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

004770

MEMORANDUM:

FROM:

EPA ID Number: . 061601; EPA Registration No. SUBJECT:

239-2460. Paraquat: Evaluation of two acute

inhalation toxicity studies with rats.

Accession No. 259755

Record No. 161046

Tox. Chem. No. 634 Project No. 735

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Toxicology Branch/HED completed an evaluation of the following studies:

- Paraquat: 4-Hour Acute inhalation toxicity study in the rat. Imperial Chemical Industries PLC, England; Reports No. CTL/P/1325 and CTL/P/1325 S (Indvidual animal data supplement); September 24, 1985.
- Paraguat: 4-Hour acute inhalation toxicity study in the rat of coarse aerosol. Imperial Chemical Industries PLC, England; Report No. CTL/P/1335; October 1, 1985.

In the first study, Wistar-derived rats, 5 males and 5 females/dose level, were exposed to the following concentrations: of paraquat dichloride (mg/m3): 0,0.2, 0.6 and 1.4, expressed as cation. More than 90% of aerosolized paraquat was respirable (particle diameter < 0.3 um). The LC 50 was between 0.6 and 1.4 mg/m^3 (0.6-1.4 ug/L).

In the second study, Wistar-derived rats, 5 males and 5 females/dose level, were exposed to the following concentrations of paraquat dichloride (mq/m³): 0, 0.93 and 3.6, expressed as cation. The aerosols generated had a median diameter of 21.5-23.0 um. The LC 50 was $\frac{1}{2}$ 3.5 mg/m³ (3.5 ug/L).

Each study was classified as Core Minimum* and in each study paraquat was very toxic (Toxicity Category I).

40 CFR 162.11(a)(3)(i) provides that a rebuttable presumption shall selse if a pesticide "....(3) Has inhalation LC50 of 0.04 mg/%iter or less as formulated." The results of both of these stables indicate, therefore, that an RPAR risk criterion has been exceeded. Since the test material used in these studies (Persequer Plus) contained 21.5% of paraquat cation, the following 6050 values are obtained when the above LC50 values are espainted from saction to test material:

In Study 1 (respirable particles):

 $LC50 = 2.8-6.5 \text{ mg/m}^3 (2.8-6.5 \text{ ug/l})**$

In Study 2 (coarse particles):

 $LC50 = 16.3 \text{ mg/m}^3 (16.3 \text{ ug/1})$

Consideration should, therefore, be given to placing this chemical into special review on the basis of these very low LC50 values.

cc: Robert Taylor, RD

^{*} Because tissues were not examined histologically in either study and because only two levels of paraquat were tested in the second study, each study was classified Core Minimum rather than Core Guideline.

^{**} Sample calculation: $\frac{0.6^{is}}{0.215^{b}} = \frac{X}{1.0}$ X = 2.8 mg of test material/m³

a = LC50, expressed as paraquat cation.

b = Percent of paraquat cation in the test material.

Tox. Chem. No. 634 Project No. 735

Study Type: Acute Inhalation

Study Title: Paraquat: 4-Hour Acute Inhalation Toxicity in the Rat. Report Nos. CTL/P/1325 and CTL/P/1325S

(Individual Animal Data Supplement).

Accession No.: 259755 .

Record No.: 161046

Sponsor: Chevron Chemical Company

Richmond, California

Testing Laboratory: Imperial Chemical Industries PLC,

Central Toxicology Laboratory, Alderley Park, Macclesfield,

Cheshire, England.

