UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

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MEMORANDUM

Subject: Data gaps in Dicamba registration standard

To: Robert Taylor / Vicki Walters, PM 25 Registration Division (TS767)

From: Stephanie P. April, Ph.D. Stephanie P. April 2/8/85
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Compound: Dicamba Tox Chem. #295
Registration No. 876-36 Registrant Velsicol
Accession Nos. 254862, 254863

Action Required: Review the additional information for the subacute inhalation experiment for the purpose of upgrading this study to be acceptable. In addition review the mutagenicity studies submitted to fill the data gap.

Data Evaluation Report

I. Subchronic Inhalation Study

This DER was exerpted from the previously completed Registration Standard for Dicamba. I considered the study supplementary for several reasons at the time. There was no report of the actual exposure concentrations, air flow rates, and animal observations as well as being conducted for two weeks rather than 90 days. The original study submitted by Velsicol was IRDC No. 163-619, Accession No. 242155.

Enclosed DER pg. 50-60 as attached herein, Addendum 1.

Velsicol submitted the requested information to upgrade this study in a submission from Chuck Ulrich who performed the study. The following comments were made on the basis of consultation with Stanley Gross, Ph.D.

(1) The particle size was derived from an analysis which is acceptable; however, although 95% of the particles were ten micrometers or less the overal size range was large.

(2) The actual exposure concentrations were: Group II 0.011 mg/L +/- 0.0048, Group III 0.14 mg/L +/- 0.045, Group IV 0.68 mg/L +/- 0.076.

The vapor pressure or boiling point would be necessary to assay if there was a significant vapor pressure exposure.

(3) The air flow rates were included: 28.3 L/min. for Groups II, III, and IV.

(4) The exposure duration was 2 weeks rather than 90 days and there were effects at all concentrations including deaths at 0.68 mg/L. In view of the actual exposure conditions of this pesticide as the use is described (4 lbs per acre) this experiment provides an adequate inhalation exposure to Dicamba.

CONCLUSION: Although no description of behavioural and pharmacological effects were not given the study is acceptable.

CLASSIFICATION: Accectable

II MUTAGENICITY

DATA EVALUATION REPORT

COMPOUND: DICAMBA

COMPOUND NO. CASWELL 295

Citation: In vitro Microbiological Mutagenicity and unscheduled DNA Synthesis Studies of Eighteen Perticides, SRI International, Menlo Park, CA Oct. 1979.

Report No. EPA-600/1-79-041; Accession No. PB80-133-222

Reviewed by: Stephanie P. April, Ph.D.
Section III, Toxicology Branch
HED(TS-769)

Core Classifications: WP2 Acceptable

Conclusion: WP2 DICAMBA is not a mutagen

Assay 1: E. coli WP2

MATERIALS:

(1) E.Coli WP2 (urrA) strain (Source: SRI from Dr. D.

McCalla). This strain is tryptophan deficient(trp) as well as deficit in repair of some physically and chemically induced DNA damage.

METHODS: The plane is supplemented with 1.25 g/L of Oxoid nutrient broth (CM67) to provide trace tryptophan to enhance mutagenic defects.

RESULTS: The number of tryptophan revertants per plate did not differ from the negative control with or without metabolic activation using 1 to 1000 micrograms of dicamba per plate.

CONCLUSION: Acceptable

Assay II: Ames Test

The SRI histidine auxotrophic strains of salmonella typhimurum that were used, TA1535, TA1537, TA1538, TA98, and TA100 were grown in a minimal (trace) histidine media in a petri dish. Only the cells that reverted to histidene independence (his) were able to form colonies. The presence of a small amount of histidine is essential for cell growth required to provide the milieu for revertant mutation to take place. The cells that did not revert easily contributed a very slight background growth in contrast to the colony formation by the revertant histidine independent cells. The spontaneous mutation frequency of each strain is relatively constant. Addition of a mutagen to the medium has been known to increase the nutation frequency from 2- to 100- fold usually in a dose response.

The source of the S.TYPHIMURIUM was Dr. Bruce Ames of U. of C. at Berkeley. This strain also had mutations (rfa) which produced a de[illegible]e polysaccharide code and a deletion of genes involved in vitamin biotin (bis) synthesis and repair of UV-induced DNA damage (urrb). These defects cause the strain to have increased permiability to large aromabatic molecules allowing them to have increased mutagenic effects and enhanced sensitivity to mutagenic agents.

