol should be discussed.

VI. BIBLIOGRAPHY

This item should contain a list of references cited in the body of the report.

VII. VERIFICATION

This item shall contain information required by §80-4(b)(2). Each test report shall be:

A. Signed by each of the senior scientific personnel, including the laboratory director responsible for performing and supervising the testing, preparing, reviewing and approving the test report and

B. Certified by the applicant or an authorized agent of the applicant as a complete and unaltered copy of the report provided by the testing laboratory whether independent or owned, operated or controlled by the applicant.

VII. ARCHIVES

This section of the final report shall contain all information required in 40 CFR 160.185.

IX. TABLES/FIGURES

X. APPENDIX(ES)

These should include individual animal data, historical control data, pathology report, analytical methods and results of analysis of the test substance, details of statistical analysis, protocol and other information as appropriate.

PESTICIDE ASSESSMENT GUIDELINES

SUBDIVISION F

HAZARD EVALUATION:

HUMANS AND DOMESTIC ANIMALS

Series 82-1 and 83-1

Subchronic and Chronic Dog

ADDENDUM ON DATA REPORTING

Prepared by:

Mission Support Section
Toxicology Branch
Hazard Evaluation Division

Project Manager:

Elizabeth M.K. Leovey, PhD
Hazard Evaluation Division

Office of Pesticide Programs
U.S. Environmental Protection Agency

Subdivision F - Subchronic and Chronic Dog

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PESTICIDE ASSESSMENT GUIDELINES

HUMANS AND DOMESTIC ANIMALS

Subchronic and Chronic Dog

Subdivision F, Series 82-1 and 83-1

DATA REPORTING

INTRODUCTION

A. Purpose

This Data Reporting Guideline (DRG) is designed to aid the petitioner/registrant in generating reports which are compatible with the Agency's review process. While following this Guideline is not mandatory, data submitters are strongly encouraged to submit complete reports which can be efficiently reviewed by the Agency. This DRG pertains to organizing and presenting the substance of the data report. 40 CFR Part 158 refers to the physical formatting of reports (which are referred to as "studies") and submittal packages. Some of its requirements are mandatory.

B. Objective

The objective of the Guideline is to provide an example of an acceptable format for reporting materials, methods, and results of chronic and subchronic dog studies. These recommendations are intended to show how the requirements of §80-4, §82-1, and §83-1, the Agency's Good Laboratory Practice Standards (40 CFR, Part 160), and the guidance offered by the Office of Pesticide Programs in its Standard Evaluation Procedures, available from the National Technical Information Center may be organized in a final report.

RESPONSE TO PUBLIC COMMENTS

The purpose of this section is to acknowledge and address the concerns expressed in the letters of comment received by the Agency in response to the public notice in the FEDERAL REGISTER (51 FR 18660) of May 21, 1986. Most of the comments concerned the organization of the different sections and of the DRG itself. The Agency has considered these comments and revised this DRG to be consistent with other DRGs for Subdivision F and with how the Agency reviews these studies. The latter is particularly the reason for the inclusion of summary tables in the RESULTS sections. Individual animal data or data for several parameters tabulated by animal is needed to allow the Agency's toxicologists to readily recognize the interrelationships of toxic effects. This is especially true in the case of gross-and histopathology observations were tthe Agency's toxicologists could easily check that gross observations haave been evaluated aand addressed by histopathology.

GUIDELINE

TITLE/COVER PAGE

Cover page and additional documentation requirements (i.e., requirements for data submission, Good Laboratory Practice statement, and statement of data confidentiality claims), if relevant to the study report, must precede the content of the study formatted below. These requirements are described in CFR 40 Parts 158 and 160.

TABLE OF CONTENTS

A concise listing, preceding the body of the report, should be contained in this item of all essential elements of the study, and the page or table number where that element is located in the report. Essential elements include a Summary, Introduction, Materials and Methods section, Results, Discussion, Bibliography, Tables, Figures, Appendices, and key subsections as appropriate.

BODY OF REPORT

The report should include all information required in §80-4(b)(2), §80-4(c), §82-1, and §83-1.

I. SUMMARY

As per §80-4(b)(1) of this Subdivision, this section of the test report shall contain a summary and analysis of the data, and a statement of the conclusions drawn from the analysis. The summary should highlight any and all positive data or observation, and any deviation from control data which may be indicative of toxic effects. The summary shuld be presented in sufficient detail to permit independent evaluation of the results.

II. INTRODUCTION

Description of the objectives of the study, name, and properties of the chemical and the rational for the type of study conducted. The rationale for any deviations from the protocol recommended in Subdivision F should be provided.

III. MATERIALS AND METHODS

A. Test Substance

1. Chemical name and chemical abstract number or code number;

2. Source of procurement, batch or lot number of each procurement;

3. Purity and identity analysis on bulk chemical;

4. Stability of test material in feed and control subtances;

5. Assay - description of method and percent of target concentration;

6. Storage/stability of test material/diet; and

7. Formulation for administration to animals.

B. Animals

1. Description:

   a. Species, strain and substrain;

   b. Age,

   c. Body weight range, and

   d. Source of supply;

2. Isolation procedures;

3. Health assessment;

4. Caging;

   a. Type of cages and

   b. Excreta collection;

5. Housing - number of animals per cage;

6. Diet - vendor or composition, if appropriate;

7. Water;

   a. Purity or source, and

   b. System; and

8. Room assignment.

C. Methods

1. Treatment groups;

   a. Dosage levels;

   b. Number of animals per group;

   c. Statistical consideration employed in selecting the number of groups, dosage levels and number of animals in each group.