Test Material: Ortho paraquat dichloride (Paraquat Plus)

containing 21.5% w/v of paraquat cation; supplied by Chevron Chemical Company,

Richmond, California

Date of Final Report: September 25, 1985

PROTOCOL

Alpk:AP (Wistar-derived) rats, five males and five females/ dose level, were exposed (nose only) to the following concentrations of aerosolized paraquat (analytical values, expressed as cation): 0 (Group 1), 0.2 (Group 2), 0.6 (Group 3), and 1.4 mg/m^3 (Group 4). The exposure time was 4 hours and the observation time 14 days. More than 90 percent of the particles (91 to 100%) were respirable (aerodynamic equivalent diameter < 0.3 um). The control groups were exposed to air. The flow rates for Groups 2, 3, and 4 were 12.0, 16.5, and 15.0 L/min of generating air and 15, 10, and 10 L/min of diluting air, respectively. Group 1 was exposed to an airflow of 12 L/min. The temperature in the exposure chamber was 18 °C for Groups 1, 2, and 3, and 19 °C for Group 4. The relative humidity was 27, 37, 38, and 41 percent for Groups 1, 2, 3, and 4, respectively. The volume of the exposure chamber was 18.4 L. The exposures were carried out on March 27, 1985, and the surviving animals were sacrificed on April 10, 1985.

The animals were obtained from the Alderley Park breeding colony. Before and after exposure, they were housed five to a cage and fed unrestricted amounts of Porton Combined Diet (pelleted; composition submitted). The temperature in the animal quarters was 20 to 23 °C and the relative humidity 36 to 60 percent. The animals were 7 weeks old at the start of the study and weighed an average of 230 g (range: 208 to 244 g; males) or 266 g (range: 192 to 223 g; females). The acclimation period was 7 days. The animals were allocated to groups by a Latin square method.

The following parameters were examined:

1. Clinical Observations

The animals were examined for abnormalities before exposure and were observed frequently during exposure. After exposure, each rat was checked daily, until the termination of the study, for the following: condition of fur, respiration, motor activity, skin color, salivation, diarrhea, condition of eyes and hearing, and the righting, corneal, pinna, and foot withdrawal reflexes.

2. Body Weight Gains

All rats were weighed on day 1 prior to exposure and then on days 2 to 8, and on day 15.

3. Food Consumption

Food consumption per cage of rats was measured daily from day 1 to 15.

4. Organ Weight

The following organs were weighed for the surviving animals: lungs with attached trachea, liver, kidneys, and testes (ovaries were not weighed). For animals which died during the study, only lungs were weighed.

5. Pathology

All animals were examined macroscopically. The following organs/tissues were preserved in 10 percent buffered formol saline but were not examined histologically: head:(for.nasal turbinates), lungs, larynx, trachea, liver, kidneys, testes, ovaries, and any abnormal tissue.

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6. Statistical Analysis

Body weight gains, organ weights, and organ/body weight ratio were analyzed statistically using a two-sided Student's t-test.

All analytical procedures used were either referenced or described. A quality assurance statement was also submitted.

RESULTS

1. Clinical Observations

Mortality. There were no deaths in the controls (Group 1) and the 0.2 (Group 2) and the 0.6 (Group 3) mg/m³ groups during the 4-hour exposure or the observation period. In the 1.4 mg/m³ group (Group 4), all animals survived the 4-hour exposure period but deaths occurred thereafter as follows:

1 male - day 3 2 males and 3 females - day 4

1 female - day 5

All of these rats were found dead. The remaining rats in Group 4 (2 males and 1 female) were killed in extremis on the observation day 6.

Toxic Signs. Immediately after exposure, abnormal respiratory noise was noted in all of the animals from Group 4 and in some animals from Groups 2 and 3. In the case of the male Groups 2 and 3, respiratory noise persisted through the observation day 8. In the case of the female Groups 2 and 3, abnormal respiratory noise persisted through the observation days 10 and 12, respectively.

The following abnormalities were also observed in rats from Group 4 before they died: irregular breathing, subdued behavior, pinched in sides, tip toe/splayed gait, ungroomed appearance, and urinary incontinence.

2. Body Weight Gains

All animals, including the controls, lost weight immediately after exposure but the greatest loss occurred in Group 4. The animals in Group 4 continued

to lose weight rapidly until they died, whereas those in Groups 1, 2, and 3 subsequently gained weight. The weight gains the in the paraquat-treated Groups 2 and 3 were similar to or greater than those of the controls. The weight gains are summarized in table I.