The test chemical solvent was used as a negative control. Various specific mutagens known to revert each strain were used as positive controls for that strain. Positive response in activated assays were indicated by reproducible, dese-related increase in the number or revertants in tested strains.

RESULTS:

DICAMBA was not found to be mutagenic to any of the strains of Salmonella Typhimurium.

CONCLUSION: acceptable

Assay III: Yeast

I Material and Methods:

The yeast Saccharomycens cerevisiae D3 which is diploid heterozygous for a defective enzyme in the adenine-metabolizing pathway was used. Should the microorganism revert by mutation from mitosic recombination to homozygous cells there is a red pigment produced in an adenine containing medium. The recombinational frequency is increased by increasing the incubating frequency with various mutagens. The number of red pigmented colonies produced indicates the degree of mutagenicity of a compound or its metabolite. A positive response is indicated by a dose-related increase in the absolute number of mitotic recombinants per ml. as well as the relative number of mitotic recombinants per thousand survivors.

RESULTS AND DISCUSSION

Dicamba did not increase the absolute number or relative number of mitotic recombinations in S. Cervisiae at 0 to 5% concentrations of Dicamba as is indicated in Table 58 p. 101 of the registrants submission of mutagenicity data. There was no positive control for this assay.

CONCLUSION: This assay is unacceptable since there was no positive control.

ASSAY IV: Unscheduled DNA Synthesis

MATERIALS AND METHODS:

Cell Culture: WI-38 cells grown in T-25 tissue culture flasks

Test Material: Dicamba at 0, 0.1, 1.0, 10, 100, 1000, 2000, and 3000 micrograms per milliliters in 0.5% DMSO along with the solvent as a negative control and 4-nitroguinoline-n-oxide as a positive control were tested with and without metabolic activation.

RESULTS: Dicamba was not able to induce UDS with or without metabolic acitivation.

CONCLUSION: These assays are acceptable. There was no indication of a mutagenic effect.

Subchronic Inhalation

Citation: Ulrich, C.E.; Rop, D.A.; Geil, R.G. et al., unpublished study

Study Type: Subchronic Inhalation Study in Rats.

Accession Number: Not available

MRID Number: 00032247

Sponsor: Velsicol Chemical Corporation, Chicago, Illinois

Contracting Laboratory: International Research and Development Corp., Mattawan, Mi.

Project No.: IRDC No. 163-619

Date: August 13, 1979

Protocol:

Material tested: Dicamba (Banvel 4S) as a clear amber liquid which is composed of the acid in water of unspecified purity was received in three 5 gallon containers on April 2, 1978. This material was tested in an inhalation experiment at nominal concentrations of 0.202 mg/liter, 2.01 mg/liter and 20 mg/liter.

Material and Methods:

Exposure Chamber: Exposures were conducted in a one cubic meter, cubical stainless steel and glass chamber with a pyramidal top and bottom. A rotary centrifugal air pump located at the exhaust side of the chamber was used to maintain a constant airflow.

Aerosol Generation: Aerosols of Banvel 4S were generated by metering the liquid with a Harvard Syringe Pump for the 0.202 mg/l aerosol and with a Dual Syringe Precision Pump for the 2.01 mg/l and 20.0 mg/l aerosols, into a positive pressure atomizer near the chamber air inlet at the top of the exposure chambers. An air pressure of 10 psig with an airflow rate of 8 l/min was applied to the atomizer. The rate of dispersion of the test product into the chamber was not given. Rats were exposed for 6 hours/day, 5 days/week for a total of 10 exposures in two weeks. The total airflow rate through the chamber was not reported.

Monitoring of Chamber Concentration: The report indicated that nominal concentration of the compound in the chamber

atmosphere was calculated from the ratio of the rate of test material dispersed/time (mg/min) to the total chamber airflow rate (l/min); however, the values for these two parameters were not available in the report.

Particle Size Distribution Analysis: The particle size distribution of the Banvel 4S aerosol was determined using an Andersan 8 stage cascade impactor. The chamber atmosphere was drawn through the sampler at a rate of 28.3 l/min. The weight of the aerosol particles impacted was determined gravimetrically and the weight-percent of each size category was calculated. The cumulative weight-percent of partcles smaller than a certain indicated diameter was plotted on logarithmic-probability graph paper. The equivalent aerodynamic mass median diameter was determined graphically. One sample was taken each day from each exposure chamber during the 10 days of exposure.