2. Treatment regimen;

   a. Route of administration;

b. Frequency;

c. Volume and concentration;

d. Carrier/solvent

e. Daily records and clinical observations

3. Experimental measurements

Describe measurements and frequency with which they are made and procedures employed.

4. Animal assignment

a. Procedure used for identification of each animal.

b. Randomization procedure for assignment to treatment groups. Housing, food, and water during experiment if different from that described in subsection "animals."

5. Statistical analysis

In presenting the statistical methods used to analyze the study data, show the method used; including computer programs and give sufficient information in order that an independent reviewer can re-evaluate and reconstruct the analysis.

IV. RESULTS

Pertinent summary table with appropriate statistical evaluations clearly indicated may be placed in the text of this section - see tables included in this package. Each parameter studied shall be addressed sequentially regardless of whether compound related effects were noted.

V. DISCUSSION/CONCLUSION

A. Discussion of incidences of effects of biological/statistical significance, relationship of related events.

b. Discussion of observations and adequacy of the tests for the intended purpose.

c. Discussion of observed toxic effects, target organ(s), dose related compound induced effects, and no observed effect levels (NOEL).

VI. BIBLIOGRAPHY

VII. VERIFICATION

This item shall contain information required by §80-4(b)(2). Each test report shall be:

A. Signed by each of the senior scientific personnel, including the laboratory director, responsible for performing and supervising the testing, preparing, reviewing, and approval of the test report; and

B. Certified by the applicant or an authorized agent of the applicant as a complete and unaltered copy of the report provided by the testing laboratory whether independent or owned, operated, or controlled by the applicant.

VIII. ARCHIVES

The section of the final report should contain all information required in 40 CFR 160.185.

IX. TABLES (Means or Lesions/Dose/Sex)

X. INDIVIDUAL ANIMAL DATA

by Parameter(s)/Dose/Sex

XI. TABLES/FIGURES (other)

XII. APPENDICES (Optional)

e.g. historical control data or any other information that may facilitate the review of a report by the Agency.

Tabular Data Format

(EXAMPLE)

A Table showing means or number of lesions should be presented for all measured parameters i.e., clinical chemistry, hematology, food consumption, etc. It is also recommended that the changes in clinical parameters over the course of the study be presented in graphical form.

Mean Summary Body Wt Gain

Groups	No. of animals in group	Initial body weight	Body Weight after 52 weeks	Weight gain
Control	4	Mean	Mean	Mean
xx ppm	4	Mean	Mean	Mean
xx ppm	4	Mean	Mean	Mean
xx ppm	4	Mean	Mean*	Mean*

* Statistical Significance

The following are examples of individual animal reporting formats for the registrants convenience.

Clinical Observation

Test Material

Animal #1 Treatment Group: Control Female

Term Sacrifice ___
Moribund Sacrifice ___
Found Dead ____

Date of Observation	Clinical Observations

Body/Organ Weights

(EXAMPLE)

Test Compound _____

Animal #1 Control Group Sex: Female

Date of Determination	Body Weight (Kg)	Body/organ wt. Ratio		
		Organ	Wt (gm)	Ratio
		brain		
		heart		
		liver		
		kidney		
		other organs		

Food (Water) Consumption

(EXAMPLE)

Test Compound _____

Animal #1 Control Group Sex:

Average Daily Diet Consumption in Grams

Week 1

(EXAMPLE)

Hematology

Test Compound _____

Animal #1 Control Group Sex:

Hematology

	Pre-test	Months on test					
		1	2	3	6	9	12
erythrocytes million/mm^3							
Hemoglobin gms/100 ml							
Hematocrit Percent							
Other Parameters*							

* Other determinations which may be necessary for an adequate Toxicological evaluation

(EXAMPLE)

Clincial Chemistry

Test Compound _____

Animal #1 Control Group Sex:

Clinical Chemistry

	Pre-test	Months on test		
	1	3	6	12
Glucose mg %				
Other* Parameters				
"				
"				
"				

* Other determinations which may be necessary for an adequate Toxicological evaluation

(EXAMPLE)

Gross/Histopathology

Animal #1 Control Group Sex:

Organ	Gross Pathology	Histopathology
Brain	Edema	Enter description of lesions or appropriate code
Pituitary	Normal	
Lungs	Hemorrhagic	
Heart	Normal	
Liver	Fatty infiltration	
Spleen	Enlarged	
Kidney	Normal	
Adrenals	Nodules	
Pancreas	Normal	
"	"	
"	"	
"	"	
"	"	
etc.	—	

PESTICIDE ASSESSMENT GUIDELINES

SUBDIVISION F

HAZARD EVALUATION:

HUMANS AND DOMESTIC ANIMALS

Series 82-1, 83-1, 83-2 and 83-5

Subchronic Oral Toxicity (90-day Study),
Chronic Toxicity Studies,
Oncogenicity Study
and Combined Chronic Toxicity/Oncogenicity Studies

(Rodent Studies)

ADDENDUM ON DATA REPORTING

Prepared by:

Orville E. Paynter, Ph.D., DABT

Project Manager:
Elizabeth M.K. Leovey, Ph.D.
Hazard Evaluation Division

Office of Pesticide Programs
U.S. Environmental Protection Agency

Subdivision F - Subchronic Oral Toxicity (90-day Study), Chronic Toxicity Studies, Oncogenicity Study and Combined Chronic Toxicity/Oncogenicity Studies (Rodent Studies)

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PESTICIDE ASSESSMENT GUIDELINES

HUMANS AND DOMESTIC ANIMALS

Subchronic Oral Toxicity (90-day Study), Chronic Toxicity Studies, Oncogenicity Study and Combined Chronic Toxicity/Oncogenicity Studies (Rodent Studies)

Subdivision F, Series 82-1, 83-1, 83-2 and 83-5

DATA REPORTING

INTRODUCTION

A. Purpose

This Data Reporting Guideline (DRG) is designed to aid the petitioner/registrant in generating reports which are compatible with the Agency's review process. While following this Guideline is not mandatory, data submitters are encouraged to submit complete reports which can be efficiently reviewed by the Agency. This DRG pertains to organizing and presenting the substance of the data report. 40 CFR Part 158 pertains to the physical formatting of reports (which are referred to as "studies") and submittal packages. Some of its requirements are mandatory.