Table I. Group Mean Body Weight Gains (g) of Male and Female Ratsa

<u>pl</u> 0		0.2		0.6		1.4	
1		2		3		4	
М	F	М	F	М	F	М	F
234.3	213.7	227.1	200.9*	227.9	206.7	234.5	205.8
-3.3	-5.8	0.3	-0.9	-2.8	-4.1	-8.9*	5.5
1.9	-0.4	10.0*	4.5	3.9	-2.7	-28.4**	-20.9**
12.0	1.1	16.9	6.7	10.2	2.2	-41.7**	-29.3**
19.8	5.3	25.7	10.0	18.8	6.0	-54.9**	-39.4**
26.4	11.1	34.8	15.5	26.7	12.6	-64.8**	-50.2**
31.3	11.0	40.7*	15.6	32.8	11.5		*
40.3	12.6	48.8	20.2	41.6	18.3		
67.5	30.7	87.7	33.6	75.7	28.3		, -
	234.3 -3.3 1.9 12.0 19.8 26.4 31.3 40.3	234.3 213.7 -3.3 -5.8 1.9 -0.4 12.0 1.1 19.8 5.3 26.4 11.1 31.3 11.0 40.3 12.6	M F M 234.3 213.7 227.1 -3.3 -5.8 0.3 1.9 -0.4 10.0* 12.0 1.1 16.9 19.8 5.3 25.7 26.4 11.1 34.8 31.3 11.0 40.7* 40.3 12.6 48.8	M F M F 234.3 213.7 227.1 200.9* -3.3 -5.8 0.3 -0.9 1.9 -0.4 10.0* 4.5 12.0 1.1 16.9 6.7 19.8 5.3 25.7 10.0 26.4 11.1 34.8 15.5 31.3 11.0 40.7* 15.6 40.3 12.6 48.8 20.2	M F M F M 234.3 213.7 227.1 200.9* 227.9 -3.3 -5.8 0.3 -0.9 -2.8 1.9 -0.4 10.0* 4.5 3.9 12.0 1.1 16.9 6.7 10.2 19.8 5.3 25.7 10.0 18.8 26.4 11.1 34.8 15.5 26.7 31.3 11.0 40.7* 15.6 32.8 40.3 12.6 48.8 20.2 41.6	M F M F M F 234.3 213.7 227.1 200.9* 227.9 206.7 -3.3 -5.8 0.3 -0.9 -2.8 -4.1 1.9 -0.4 10.0* 4.5 3.9 -2.7 12.0 1.1 16.9 6.7 10.2 2.2 19.8 5.3 25.7 10.0 18.8 6.0 26.4 11.1 34.8 15.5 26.7 12.6 31.3 11.0 40.7* 15.6 32.8 11.5 40.3 12.6 48.8 20.2 41.6 18.3	M F M F M F M 234.3 213.7 227.1 200.9* 227.9 206.7 234.5 -3.3 -5.8 0.3 -0.9 -2.8 -4.1 -8.9* 1.9 -0.4 10.0* 4.5 3.9 -2.7 -28.4** 12.0 1.1 16.9 6.7 10.2 2.2 -41.7** 19.8 5.3 25.7 10.0 18.8 6.0 -54.9** 26.4 11.1 34.8 15.5 26.7 12.6 -64.8** 31.3 11.0 40.7* 15.6 32.8 11.5 40.3 12.6 48.8 20.2 41.6 18.3

a This table is based on TABLE 5 of the submission.

3. Food Consumption

Exposure to paraquat had no effect on the food consumption of rats in Groups 2 and 3. However, rats in Group 4 ate very little food following exposure (males, 1.0 to 1.5 g/animal/day and females, 0.2 to 2.0 g/animal/day).

b Paraquat cation, mg/m3.

c Starting weight before exposure.

^{*} Significantly different from control; p < 0.05.

^{**} Significantly different from control; p < 0.01.

M = males F = females

4. Organ Weights

There were no statistically significant differences in the group mean absolute weights of lungs, kidneys, liver, and testes when the animals in Groups 2 and 3 were compared with those in Group 1 (controls). The organ/body weight ratios were also unaffected in Groups 2 and 3.