CD-1 rats, 20/sex approximately 6-8 weeks of age (males 201-227 g; females 208-229 g) from Charles River Breeding Laboratories, Portage, Michigan, were housed in wire mesh cages for an acclimatization period of 8 days with food and water ad libitum at controlled but unspecified temperature and humidity.

Animals were randomized using the IRDC computer radomization program into 4 groups of 5 rats each as described in the Summary of Experimental Design (Table 1).

Table 1. Summary of Experimental Design.

Nominal Concentration (mg/l)	Initial No. of Animals		No. of Animals for Terminal Laboratory Studies		Histopathology
	Male	Female	Male	Female	
Control	5	5	5	5	Complete
0.202	5	5	5	5	Partial
2.01	5	5	5	5	Partial
20.0	5	5	5	5	Complete

Observations:

The following observations were made at the specified times:

	Event	When Performed
1.	Pharmacotoxic signs	Twice daily, before and after exposure
2.	Individual body weights	Twice weekly during the two weeks of exposure
3.	Hematology tests[a]	Terminal sacrifice
4.	Biochemical tests[b]	Terminal sacrifice
5.	Urinalysis[c]	Terminal sacrifice
6.	Terminal sacrifice[d]	Two weeks
7.	Gross necropsy examination[e]	Termination
8.	Organ weights[f]	Termination
9.	Histopathology[g]	Termination

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[a]Parameters measured included hemoglobin, hematocrit, erythrocyte count, total and differential leukocyte count, and bone marrow smear.

[b]Parmeters measured included alkaline phosphatase, blood urea nitrogen, serum glutamic pyruvic transaminase and fasting blood glucose.

[c]Parameters measured included volume, appearance, specific gravity, pH, glucose, acetone, protein, bilirubin, and occult blood.

[d]Performed on all surviving rats at two weeks by carbon dioxide asphyxiation.

[e]Performed examination for gross abnormalities of organs and tissues on all terminal sacrifice animals as well as all animals that died during the study.

[f]Weights were recorded for terminal sacrifice animals for the following tissues: adrenals, brain, testes/ovaries, kidneys, liver, pituitary, spleen, and thyroid.

Tissues from rats in the control and 20.0 mg/l exposure level groups were embedded in paraffin, sectioned, and stained with hematoxylin and eosin and examined microscopically. Animals from terminal sacrifice as well as those animals dying during the study. Tissues were prepared and examined by IRDC. Tissues examined for the control and 20.0 mg/l exposure level groups were:

adrenals	mammary gland	urinary bladder
aorta	nasal turbinate	uterus
bone	pancreas	trachea
brain	pituitary	
esophagus	peripheral nerve	
gonad	skeletal muscle	
heart	spinal cord	
intestine (colon, duodenum, ileum, jejunum)	salivary gland	
	skin	
	spleen	
kidneys	stomach	
liver	thymus	
lung	thyroid	
mesenteric lymph nodes		

The following tissues were examined from the 0.2 and 2.0 mg/l exposure level groups:

brain	lung	skin	stomach
kidney	nasal turbinate	spleen	trachea
liver	mammary gland		

Statistics:

All statistical analyses compared the treatment groups with the control group. Body weights, hematology, biochemistry, absolute and relative organ weights were compared by analysis of variance (one-way classification), Barlett's test for homogeneity of variances and the appropriate t-test (for equal or unequal variances) using Dunnett's multiple comparison tables to determine significance of differences.

Results:

Chamber concentrations:

Animals were exposed to aerosols of test material which had average nominal concentrations of 0.202, 2.01, and 20.0 mg/l. However, these nominal concentrations could not be verified due to the lack of data on the quantity of test material injected into the chamber and on the total chamber air flow rate. Actual concentrations in the breathing zones

of the animals were not reported. The average aerodynamic mass median diameter of the delivered test material was 4.25 um with a geometric standard deviation of 2.07 um which indicated that 92-95% of the particles were less than 10 um in diameter. No analytical determinations of test material in the exposure chamber were made.

Clinical Observations and Mortality:

No data were present for observations of ocular and nasal irritation, dyspnea, and other pharmacotoxic signs. However, the final report indicated that at the high concentration, "the rats exhibited reddish ocular discharge, eye squint, dyspnea, and general physical weakness." In addition, the final report indicated that "the fur of the rats exposed to this concentration was heavily coated with the dried compound after each exposure." At the intermediate concentration rats exhibited a "dried reddish discharge around the nares." No adverse effects were noted at the low concentration.