B. Objective

The objective of the Guideline is to provide an example of an acceptable format for reporting materials, methods, and results of toxicity and rodent oncogenicity studies. These recommendations are intended to show how the requirements of §80-4, 82-1, 83-1, 83-2, and 83-5, the Agency's Good Laboratory Practice Standards (40 CFR, Part 160), and the guidance offered by the Hazard Evaluation Division's SEP Toxicity Potential (EPA 540/9-85-020) and Oncogenicity Potential (EPA 540/9-85-019), available from the National Technical Information Center may be organized in a Final Report.

RESPONSE TO PUBLIC COMMENT

This document incorporates the public comments received by the Agency in reposnse to publication in the FEDERAL REGISTER (54 FR 3136, 1/23/89).

GUIDELINE

The Final Report should contain the following items.

COVER PAGE

Cover page and additional documentation requirements (i.e., requirements for data submission, Good Laboratory Practice statement, and statement of data confidentiality claims), if relevant to the

study report, must precede the content of the study formatted below. These requirements are described in PR Notice 86-5.

TABLE OF CONTENTS

This item should be a concise listing of the essential elements of the Final Report including the page numbers for each. Essential elements should include a Summary, Introduction, Materials and Methods section, Results, Discussion, Bibliography, Tables, Figures, Appendices, and key subsections as appropriate.

BODY OF THE REPORT

This item shall include all information required in §80-4(b)(2), §80-4(c), §82-1(1)(3), §83-1(3), §83-2(f)(1)(i)-(ii), and §83-2(3). If the study is a combined chronic/ oncogenicity study, the report shall meet the requirement of §83-5(c)(1)(i)(ii) and §83-5(3) in addition to the §80-4 requirements.

I. SUMMARY

As per §80-4(b)(1) of this Subdivision, this section of the test report shall contain a summary and analysis of the data, and a statement of the conclusions drawn from the analysis. The summary should highlight any and all positive data or observations, and any deviations from control data which may be indicative of toxic effects.

II. INTRODUCTION

Includes the objective of the study and any deviations from the protocol recommended in §83-2 or §83-5. The rationale for the deviations should be provided.

III. MATERIALS AND METHODS

A. Test Substance

1. Chemical name and chemical abstract number or code number;

2. Source of procurement, batch or lot number of each procurement;

3. Purity and identity analysis on bulk chemical;

4. Stability of test material in feed and control substances;

5. Assay--description of method and percent of target concentration;

6. Storage/stability of test material/diet; and

7. Formulation for administration to animals.

B. Animals

1. Description:

   a. Species, strain, and substrain,

   b. Age,

   c. Body weight range, and

   d. Source of supply;

2. Isolation procedures;

3. Health assessment;

4. Caging--type of cages;

5. Housing--number of animals per cage;

6. Diet;

   a. Vendor and

   b. Composition;

7. Water;

   a. Purity or source, and

   b. Delivery System to Animals;

8. Room assignment.

C. Methods

1. Treatment groups:

   a. Dosage levels, and

   b. Number of animals per group;

2. Treatment regimen:

   a. Route of administration;

   b. Frequency;

   c. Volume and concentration;

   d. Carrier/solvent; and

e. Daily records and clinical observations.

3. Experimental measurements:

Describe measurements and frequency with which they are made and cite procedures employed.

4. Animal assignment:

a. Procedure used for identification of each animal.

b. Randomization procedure for assignment to treatment groups. Housing, food, and water during experiment if different from that described in subsection "Animals."

5. In presenting the statistical methods used to analyze the study, cite the method used, and give sufficient information in order that an independent reviewer can reevaluate and reconstruct the analysis.

IV. RESULTS

Pertinent summary table with appropriate statistical evaluations clearly indicated may be placed in the text of this section. Each parameter studied shall be addressed sequentially. It is sufficient to state that there were no significant inter-group differences in certain parameters where appropriate.

V. DISCUSSION/CONCLUSION

A. Discussion of observations and adequacy of the tests for the intended purpose.

B. Discussion of observed toxic effects, target organ(s), dose-related compound-induced effects, and no-observed-effect levels (NOEL).

C. The following major considerations for analysis and evaluation of oncogenicity (see SEP - Oncogenicity Potential for further discussion), as relating to the species and strain of rodents used, should be specifically addressed in this part.

1. Spontaneous neoplasm/incidence in untreated animals (concurrent and historical controls);

2. Presence and incidence of neoplasms not usually observed (rare tumors);

3. Increased incidence of benign and/or malignant neoplasms that are usually found;

4. Dose-response relationships; and

5. Decrease in latency (time to tumor discovery) of neoplasms

that are usually found, in so far as can be assessed.

VI. SUMMARY TABLE

See tables 1 and 2 for examples for presenting historical control data summaries and table 3 for summarizing tumor incidence data.