Male and female rats in Group 4 were not evaluated statistically because all died (were found dead or were sacrificed in extremis) on days 3 to 6 of the observation period. However, data reported for three rats (2 males and 1 female) which were sacrificed in extremis on day 6 after exposure indicated that the lung weight was increased and the weights of kidneys, liver, and testes were decreased when related to the controls. The ratios of lung, kidney, or testes/body weight were also increased in Group 4. Data for these three rats from Group 4 and the controls are summarized in table II.

Table II. Absolute Organ Weights and Organ/Body Weight
Ratios for Group 1 (controls) and Group 4 (1.4 mg
paraquat ion/m3)a

Animals			Group Mean Organ Weights (g)				
	,		Lungs	Kidneys	Liver	Testes	
Males: Females:	Group 4	(5 rats)D	1.480 3.275 1.377 4.030	2.382 1.579 2.001 1.271	13.631 7.250 10.443 6:100	3.025 2.550 	
			Organ/Body Weight Ratios				
Males: Females:	Group 1 Group 4 Group 1 Group 4	•	0.491 1.928 0.564 2.756	0.790 0.929 0.818 0.869	4.490 4.267 4.272 4.172	1.008 1.501 	

a This table is based on TABLES 7, 8, and 9 of the submission. b These rats were killed on day 15 of the observation period.

The lungs of the three male rats in Group 4 which were found dead on days 3 and 4 after exposure weighed 3.969 to 4.155 g and the lung/body weight ratios ranged from 1.990 to 2.164. The lungs of the four females in Group 4 which were found dead on days 4 and 5 after exposure weight 2.951 to 3.924 g and the lung/body weight ratios ranged from 1.639 to 2.231. Organs other than lungs were not weighed for rats which were found dead in their cages.

5. Pathology

One male rat in Group 2 had dark red spots on the surface of the lungs. No other abnormalities were observed in Group 2 and none were noted in Groups 1 and 3.

Males and females in Group 4 which died on days 3 to 5 after exposure to paraguat (total of 7 rats) and animals which were sacrificed in extremis on day 6 (remaining 3 rats) had dark red, mottled lungs. Most of the lungs were not fully deflated. Also, two male rats had froth exuding from the tracheae.

SUMMARY

Wistar-derived male and female rats, exposed to respirable particles (< 0.3 µm) of aerosolized paraguat dichloride for 4 hours, suffered from irritation of the respiratory tract (noisy and irregular breathing). In the case of Groups 2 and 3, the irritation persisted for 8 to 10 days following exposure. Rats in Group 4 had respiratory distress until they died but none occurred in the controls immediately after exposure (abnormal respiratory noise was reported for one control female on days 12 and 13). The exposure levels used were 0 (Group 1):0.2 (Group 2), 0.6 (Group 3), and 1.4 (Group 4) of paraguat ion/m³. Each group had five animals of each sex. The control groups were exposed to air.

With one exception*, toxic effects other than irritation of the respiratory tract were observed only in Group 4, as follows:

- All animals died before day 7 of the observation period; (7 were found dead and 3 were killed in extremis).
- There were significant reductions in body weight gains and food consumption.

^{*}One male rat in Group 2 had an increased lung weight and red spots all over the lungs.

The mean absolute lung weight was increased whereas the weights of kidneys, liver, and testes were decreased when compared with the controls. Ovaries were not weighed.

The ratios of lung, kidneys, and testes/body weight were increased when compared with the controls. (Liver/body weight ratios were slightly decreased.)

The lungs were dark red, mottled and in two male rats froth was exuding from the tracheae.

 $\frac{LC}{cation}$ = 0.6 to 1.4 mg/m³ (0.6 to 1.4 ug/L), expressed as paraquat

Toxicity Category: I

Core Classification: Minimum

Tox. Chem. No. 634
Project No. 735 004770

Study Type: Acute inhalation.

Study Title: Paraquat: '4-Hour Acute Inhalation Toxicity Study in the Rat of a Coarse Aerosol. Report No. CTL/P/1335.