No deaths were reported for the control, low, and intermediate concentrations. Table 2 summarizes the mortality data. Exposure to the high concentration (20.0 mg/l) resulted in 80% mortality in both sexes. The NOEL for mortality was 2.01 mg/l for both sexes. The LEL was 20.0 mg/l for both sexes.

Table 2. Mortality Data

Group/Sex	Deaths Recorded During Days 1-5	Deaths Recorded During Days 6-10	% Survival at 10 days	Deaths Recorded During Days 11-14	% Surviva at 14 Day
Control M	0	0	100	0	100
0.202 mg/l M	0	0	100	0	100
2.01 mg/l M	0	0	100	0	100
20.0 mg/l M	0	4	30	0	20
Control F	0	0	100	0	100
0.202 mg/l F	0	0	100	0	100
2.01 mg/l F	0	0	100	0	100
20.0 mg/l F	1	2	40	1	20

Body Weights and Food Consumption:

Individual and group mean body weights were present for all animals for days 1, 2, 5, 9, 12, 14, and 15. Male and female rats in the low and intermediate dose groups had body weight gain comparable to the controls. The high concentration (20.0 mg/l) group had statistically significant depressed

body weights at day 5 compared to controls for both sexes. By day 9, four of five male rats and three of five female rats had died in the high dose group and the remaining rats showed a slight increase in body weight during the rest of the study period. Based on these findings, the NOEL for body weights was 2.01 mg/l for both sexes. The LEL was 20.0 mg/l for both sexes.

There was no food consumption data present for this study. Therefore, a NOEL could not be determined for this parameter.

Hematology:

Hematology data consisting of erythrocyte count, hemoglobin, hematocrit, total and differential leukocyte counts were reported for all terminal sacrifice animals. Group mean data for selected hematologic parameters for each sex and statistical analysis of this data were present in the final report. No statistically significant differences were seen for erythrocyte count, hemogloglobin, hematocrit, or leukocytes for males. For females, erythrocyte count was significantly decreased ($p = 0.05$) at the intermediate concentration level (2.0 mg/l) compared to controls. Hemoglobin was also significantly depressed at the intermediate concentration level compared to controls ($p = 0.05$). Both decreases were compound-related with decreases also noted at 0.2 mg/l. Data from the 20.0 mg/l groups of both sexes were not included in the statistical analysis since only one animal survived in each of these groups. No statistically significant differences for males were noted for either hematocrit or total leukocyte count. Based on these findings and since the 20.0 mg/l group was not included in the statistical analysis, the NOEL for hematology for males was 2.0 mg/l. For females the NOEL for hematology was 0.2 mg/l (LEL 2.0 mg/l).

Biochemistry:

Biochemistry data consisting of glucose, BUN, alkaline phosphatase and SGPT were reported for all terminal sacrifice animals. Group mean data for each sex and statistical analysis of this data were present in the final report. For males, glucose was significantly depressed at 0.2 mg/l and 2.0 mg/l compared to control and the effect was compound-related. No other statistically significant differences were noted for males. For females, glucose was significantly depressed at 2.0 mg/l and the effect appears to be compound-related. No other significant differences were noted for females. Based on these findings, the NOEL for Biochemistry was less than 0.2 mg/l for males (LEL 0.2 mg/l) and the NOEL for females was 0.2 mg/l (LEL 2.0 mg/l).

Urinalysis:

Urinalysis data consisting of volume, color and appearance, pH, specific gravity, glucose, acetone, protein, bilirubin, and occult blood were present for all terminal sacrifice animals. Group mean data and statistical analysis of the data were present in the final report.

No statistically significant differences were noted for females. However, the 20 mg/l group was not included in the statistical analysis since only one animal in this group survived. For males, pH was significantly decreased at 2.0 mg/l compared to controls and the effect appeared to be compound-related since a decrease (although not significant) was also noted at 0.2 mg/l. Based on these findings the NOEL for females was 2.0 mg/l. For males the NOEL was 0.2 mg/l (LEL 2.0 mg/l).