VII. INDIVIDUAL ANIMAL TUMOR DATA

See table 4. In addition to animal number, the time to tumor discovery or animal death (in days) should be contained in the column heading for each animal.

VIII. VERIFICATION

This item shall contain information required by §80-4(b)(2). Each test report shall be:

A. Signed by each of the senior scientific personnel, including the laboratory director, responsible for performing and supervising the testing, preparing, reviewing, and approval of the test report; and

B. Certified by the applicant or an authorized agent of the applicant as a complete and unaltered copy of the report provided by the testing laboratory whether independent or owned, operated, or controlled by the applicant.

IX. ARCHIVES

This section of the Final Report shall contain all information required in 40 CFR 160.185.

X. TABLES/FIGURES

XI. APPENDIX(CES)

These should include individual animal data, historical control data, analytical method and results of analyses on the test substance, and test diet (if the test material is administered via the diet), and other appropriate information.

EXAMPLES TO ILLUSTRATE TABLES MOST USEFUL IN REPORTING ONCOGENICITY STUDIES

Table 1. Incidence (Percent) of Female Control Rats Bearing Thyroid C-Cell Tumors Among Animals Sacrificed Post 12-Months (Same Lab)

Study*		Adenoma or Carcinoma	Adenoma	Carcinoma
1.	Group A	10/58 (17.2)	10/58 (17.2)	0/58 (0)
	Group B	7/59 (11.9)	6/59 (10.2)	1/59 (2)
2.	Group A	5/59 (8.5)	5/59 (8.5)	0/59 (0)
	Group B	6/58 (10.3)	6/58 (10.3)	0/58 (0)
3.	Group A	9/57 (15.8)	6/57 (10.5)	3/57 (5)
	Group B	6/55 (10.9)	5/55 (9.0)	1/55 (2)
4.	Group A	2/58 (3.4)	2/58 (3.4)	0/58 (0)
	Group B	0/55 (0)	0/55 (0)	0/55 (0)
	Total	45/459(9.8)	40/459(8.7)	5/459(1.1)

*Each listed study had two control groups, identified as Group A or B. The rat strain is Sprague-Dawley.

Table 2. Historical Control Incidence of Lung Tumors in Male B6C3F$_1$ Mice Receiving Corn Oil by Gavage (Different Labs)

Laboratory	Alveolar/ Bronchiolar Adenoma	Alveolar/ Bronchiolar Carcinoma	Alveolar/ Bronchiolar Adenoma or Carcinoma
A	8/100(8.0%)	6/100(6.0%)	14/100(14.0%)
B	12/235(5.1%)	17/235(7.2%)	29/235(12.3%)
C	5/120(4.2%)	3/120(2.5%)	8/120(6.7%)
D	19/150(12.7%)	4/150(2.7%)	22/150(14.7%)
E	4/49(8.2%)	3/49(6.1%)	7/49(14.3%)
F	32/248(12.9%)	11/248(4.4%)	43/248(17.3%)
Total	80/902(8.9%)	44/902(4.9%)	123/902(13.6%)

TABLE 3 (EXAMPLE)

	GROUP I			GROUP II			GROUP III			GROUP IV		
	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total	Scheduled Sacrifice	Moribund Sacrifice & Deaths	Total
Liver (No. Examined)	(22)	(52)	(74)	(34)	(42)	(76)	(24)	(52)	(76)	(22)	(53)	(75)
Hepatocellular Carcinoma		4	4	2	1	3	2	1	3	1	1	2
Hepatocellular Adenoma*	2/2	1/1	3/3	1/1	4/3	5/4	30/12	24/11	54/23	54/17	21/12	75/29
Malignant Lymphoma	3	9	12	2	7	9	1	7	8		6	6
Granulocytic Leukemia		1	1								1	1
Angiosarcoma								2	2		1	1
Carcinoma, Metastatic											1	1
Sarcoma, Metastatic		1	1		1	1						
Reticulum Cell Sarcoma				1		1		1	1			
Hepatocholangio-carcinoma												
Multifocal Hepatocellular												
Degeneration		1	1				1	2	3		3	3
Basophilic Foci						1				1	2	3
Mononuclear Cell Infiltration	6	9	15	9	1	10	9	2	11	8	8	16
Foci of Mononuclear Cells				1		1					1	1
Angiectasis	1		1	2	1	3		1	1	2	3	5
Focus of Cellular Change				3		3				1		1
Multifocal Hepatitis	16	10	26	23	4	27	13	7	20	14	9	23
Multifocal Necrosis	3		8	3	8	11	1	6	7	2	6	8

TABLE 4 (EXAMPLE)

Liver (Animal No.)																						
Hepatocellular Carcinoma																						P
Hepatocellular Adenoma (No. Present)	1	6	2	5	1	4	5		4		1	5		2	7	1	N	1	1		4	4
Malignant Lymphomas																						
Granulocytic Leukemia																						
Angiosarcoma																						
Carcinoma, Metastatic																						
Sarcoma, Mestastatic																						
Reticulum Cell Sarcoma																						
Hepatochol-angiocarcinoma																						
Multifocal Hepatocellular																						
Degeneration																						
Basophilic Foci			2																			
Mononuclear Cell Infiltration	1					2				3		1	1		2	1				1		
Foci of Mono-nuclear Cells																						
Angiectasis						2							3									
Focus of Cellular Change														3								
Multifocal Hepatitis	2	2	4		3	3	3	1		3		2	2	2		3			2			4
Multifocal Necrosis												2										2