Accession No. 259755 Record No. 161046

Sponsor: Chevron Chemical Company Richmond, California

Testing Laboratory: Imperial Chemical Industries PLC, Central Toxicology Laborartory, Alderley Park, Macclesfield, Cheshire, England.

Test Material: Ortho paraquat dichloride (Paraquat Plus) containing 21.5% w/v of paraquat cation; supplied by Chevron Chemical Company, Richmond, California

Date of Final Report: October 1, 1985

PROTOCOL

Alpk:AP (Wistar-derived) rats, five males and five females/ dose level, were exposed (nose only) to the following concentrations of aerosolized paraquat (analytical values, expressed as cation): 0 (Group 1), 0.93 (Group 2), 0 (Group 3) and 3.5 mg/m3 (Group 4). The exposure time was 4 hours and the observation time 14 days. Two control groups were used because the acclimation time for Groups 1 and 2 was 7 days and for Groups 3 and 4, 15 days. Groups 3 and:4 were exposed a weeks later in order to allow assessment of the results obtained for Groups 1 and 2.

The volume of an exposure chamber was approximately 18.4 liters. The total air flow in the chambers was 40 liters/minute (generating and diluting air). The air flow through the control chambers was also 4J liters/minute. (The control groups were exposed only to air). The aerosols generated had a median diameter of 21.5-23 um and contained < 32% of inspirable particles (diameter < 15 um) and only 0.12-0.25% of respirable particles (diameter < 2.5 um). The temperature in the exposure chambers for Groups 1, 2, 3 and 4 was 21, 21, 13 and 14°C, respectively. The relative humidity for the same groups was 29, 44, 43 and 49%, respectively.

The animals were obtained from the Alderley Park breeding colony. Before and after exposure, they were housed five to a cage and fed unrestricted amounts of Porton Combined Diet (pelleted, composition submitted). The temperature in the animal guarters was 20.5-25.0°C and the relative humidity 35-61%. The animals were 658 weeks old at the start of the study and weighed as follows:

Groups 1 and 2: .males, 231g* (range 221-245g) females, 215g* (range 189-234g) Groups 2 and 3: males, 296g* (range 281-314g) females, 236g* (range 220-257g)

*Group mean values.

The animals were allocated to groups by a Latin square method.

The following parameter were examined.

1. Clinical Observations

The animals were examined for abnormalities before exposure and were observed frequently during exposure. After exposure, each rat was checked daily, until the termination of the study, for the following: condition of fur, respiration, motor activity, skin color, salivation, diarrhea, condition of eyes and hearing, and the righting, corneal, pinna, and foot withdrawal reflexes.

Body Weight Gains

All rats were weighed on day 1 prior to exposure and then on days 2 to 8, and on day 15. Animals in Groups 1 and 2 were also weighed on day 9.

3. Food Consumption

Food consumption per cage of rats was measured daily from day 1 to 15.

4. Organ Weights

The following organs were weighed for all animals: lungs with attached trachea, live, killeys and testes (ovaries were not weighed).

5. Pathology

All animals were examined macroscopically. The following organ tissues were preserved in 10 percent buffered formol saline but were not examined histologically: head (for nasal turbinates), lungs, larynx, trachea, liver, kidneys, testes, cvaries, and any abnormal tissue.

6. Statistical Analysis

Body weight gains, organ weights, and organ/body weight ratio were analyzed statistically using a two-sided Student's t-test.

All analytical procedures used were either referenced or described. A quality assurance statement was also submitted.

RESULTS:

1. Clinical Observations:

Mortality. There were no death in the 0.93 mg/m³ group or in either control groups. All rats in the 3.5 mg/m³ group survived the 4-hour exposure period but 5/10 were dead on day 3 of the observation period (3 males and 1 female were killed in extremis, and another male died on that day). The remaining 5 animals (1 male and 4 females) in the 3.5 mg/m³ group survived until the termination of the study.