Organ Weights:

Organ weight data for adrenals, brain, ovaries/testes, kidneys, liver, pituitary, spleen, and thyroid were present for all terminal sacrifice animals. Mean group absolute (actual) and relative (% of body weight) organ weight data and statistical analysis of these data were present in the final report. Absolute and relative organ weights for both males and females showed some incidences of statistically significant differences when compared to controls.

Organ	Exposure Level (mg/l)	Sex	Weight	Change	p
Kidney	2.0	F	relative	increase	0.05
Liver	2.0	M	relative	increase	0.05
Pituitary	0.2	F	absolute	decrease	0.05
Thyroid	0.2	F	absolute/ relative	decrease	0.01/0.01
Thyroid	2.0	F	absolute/ relative	decrease	0.01/0.05

Of these significant differences the increase in the mean relative kidney weight of the 2.0 mg/l females and the increase of the mean relative liver weight of the 2.0 mg/l males are the primary findings with possible biological significance. Both effects appear to be compound related.

Based on the statistical significance of kidney and liver effects at the intermediate exposure level, the NOEL for organ weights was 0.2 mg/l (LEL 2.0 mg/l) for both sexes.

Gross Necropsy Examinations:

All animals were examined for gross pathological findings. External findings consisting primarily of yellow crystalline material on hair and blood around nose/eyes was increased at the high exposure level compared to the control. Lymph node findings consisting of red lymph nodes were increased at the low and intermediate exposure levels compared to controls for males and increased at intermediate exposure levels compared to the control group for females. Stomach findings of primarily brown red and/or hemorrhagic foci were increased at the high exposure level compared to control for males and at the intermediate and high exposure levels for females. Liver findings consisting primarily of yellow foci and dark red/brown coloration were increased at the high exposure level compared to controls for males and females. No obvious exposure-related effect was seen for males or females.

Histopathology Evaluation:

Complete histopathology was performed on all control and 20.0 mg/l animals. A partial list of tissues was examined for the 0.2 and 2.0 mg/l groups. The histopathology was prepared by IRDC and evaluated by Dr. R.G. Geil, consulting pathologist.

The number of lesions in the lung for males was increased at low, intermediate, and high exposure levels compared to controls. In females the number of lesions in the lung was increased only at the high exposure level (20.0 mg/l). Lung findings reported included parenchymal hemorrhage, interstitial inflammatory cell infiltrate, capillary/vascular congestion, microgranuloma, perivascular inflammatory cell accumulation, alveoli macrophages, and edema.

In the lungs, capillary/vascular congestion was significantly increased at 20.0 mg/l compared to controls for both male and females. Edema was increased at 0.2, 2.0, and 20.0 mg/l for males and at 2.0 and 20.0 mg/l for females compared to controls. This effect appeared to be treatment related.

In males, the number of lesions in the stomach were increased at the low, intermediate, and high exposure levels compared to controls. For females, the number of lesions in the stomach were increased at the intermediate and high doses compared to controls.

In the liver, the incidence of hepatocellular necrosis was increased at 20.0 mg/l in males and at 2.0 and 20.0 mg/l in females compared to controls. In the spleen the incidence of focal necrosis was increased at 20.0 mg/l for both sexes

compared to controls. This effect was probably compound related since the finding was not present in either of the control groups.

Based on the treatment-related effect of edema in lungs, the NOEL for histopathology for males was less than 0.2 mg/l (LEL 0.2 mg/l) and the NOEL for females was 0.2 mg/l (LEL 2.0 mg/l).

Discussion:

A two-week subchronic inhalation study was conducted to evaluate the toxicity of an aerosol atmosphere of Dicamba (Banvel 4S) in CD-1 rats. Four test groups, 10 rats/sex group, were exposed to a nominal concentration of 0, 0.202, 2.01, and 20.0 mg/liter of Banvel 4S for 6 hours/day, 5 days/week for a total of 10 exposures in two weeks. Airflow rate through the exposure chamber was not reported. Aerosol particle size distribution analyses were performed daily and the results indicate that 92-95% of the particles had a diameter less than 11uM. Parameters monitored during the in-life phase of the study included observations of pharmacotoxic signs and body weights. Food consumption data were not recorded. Hematology, biochemistry, urinalysis, organ weights, gross and microscopic pathologic examinations were performed at the end of the study.

Although the nominal concentrations of test material in the atmosphere of the test chamber were specified in the report and the airflow through the atomizer was given (9 l/min), the nominal concentration values cannot be verified. This is due to the absence of data in the report on the rate of test material dispersion into the chamber and on the total chamber airflow rate. This is basic information to the determination of the nominal concentrations.