Key: P = Present N = No Section A = Autolysis X = Not Remarkable 1 = Incomplete Section
1 = Minimal 2 = Slight 3 = Moderate 4 = Moderately Severe High 5 = Severe/High

PESTICIDE ASSESSMENT GUIDELINES

SUBDIVISION F

HAZARD EVALUATION

HUMAN AND DOMESTIC ANIMALS

Series 82-2 and 82-3

Repeated Dose Dermal Toxicity: 21-Day Study

and

Subchronic Toxicity Study: 90-Day Study

ADDENDUM ON DATA REPORTING

Prepared by:

Robert P. Zendzian Ph.D.

for

Health Effects Division

Office of Pesticide Programs
US Environmental Protection Agency

Subdivision F - Repeated Dose Dermal Toxicity Studies
(21-day and 90-day)

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Repeated Dose Dermal Toxicity

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PESTICIDE ASSESSMENT GUIDELINES

HUMAN AND DOMESTIC ANIMALS

Repeated Dose Dermal Toxicity (21-days and 90-days)

Subdivision F, Series 82-2 & 82-3

DATA REPORTING

INTRODUCTION

A. Purpose

The purpose of this addendum to the guideline is to provide a data reporting format for repeated dose dermal toxicity studies. Subpart F, Series 82-2 and 82-3 provide guidelines for carrying out the repeated dose dermal toxicity studies.

B. Objective

The objective of the Data Reporting Guidelines (DRGs) is to provide an example of an acceptable general reporting format that can be reviewed effectively and expeditiously in accordance with the Agency's review process. The recommendations are intended to be consistant with the guidelines for data reporting as described in Sections 80-4, 82-2 and 82-3 and those described in the Agency's Good Laboratory Practive Standards (40 CFR Part 160).

While following this Guideline is not mandatory, data submitters are encouraged to submit complete reports which can be effectively reviewed by the Agency. 40 CFR Part 158 pertains to the physical formatting of reports (which are referred to as "studies") and submitted packages. Some of its requirements are mandatory.

RESPONSE TO PUBLIC COMMENTS

The Agency received one response to its request for public comments on these documents published in the FEDERAL REGISTER of March 8, 1989 (54 FR 9886). These comments were considered in the final form of this DRG.

GUIDELINE

The Final Report should contain the following items.

COVER PAGE

The title page and additional documentation (i.e., requirements for data submission, Good Laboratory Practices statement and statement of data confidentiality claims), if relevant to the study report, must precede the content of the study format below. These requirements are described in 40 CFR Part 158.

TABLE OF CONTENTS

The table of contents should include a listing of the elements of the final report such as the Summary, an Introduction, the Materials and Methods, Results, Discussion Bibliography, Tables, Figures, Appendices and key subsections as appropriate.

BODY OF THE REPORT

This item shall include all information required in §80-4(b)(2), 80-4(c), 82-2(h) and 82-3(h) of this subdivision and should be provided in such detail that the reviewer can assess the quality of the study and conformity to the repeated dose dermal toxicity Guideline. It should contain the following sections.

I. SUMMARY

As per §80-4(b)(1) of this subdivision, the test report shall contain a summary including a brief description of the study protocol, chemical used, the animals tested and the highlights of the results of the study relative to the positive findings. Any deviations from the intended protocols should be noted.

II. INTRODUCTION

Include the objectives of the study and the Guideline reference. The overall experimental design should be explained.

III. MATERIALS AND METHODS

A. Test substance

Test material (chemical name)
source
lot number
CAS No.
purity

state
Ionization constant (if applicable)
pH (if applicable)
octanol/water partition coefficient (if known)
vapor pressure at 20° C (if known)

vehicles used

B <u>Test Animals</u>

species and strain
source
sex
body weight
number of test animals
number of control animals

pre-test condition
housing conditions
test environment

C. Experimental Design

Doses and duration of exposure
Number and sex of animals per dose group
Application site, preparation and method(s) of protection
Observations, type and time
Termination

D. Evaluation Procedures

The final report should describe the types of observations of the animals for toxic signs, body weights, the frequency of observations, the gross pathological examination procedures, histopathology and any other observations performed.

E. Deviation from protocol

Deviations from the protocol recommended in § 82-2 or 82-3 should be described along with the rational for the changes.

IV. RESULTS

This sections should provide a summary of the toxic signs, mortality, body weight changes, gross pathology and other observations performed associated with the doses tested. Typically, these results are summarized in tabular form.

V. DISCUSSION

This section should provide an assessment of the results of the study, an interpretation of the toxicity observed, any the dose-response effects and should try to explain unexpected findings. The impact of any deviation from the Guideline protocol should be discussed.

VI. BIBLIOGRAPHY

This item should contain a list of references cited in the body of the report.

VII. VERIFICATION

This item shall contain information required by §80-4(b)(2). Each test report shall be:

A. Signed by each of the senior scientific personnel, including the laboratory director responsible for performing and supervising the testing, preparing, reviewing and approving the test report and

B. Certified by the applicant or an authorized agent of the applicant as a complete and unaltered copy of the report provided by the

testing laboratory whether independent or owned, operated or controlled by the applicant.

VII. ARCHIVES

This section of the final report shall contain all information required in 40 CFR 160.185.

IX. TABLES/FIGURES

X. APPENDIX(ES)

These should include individual animal data, historical control data, pathology report, analytical methods and results of analysis of the test substance, details of statistical analysis, protocol and other information as appropriate.