Toxic Signs. During exposure, treatment-related abnormalites were observed only in the 3.5 mg/m^3 group, as follows:

- Slightly labored breathing in 3 rats (sex not specified) t 77 minutes of exposure and in 2 rats during 114-199 minutes of exposure.
- o Slightly reduced response to noise (normal animal will jump) in all male and female rats at the termination of the exposure (at 238 minutes).

During the observation period, treatment-related abnormalities were need mostly in the 3.5 mg/m³ group, as follows:

- o Respiratory tract irritation (irregular breathing, gasping and abnormal respiratory noise) in most animals on day 3.
- General debility (hunched, sides pinched-in, and subdued) also in most animals on day 3.

Males appeared to be more severly affected than females in the 3.5 mg/m³ group. The only male surviving beyond the observation day 3 was hunched until day 7, had abnormal respiratory noise until day 13, and was subdued at times until the termination of the study. Of the 4 surviving females, 3 had no toxic signs after day 6 but 1 had abnormal respiratory noises until day 11.

In the 0.93 mg/m³ group, 2 females had treatment-related abnormalities, as follows:

- One had abnormal respiratory noise on the observation days 4, 5 and 6.
- O Another showed signs of general debility (emaciation, reduced righting reflex, and piloerection) throughout the observation period.

2. Body Weight Gains

All animals, including the controls, lost weight immediately after exposure but those ir Group 2 (0.93 mg paráquat ion/m³) and its control (Group 1) began gaining weight again on the observation day 3 (males) and day 4 (females). The overall group mean weight gains at the termination of the study (day 15) were as follows:

Group 1: males 94 g
females 22 g
Group 2: males 89.8 g
females 30.4 q*

^{*}Significantly different from control; P< 0.05.

Although the initial weight losses in Group 4 (3.5 mg paraquat ion/m^3) and its control (Group 3) were similar, the weight losses in Group 4 became more severe on day 3, at which time 4 males and 1 female died. The surviving animals gained weight after the observation day 4 (1 male) and after day 5 (females). The overall weight gain for the male was 18.3% less than for the controls. The overall gain for the females was 22% greater than that for the controls. These data are summarized in Table I.

Table I. Weight Gains in the Group 4 and Group 3 Ratsa

	Male	Females				
Paraquat ion (mg/m³)	0	0 3.5		_	3.5	
Group	3	4	3		4	
Observation Day	Grou	Mean	Weight	Ga	in (g)	
1b	300.2	292.6	232	. 2	240.4	
2	-9.4	-11.4	-3	.0	-5.2	
3	3.8	-24.6		.8	-6.2	
4C	12.2	-1.01	** 3	, 4	-7.7	
5	13.4	6.0	4	. 2	-3.0	
6	20.2	13.0	6	. 2	4.0.	
7	26.2	17.0	6	.8	6.0,	
8	31.2	20.0	11	. 2	5.8	
15	73.4	60.0	17	.6	21:5	

- a This table is based on TABLE 5 of the submission.
- b Starting weight.
- c Strating with day 4, only 1 male and 4 females remained in the study. Each of the control groups had 5 animals.
- ** Significantly different from control; P < 0.01.

3. Food Consumption

Exposure to paraguat had no effect on food consumption of the male and female rats in Group 2 (0.93 mg/m³). However, male and female rats in Group 4 (3.5 mg/m³) consumed 52% and 20%, respectively, less food than did their controls on day 2 after exposure. After day 3, the food consumption of the single surviving male in Group 4 was similar to that of the controls (30-36 g/day vs 31-37g/animal/day). The food consumption of the four surviving females in Group 4 was also similar to that of their controls (21-29 vs 19-26 g/animal/day).

4. Organ Weights

Group mean absolute weights and organ/body weight ratios (g/100 g) were reported for lungs, kidneys, liver and tests. There were no statistically significant differences in these weights and ratios between animals in the 0.93 mg/m³ group (Group 2) and their controls (Group 1), and, with one exception, between animals in the 3.5 mg/m³ group (Group 4) and their controls (Group 3). In the 3.5 mg/m³ female group, there was a statistically significant (P< 0.01), although small (12.2%), increase in the mean lung weight. However, there were no statistically significant differences in the lung/body weight ratio in this group.