Analysis of the chamber respirable atmosphere should have been performed as stated in the Guidelines.

No data were present for observation of pharmacotoxic signs; however, the final report indicated pharmacotoxic signs occurred at 2.0 mg/liter and 20.0 mg/liter. No adverse reactions were noted at 0.20 mg/liter.

No deaths were reported for the control, low, and intermediate concentrations. Exposure to the high concentration 20.0 mg/l resulted in 80% mortality in both sexes (LEL 2.0 mg/l).

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Male and female rats in the low and intermediate dose groups had body weight gain comparable to the controls. At the high concentration (20.0 mg/l) there was significant depression of body weights at day 5 for both sexes. Based on these findings, the NOEL for body weights was 2.0 mg/l and the LEL was 20.0 mg/l for both sexes.

With respect to hematology, erythrocyte count was significantly depressed at 2.0 mg/l for females. Hemoglobin was also significantly depressed at 2.0 mg/l for females. Both decreases were compound-related with decreases also reported at 0.20 mg/l which were not significantly different from control values. No statistically significant changes were observed for males for any of the hematological parameters tested. Data from the 20.0 mg/l group of both sexes were not included in the statistical analysis since only one animal survived in each group. Based on these findings, the NOEL for hematology for males was 2.0 mg/l. For females, the NOEL for hematology was 0.2 mg/l (LEL 2.0 mg/l).

With respect to biochemistry, glucose levels for males were significantly depressed at 0.2 mg/l and 2.0 mg/l compared to control. For females glucose was significantly depressed at 2.0 mg/l and the effect was compound-related. Therefore, the NOEL for females was 2.0 mg/l and the NOEL for males was 0.2 mg/l (LEL 2.0 mg/l).

For urinalysis, no statistically significant differences were noted between control and dosed females. However, data from the female 20 mg/l group were not included in the statistical analyses since only one animal survived in this group. In males, the pH was significantly decreased at 2.0 mg/l compared to controls and the effect was compound-related. Therefore, the NOEL for females was 2.0 mg/l and the NOEL for males was 0.2 mg/l (LEL 2.0 mg/l).

For organ weights, a significant increase in the mean relative (% of body weight) kidney weight at 2.0 mg/l for females and a significant increase in the mean relative liver weight for males at 2.0 mg/l were both compound-related effects. Based on these findings, the NOEL for organ weights was 0.2 mg/l (LEL 2.0 mg/l) for both sexes.

With respect to gross pathology, no exposure-related effect was seen for males or females. Therefore, the NOEL for gross pathology was 20.0 mg/l for both sexes.

For histopathology in the lungs, edema was increased at 0.2, 2.0, and 20.0 mg/l for males and at 2.0 and 20.0 mg/l for females compared to controls. The effect appeared to be treatment-related. Based on these findings, the NOEL for

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histopathology for males was less than 0.2 mg/l (LEL 0.2 mg/l) and the NOEL for females was 0.2 mg/l (LEL 2.0 mg/l).

Conclusion:

The NOELs and LELs for the biological parameters measured based on the stated nominal concentrations (calculations unverifiable) were as follows:

Parameter	Individual Data Present	NOEL (mg/l) M	NOEL (mg/l) F	LEL (mg/l) M	LEL (mg/l) F
Observations	no	--	--	--	--
Mortality	yes	2.0	2.0	20.0	20.0
Body Weights	yes	2.0	2.0	20.0	20.0
Food Consumption	no	--	--	--	--
Hematology	yes	2.0	2.0	--[a]	2.0
Biochemistry	yes	<0.2	0.2	0.2	2.0
Urinalysis	yes	0.2	0.2	2.0	--[a]
Organ Weights	yes	0.2	2.0	2.0	2.0
Gross Pathology	yes	20.0	20.0	--	--
Histopathology	yes	<0.2	0.2	0.2	2.0

[a]Data from the 20 mg/l group of both sexes were not included in the statistical analysis since only one animal survived in each group. Therefore, an LEL could not be set for this parameter.

The systemic NOEL for subchronic inhalation was <0.2 mg/l for this study.

Classification: Supplementary

This study did not report actual exposure concentrations, air flow rates and animal observations. This study was conducted with a two week exposure rather than the recommended 90 days.

END