PESTICIDE ASSESSMENT GUIDELINES

SUBDIVISION F

HAZARD EVALUATION

HUMAN AND DOMESTIC ANIMALS

Series 83-4

Reproductive and Fertility Effects

ADDENDUM ON DATA REPORTING

Prepared by:

Roger Gardner

for

Health Effects Division

Office of Pesticide Programs
US Environmental Protection Agency

Subdivision F - Reproductive and Fertility Effects

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PESTICIDE ASSESSMENT GUIDELINES

HUMAN AND DOMESTIC ANIMALS

Reproductive and Fertility Effects

Subdivision F, Series 83-4

DATA REPORTING

INTRODUCTION

A. Purpose

The purpose of this addendum to the guideline is to provide a data reporting format for the rat multigeneration reproduction study. Subpart F, Series 83-4 provides guidelines for carrying out this study.

B. Objective

The objective of the Data Reporting Guidelines (DRGs) is to provide an example of an acceptable general reporting format that can be reviewed effectively and expeditiously in accordance with the Agency's review process. The recommendations are intended to be consistant with the guidelines for data reporting as described in Sections 80-4 and 83-4 and those described in the Agency's Good Laboratory Practice Standards (40 CFR Part 160).

While following this Guideline is not mandatory, data submitters are encouraged to submit complete reports which can be effectively reviewed by the Agency. 40 CFR Part 158 pertains to the physical formatting of reports (which are referred to as "studies") and submitted packages. Some of its requirements are mandatory.

RESPONSE TO PUBLIC COMMENTS

The Agency received one response to its request for public comments on these documents published in the FEDERAL REGISTER of March 8, 1989 (54 FR 9886). These comments were considered in the final form of this DRG.

GUIDELINE

The Final Report should contain the following items.

COVER PAGE

The title page and additional documentation (i.e., requirements for data submission, Good Laboratory Practices statement and statement of data confidentiality claims), if relevant to the study report, must precede the content of the study format below. These requirements are described in PR Notice 86-5.

TABLE OF CONTENTS

The table of contents should include a listing of the elements of the final report such as the Summary, an Introduction, the Materials and Methods, Results, Discussion Bibliography, Tables, Figures, Appendices and key subsections as appropriate.

BODY OF THE REPORT

This item shall include all information required in §80-4(b)(2), 80-4(c) and 83-4(f) of this subdivision and should be provided in such detail that the reviewer can assess the quality of the study and conformity to the Reproductive and Fertility Effects Guideline. It should contain the following sections.

I. SUMMARY

As per §80-4(b)(1) of this subdivision, the test report shall contain a summary including a brief description of the experimental design, chemical used, the animals tested and the highlights of the results of the study relative to the positive findings. Any deviations from the intended protocols should be noted.

II. INTRODUCTION

Include the objectives of the study and the Guideline reference. The overall experimental design should be explained.

III. MATERIALS AND METHODS

A. Test substance

Test material (chemical name)
Form (technical, manufacturing-use product or formulation)
source
lot number
CAS No.
purity

state
Ionization constant (if applicable)
pH (if applicable)
octanol/water partition coefficient (if known)

vehicles used

B <u>Test Animals</u>

species and strain
sex
source
body weight
pre-test condition

housing conditions
test environment

C. Experimental Design

Dosing and breeding schedule
Mating procedure
Doses used
Route of administration
Number and sex of animals per dose group
Observations, type and time
Termination and tissue collection

D. Evaluation Procedures. The final report should describe:

(A) Observations and procedures used to calculate percentages, weight changes, or mating, gestation, viability, and lactation indices.

(B) Methods for adjusting data (censoring, pooling, or transforming results) prior to statistical analysis,

(C) Statistical procedures as recommended in §80-4(c) of this subdivision.

E. Deviation from protocol

Deviations from the protocol recommended in § 83-4 should be described along with the rationale for the changes.

IV. RESULTS

This section should provide a summary of the toxic signs, mortality, body weight changes, gross pathology, histopathology and other observations associated with the doses tested. Typically, these results are summarized in tabular form. Example formats in this section are generalized from those commonly submitted to the Agency. They do not represent required or preferred formats, but they are provided as a guide.

V. DISCUSSION

This section should provide an assessment of the results of the study, an interpretation of the toxicity observed, the consistency of the dose-response effects and should try to explain unexpected findings. The impact of any deviation from the Guideline protocol should be discussed.

VI. BIBLIOGRAPHY

This item should contain a list of references cited in the body of the report.

VII. VERIFICATION

This item shall contain information required by §80-4(b)(2). Each test report shall be:

A. Signed by each of the senior scientific personnel, including the laboratory director responsible for performing and supervising the testing, preparing, reviewing and approving the test report and

B. Certified by the applicant or an authorized agent of the applicant as a complete and unaltered copy of the report provided by the testing laboratory whether independent or owned, operated or controlled by the applicant.

VII. ARCHIVES

This section of the final report shall contain all information required in 40 CFR 160.185.

IX. TABLES/FIGURES

(1) Summary Tables. Paragraph 83-4(f) and §80-4 require results to be summarized in tabular form. Example Formats 1-3 show common presentations of summary data that are accepted by the Agency.

X. APPENDIX(ES)

These should include individual animal data (Example Formats 4 through 7), historical control data, pathology report, analytical methods and results of analysis of the test substance, details of statistical analysis, protocol and other information as appropriate.