The organ weights of the rats which died or were killed in extremis on the observation day 3 (four males and one female in Group 4) were not compared statistically with the controls. However, there were considerable increases in the lung/body weight ratios in the males, when the ratios of the paraquat-treated animals were related to those of the controls. These data are summarized in Table II.

Table II . Lung and Kidney/Body Weight Ratios (g/100g) for Rats Which Did Not Survive the Study and for the Controls :

	0 3	3.5		Percent Increase
Ratio 0.420 0.493	Rats ^b 5 5	Ratio 0.626 0.644	Ratsb 0 1	50.0 30.6
0.753	5	0.938	4	24.6
0.752	5	0.826	1	8.2
	0.420	0.420 5	0.420 5 0.626	0.420 5 0.626 0
	0.493	0.493 5	0.493 5 0.644	0.493 5 0.644 1
	0.753	0.753 5	0.753 5 0.938	0.753 5 0.938 4

This table is based on TABLE 8 of the submission.

Number of rats for which group mean ratios were reported. Rats in the control group were killed at the termination of the study (day 15 of the observation period). Rats in the 3.5 mg/m³ group were killed or died on day 3 after exposure.

Pathology

No abnormalities were observed in the male and female rats from Group 2 (0.93 mg pacaquat ion/m³) and in their controls (Group 1). No abnormalities were also observed in the surviving rats from Group 4 (3.5 mg paraquat ion/m³) and in 50% of their controls (Group 3). In Group 3,2 rats had slight pelvic dilatation of the right kidney and the remaining 3 rats had one of the following: distended bladder, small cyst on the left ovary or one dark area (1 mm in diameter) on the left lung.

Rats in Group 4 which died or were killed in extremis on the observation day 3 had red lungs (2 males) or dark red and blotchy thymus (2 males and 1 female).

SUMMARY

Wistar-derived rats (6-8 weeks of age), five males and five females/dose level > were exposed to coarse particles of aerosolized paraquat dichloride for four hours and then were observed for 14 days before they were sacrificed. The aerosols generated had a median diameter of 21.5-23 um and contained < 32% of inspirable particles (diameter < 15 um) and only 0.12-0.25% of respirable particles (diameter < 2.5 um). exposure levels, expressed as paraquat ion, were 0 (Group 1), 0.93 mg/m3 (Group 2), 0 (Group 3) an 3.5 mg/m3 (Group 4). Two control groups were used because the acclimation period for Groups 1 and 2 was 7 days, and for Groups 3 and 4, 15 (The control groups were exposed to air). The following parameters were examined: clinical observations, body weight gains, food consumption, obsolute organ weights (lungs, liver, kidneys and testes), organ/body weight ratios, and gross necropsy. Tissues were not examined histologically. When appropriate, data were analyzed statistically using a two-sided Student's t-test. The following findings were reported:

- o Deaths occurred only in the 3.5 mg/m³ group on the observation day 3 (1 male died and 1 female and 3 males were killed in extremis).
- Treatment-related effects (iregular breathing, gasping, abnormal respirtory noise and general debility (hunched, sides pinched-in, subdued)) were observed in most animals from the 3.5 mg/m³ group through day 3 after exposure. However, one female and one male had respiratory noise until day 11 and day 13, respectively, after exposure.
- o The above effects and weight loss, decreased food consumption, increased lung/body weight and kidney/body weight ratios, red lungs, and dark red and blotchy thymus were observed only in the 3.5 mg/m³ rats which died or were killed in extremis on day 3 after exposure.
- o In the 0.93 mg/m³ group, treatment-related effects were observed in two females. One rat had abnormal respiratory noise through the observation day 6 and another showed signs of general debility (emaciation, reduced righting reflex, piloerection) throughout the observation period.

 $LC 50 = > 3.5 \text{ mg/m}^3$ (3.5 ug/L), expressed as paraquat cation

Toxicity Category, I

Core Classification: Mimimum.