

Reviewer: Eugenia McAndrew
Product Manager: 22

August 26, 2004

STUDY TYPE: Acute Inhalation Toxicity -S-D rat; OPPTS 870.1300; OECD 403

TEST MATERIAL: Chlorothalonil Technical (Lot # 218/87; 98.63 % purity; white powder)

CITATION: Danks, A. Chlorothalonil Technical: Acute Inhalation Study in the Rat. Life Science Research Limited, Suffolk, England. Laboratory Report Number 88/CFA001/185. July 21, 1988. MRID 45710204. Unpublished.

SPONSOR: Chlorothalonil Technical (Lot # 218/87; 98.63 % purity; white powder)

EXECUTIVE SUMMARY: In an acute inhalation toxicity study (MRID 45710204), four groups of five male and five female young adult CD albino rats (Age 7-12 weeks; Source: Charles River UK Limited; 230-270 g males and 212-245 g females) were exposed nose only via the inhalation route to Chlorothalonil Technical (Lot # 218/87; 98.63 % purity; white powder) for 4 hours at concentrations of 0.658, 0.127, 0.223 or 0.376 mg/L. Animals were then observed for 14 days.

LC₅₀ Males = 0.230 mg/L (95% C.I. 0.155-0.304 mg/L)

LC₅₀ Females = 0.205mg/L (95% C.I. 0.139-0.271 mg/L)

LC₅₀ Combined = 0.217mg/L (95% C.I. 0.174-0.260 mg/L)

At 0.658 mg/L, all rats died by day 3. At 0.376 mg/L, all rats died by day 5. At 0.223 mg/L, four rats died by day 4. At 0.127 mg/L, one female rat was found dead on day 3. Clinical signs noted during the exposure included exaggerated respiratory movements, reduced respiratory rate, struggling in restraint tubes, gasping, pallor of the extremities, irregular respiration. The following clinical signs were noted during the first three hours following exposure: exaggerated respiratory movements, gasping, rales, torpidity, eyes closed or partially closed, dark eyes, hypothermia, brown staining on the fur and test material on the fur. Signs that persisted for several days included exaggerated respiratory movements, reduced respiratory rate, gasping, rales, brown staining on the head, dark eyes, eyes closed or partially closed, hypothermia, torpidity, yellow staining in the urogenital region, swollen abdomen and emaciation. Most of the surviving rats recovered from these symptoms by day 5. The rats that died on test lost bodyweight rapidly before death. Rats that survived either lost weight or gained weight slowly for the four days following exposure. Gross necropsy of the decedents revealed blockage of partial blockage of the larynx or anterior trachea with flexible solid material or viscous liquid, incomplete collapse of the lungs when the trachea was cut, firm lungs and dark appearance of the lungs. Gross necropsy of the surviving rats showed a pale appearance to the lungs, dark areas on the lungs, enlargement of the cervical lymph nodes, dark cervical lymph nodes and the presence of dark foci on the cervical lymph nodes.

EPA Toxicity Category cannot be determined.

This acute inhalation study is classified as unacceptable. It does not satisfy the guideline requirement for an acute inhalation study (OPPTS 870.1300; OECD 403) in the rat. The mass median aerodynamic diameter (MMAD) and the geometric standard deviation (GSD) were not calculated and reported as required in OPPTS Guideline 870.1300. If the laboratory has retained the original records for the study and can provide the MMAD and GSD, the study is potentially upgradable.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Nominal Concentration (mg/L)	Gravimetric Concentration (mg/L)	MMAD μ m	GSD μ m	Mortality/Number Tested		
				Males	Females	Combined
1.377	0.658	not reported	not reported	5/5	5/5	10/10
0.723	0.376	not reported	not reported	5/5	5/5	10/10
0.382	0.223	not reported	not reported	2/5	2/5	4/10
0.245	0.127	not reported	not reported	0/5	1/5	1/10

Statistics - The LC_{50} and 95% confidence limits were calculated by the method of Finney (Finney, 1971).

Test Atmosphere / Chamber Description:

Chamber Volume: 60 L
 Airflow: 30 LPM
 Temperature: 23°C
 Relative Humidity: 15-24%
 Time to Equilibrium: not reported

A. Mortality - as noted in table.

B. Clinical observations - Clinical signs noted during the exposure included sagging eyelids, tachypnea, closed eyelids, coating of the fur with test article and hunched posture. Lethargy, sagging eyelids, few feces, chromorhinorrhea, soiling of the anogenital area, chromodacryorrhea, wetness of the anogenital area, wetness of the nose/mouth area, red staining of the abdomen, emaciation, dyspnea, piloerection, tremors, tachypnea, red staining of the nose/mouth area, ocular discharge and crusting, hunched posture, brown staining of the nose/mouth area, vocalization when handled, red areas and eschar on the tail, red staining of the front paws, localized alopecia and malocclusion of the incisors were noted during the extended 28 day observation period. Some animals lost weight during the first 14 days but all animals gained weight by day 28.

C. Gross Necropsy - Gross necropsy of the decedents revealed blockage of partial blockage of the larynx or anterior trachea with flexible solid material or viscous liquid, incomplete collapse of the lungs when the trachea was cut, firm lungs and dark appearance of the lungs. Gross necropsy of the surviving rats showed a pale appearance to the lungs, dark areas on the lungs, enlargement of the cervical lymph nodes, dark cervical lymph nodes and the presence of dark foci on the cervical lymph nodes.

D. Reviewer's Conclusions: This study is classified as unacceptable because the mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) were not calculated and reported. If the laboratory has retained the original records for the study and can provide the MMAD and GSD, the study is potentially upgradable.

ACUTE TOX ONE-LINERS

1. DP BARCODE: D302849
2. PC CODES: 081901
3. CURRENT DATE: 26/AUG/2004
4. TEST MATERIAL: Chlorothalonil Technical (Lot # 218/87; 98.63 % purity; white powder)

Study/Species/Lab Study # /Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity/rat Life Science Research Rome Toxicology Centre 88/CFA002/276 3-29-88	45710203	LD ₅₀ > 5000 (males, females combined)	IV	A
Acute inhalation toxicity/rat Life Science Research Limited 88/CFA001/185	45710204	No LD ₅₀ was determined MMAD and GSD were not calculated and reported.	--	U

Core Grade Key: A = Acceptable, S = Supplementary, U = Unacceptable, W = Waived