Example Format 1

Example of frequently submitted
summary table presentations of clinical signs

Observation	Dose (mg/kg/day) 0	Y	5Y	10Y
Behavioral changes; clinical signs; signs of difficult or prolonged parturition; clinical signs; mortalities;	X	X	X	X
Number of animals	N	N	N	N
Number of males mated; number of females mated; number pregnant; number of males and females that died; number aborted; number not pregnant	X	X	X	X
Duration (days) of gestation; number of pups; stillbirths; live pups; pups with gross alterations; litter weights; individual pup weights at birth as well as at Days 4, 7, 14, and 21 after birth (Day 0);	Mean S. D. N	Mean S. D. N	Mean S. D. N	Mean S. D. N

Example Format 2

Example of a frequently submitted summary table format for
maternal body weight results in a Reproduction Toxicity Study

Observation	Dose (mg/kg/day) 0	Y	5Y	10Y
Body weight (g) at				
Week 0	Mean S. D. N	Mean S. D. N	Mean S. D. N	Mean[b] S. D. N
Each treatment week when weights are obtained.	Mean S. D. N	Mean S. D. N	Mean S. D. N	Mean[b] S. D. N
Day of sacrifice	Mean S. D. N	Mean S. D. N	Mean S. D. N	Mean[b] S. D. N
Body weight change, food and water consumption	Mean S. D. N	Mean S. D. N	Mean S. D. N	Mean S. D. N

[b]Means that are statistically significantly different from control group means should be highlighted.

Example Format 3

Presentation of some optional parental toxicity end points such as liver weight[a] and weight ratios (% body weight)

Dosee (mg/kg/day)	Body weight (g) at Day 0	Body weight (g) at Sacrifice	Liver wt parameters Absolute	Liver wt parameters Relative*
0	Mean S. D. N	Mean S. D. N	Mean S. D. N	Mean[b] S. D. N
Y	Mean S. D. N	Mean S. D. N	Mean S. D. N	Mean[b] S. D. N
5Y	Mean S. D. N	Mean S. D. N	Mean S. D. N	Mean[b] S. D. N
10Y	Mean S. D. N	Mean S. D. N	Mean S. D. N	Mean[b] S. D. N

[a]May include other organs as appropriate.

[b]Means that are statistically significantly different from control group means should be highlighted.

*Expressed as % body weight at sacrifice.

Example Format 4

Example of a format for reporting individual survival and toxic signs results

Dose group	Animal no.	Day of death or sacrifice	Toxic signs: Onset day	Toxic signs: Duration	Toxic signs: Description
Y	1	X	X	X	Brief description of changes in behavior, appearance, or other clinical signs.
	2	X	X	X	
	3	X	X	X	
	.	.	.	.	
	.	.	.	.	
	.	.	.	.	

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401 M ST., S.W., TS-793
WASHINGTON, D.C. 20460

Example Format 5

An example of a format for reporting individual maternal body weight data

Week	Animal number ###	Animal number ###	.....	Animal number ###
(Premating)				
1				
:	XXX	XXX	...	XXX
:	---	---	...	---
:	---	---	...	---
10	XXX	XXX	...	XXX
(Gestation)				
12	XXX	XXX	...	XXX
13	XXX	XXX	...	XXX
14	XXX	XXX	...	XXX
(Lactation)				
15	XXX	XXX	...	XXX
16	XXX	XXX	...	XXX
17	XXX	XXX	...	XXX
Sacrifice	XXX	XXX	...	XXX

Example Format 6

An example of the presentation of individual animal data for postnatal observations to be reported for each mating in each generation of the multigeneration reproduction study

At birth, Day 4 (before culling of litters), and on lactation days 7, 14, and 21

Animal number	Number alive		Number dead		Per cent alive	Mean pup weight (g)	Sex ratio*
	Males	Females	Males	Females			
xxxxxx	X	X	X	X	X	X	X
xxxxxx	X	X	X	X	X	X	X
xxxxxx	X	X	X	X	X	X	X
:	:	:	:	:	:	:	:
:	:	:	:	:	:	:	:
:	:	:	:	:	:	:	:

Day 4 (after culling of litters)

Animal number	Number alive		Mean pup weight (g)	Sex ratio*
	Males	Females		
xxxxxx	X	X	X	X
xxxxxx	X	X	X	X
xxxxxx	X	X	X	X
:	:	:	:	:
:	:	:	:	:
:	:	:	:	:

* Expressed as a percentage for one sex or as a ratio of the number of males to females.

Example Format 7

Example format for presentation of clinical observations of offspring from each mating in each generation of a multigeneration reproduction study

Animal number	Number of pups		Day	Observations
	Males	Females		
				Group Y
xxxxxx	X	X	X	Description of clinical observation 1
	X	X	X	Description of clinical observation 2
	X	X	X	Description of clinical observation n
xxxxxx	X	X	X	Description of clinical observation 1
	X	X	X	Description of clinical observation 2
	X	X	X	Description of clinical observation n
xxxxxx	X	X	X	Description of clinical observation 1
	X	X	X	Description of clinical observation 2
	X	X	X	Description of clinical observation n

PESTICIDE ASSESSMENT GUIDELINES

SUBDIVISION F

HAZARD EVALUATION

HUMANS AND DOMESTIC ANIMALS

Series 84

Mutagenicity Studies

ADDENDUM ON DATA REPORTING

Office of Pesticide Programs
U.S. Environmental Protection Agency

Subdivision F - Mutagenicity Studies

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PESTICIDE ASSESSMENT GUIDELINES

HUMANS AND DOMESTIC ANIMALS

Mutagenicity Studies

Subdivision F, Series 84

DATA REPORTING

INTRODUCTION

A. Purpose

This Data Reporting Guideline (DRG) is designed to aid the petitioner/registrant in generating reports which are compatible with the Agency's review process. This DRG pertains to organizing and presenting the substance of the data report. 40 CFR Part 158 pertains to the physical formatting of reports (which are referred to as "studies") and submittal packages. Some of its requirements are mandatory.

B. Objective

The objective of the Guideline is to provide an example of an acceptable format for reporting materials, methods, and results of mutagenicity studies. These recommendations are intended to show how the requirements of Series 84 of Subdivision F, the Agency's Good Laboratory Practice Standards (40 CFR, Part 160), and the guidance on mutagenicity testing offered by the Health Effects Testing Guidelines (Subpart F - Genetic Toxicity of 40 CFR, Part 798) may be organized in a Final Report. While following this Guideline is not mandatory, data submitters are encouraged to submit complete reports which can be efficiently reviewed by the Agency.

RESPONSE TO PUBLIC COMMENTS

The Agency received no response to its request for public comments on these documents published in the FEDERAL REGISTER of March 8, 1989 (54 FR 9886).

GUIDELINE

The final report should contain the following items.

COVER PAGE

Cover page and additional documentation requirements (i.e. requirements for data submission, Good Laboratory Practice statement, Quality Assurance statement and procedures for claims of confidentiality of data), if relevant to the study report, must precede the content of the study formatted below. These requirements are described in 40 CFR Part 160.

TABLE OF CONTENTS

This item should be a concise listing of the essential elements of the Final Report including the page numbers for each. Essential elements should include a Summary, Introduction, Materials and Methods section, Results, Discussion/Conclusion(s), Bibliography, Tables, Figures, Appendices, and key subsections as appropriate.

BODY OF REPORT

This item shall include all information required in Series 80-4(b)(2), Series 80-4(c) and Series 84 of this Subdivision. Additional guidance is provided in the Health Effects Testing Guidelines for mutagenicity testing (40 CFR, Part 798, Subpart F - Genetic Toxicity; hereafter referred to as the Health Effects Testing Guidelines).

I. SUMMARY

As per Series 80-4(b)(1) of this Subdivision, this section of the test report shall contain a summary and analysis of the data, and a statement of the conclusions drawn from the analysis. The summary should highlight any and all positive data or observations, and any deviations from control data which may be indicative of toxic effects.

II. INTRODUCTION

Includes the objective of the study and any deviations from the protocol recommended in the Health Effects Testing Guidelines. The rationale for the deviations should be provided.

III. MATERIALS AND METHODS

A. Test Substance; Negative and Positive Control Substances

1. Chemical name and chemical abstract number; any code numbers.

2. Source of procurement, batch or lot number of each procurement; procurement date.

3. Purity and identity analysis on bulk chemical.

4. Physical description.

5. Solvent(s)/vehicle(s) used and percent of final solution.

6. Stability (e.g. shelf life) and stability in solvent/vehicle.

7. Additional for in vivo tests: storage/stability of test substance/diet; formulation for administration to animals; percent of target concentration.

B. Test System

1. Description:

a. In vitro: Cell type; maintenance; source.

b. In vivo: Species, strain, substrain; age; body weight range; sex; source; maintenance (including isolation procedures, health assessment, caging with types of cages, housing - number of animals per cage, diet - vendor and composition, water).

2. Metabolic activation system (if required)

a. Description of source and derivation.

b. Composition of final preparation.

C. Methods

In this item, present description of protocol, include the following where appropriate for in vitro or in vivo situations:

1. Treatment groups

a. Concentration/dosage levels; present rationale for selection of concentrations/doses used (e.g. preliminary toxicity test).

b. Number of cultures/animals per test group.

c. Replicates per test group.

2. Treatment regimen

a. Method of administration/exposure.

b. Frequency.

c. Volume and concentration.

d. Daily records and observations (e.g. cell condition; clinical observations).

3. Experimental measurements

Describe measurements and frequency with which they are made and cite procedures employed.

4. In presenting the statistical methods to analyze the study, cite the method used and give sufficient information in order that an independent reviewer can reevaluate and reconstruct the analysis.

IV. RESULTS

A pertinent summary table(s) with appropriate statistical evaluations clearly indicated may be placed in the text of this section. Each parameter studied shall be addressed. Due to the large number of mutagenicity test types, a single Example table is not appropriate. Indicate in the table all pertinent information from which an unambiguous conclusion can be made.

V. DISCUSSION/CONCLUSION

1. Discussion of observations and adequacy of the tests for the intended purpose.

2. Discussion of observed effects of endpoint of interest, toxic effects, concentration-/dose-related compound-induced effects and statistical and biological significance.

3. Discussion of necessity for repeat, if warranted.

4. Overall conclusion(s) of the study.

VI. BIBLIOGRAPHY

This item should contain a list of references cited in the body of the report. They should be complete so that an independent reviewer may readily identify and obtain any reference.

VII. VERIFICATION

This item shall contain information required by Series 80-4(b)(2). Each test report shall be:

1. Signed by each of the senior scientific personnel, including the laboratory director, responsible for performing and

supervising the testing, preparing, reviewing, and approval of the test report; and

2. Certified by the applicant or an authorized agent of the applicant as a complete and unaltered copy of the report provided by the testing laboratory whether independent or owned, operated, or controlled by the applicant.

VIII. ARCHIVES

This section of the Final Report shall contain all information required in 40 CFR Part 160.185.

IX. TABLES/FIGURES

If a summary table was not included in the results section of the Final Report, include a summary table(s) here.

X. APPENDIX(CES)

These should include individual data, historical control data, analytical method and results of analyses on the test substance and test diet (if the test substance is administered via the diet), details of statistical analyses, complete protocol (if not already described completely in body of Final Report), and other information as appropriate.