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TXR#:0051475

Updated Executive Summary for
DATA EVALUATION RECORD
TXR# 0052720

STUDY TYPE: 28- Day Inhalation Toxicity - [rat]; OPPTS 870.3465 [§82-4]; OECD 413.

PC CODE: 068103

DP BARCODE: 303925
SUBMISSION NO.: 332274

TEST MATERIAL (PURITY): Methyl Isothiocyanate 96.9%

SYNONYMS: MITC

CITATION: Klimisch, H.J. (1987). Study of the Subchronic Inhalation Toxicity of Methyl Isothiocyanate in Wistar Rats (4 weeks study). Department of Toxicology. BASF Aktiengesellschaft, D-W6700 Ludwigshafen, Federal Republic of Germany. Project No 4010231/8539, BASF Reg. Document Number 87/0244, January 29, 1987. MRID 45314802. Unpublished.

SPONSOR: BASF Corporation, Agricultural Products, 26 Davis Drive. P.O. Box 13528. Research Triangle Park, NC 27709-3528

EXECUTIVE SUMMARY: In a 28 day inhalation toxicity study (MRID 45314802), Methyl Isothiocyanate [96.9 % a.i.] was administered to 5/sex/dose of SPF Wistar/Chubb:THOM rats by whole body exposure at analytical concentrations of 0, 5.0, 20, or 100 mg/m³ equivalent to 0, 5.0, 20, or 100 ug/L (measured concentrations 0, 5.1, 19.9 or 100 ug/L) and (equivalent to concentrations of 0, 1.7, 6.8, and 34 ppm) for 6 hours per day, 5 days/week for a total of 28 days.

All animals survived to study termination. Mid and high dose rats demonstrated clinical signs during exposure from the third exposure period day. No clinical signs were observed in the low dose animals. According to the study report,

"During exposure, the animals of test group 2 showed eyelid closure, somnolence, and ruffled fur from the third day of exposure onwards. On the next morning before exposure nothing abnormal was found in the animals.....At 20 mg/m³ the animals showed first indications of an irritating effect of the test substance and a slightly deteriorated general state of health."

Additional clinical signs observed at the high exposure concentration included reddish nasal discharge, salivation, eye discharge, and difficulty in breathing or whooping respiration, and stretched posture. In the high dose rats, although signs recovered between exposures at the beginning of the study, towards the end of the study ruffled fur and respiratory sounds were no longer reversible.

Body weight and body weight gain were significantly decreased ($p < 0.05$) at the high dose. Food consumption and feed efficiency were not measured. There were decreases in plasma urea, glucose, triglyceride, and albumin the high dose males. In high dose females, urea and glucose were also decreased. In the males of mid exposure group, there was a decrease in urea concentration in the plasma.

At the mid and high exposure concentrations, increase in neutrophilic polymorphonuclear granulocytes in the peripheral blood was observed in males; this was also observed in the high exposure concentration for females.

There was increased lung weight at the high exposure concentration. Histopathology revealed an increase in incidence and severity of rhinitis in the nasal cavity at the high exposure concentration in both sexes (incidence in males: 2/5, 2/5, 2/5, 5/5; females: 0/5, 3/5, 1/5, 5/5). Other histopathologic findings at the high exposure concentration included: atrophy of the olfactory epithelium, metaplasia of the nasal respiratory epithelium (3 males in section plane 1 only, 5 females in section planes 1 and, to a lesser extent, section plane 2), tracheal epithelial proliferation and single cell necrosis (all high exposure concentration), bronchopneumonia and bronchial and bronchiolar epithelial proliferation (5 males, 2 females), and emphysema (3 males, 2 females).

The systemic LOAEL is 19.9 mg/m^3 (6.8 ppm), based on clinical signs consistent with irritation in both sexes and increased neutrophilic polymorphonuclear granulocytes in the blood of males. The systemic NOAEL is 5 mg/m^3 (1.7 ppm).

The LOAEL for effects in the extrathoracic (ET) region is 100 mg/m^3 (34 ppm), based on observation of pathological changes of the nasal cavity (metaplasia of respiratory epithelium and atrophy of the olfactory epithelium). The ET NOAEL is 19.9 mg/m^3 (6.8 ppm).

The LOAEL for effects in the tracheobronchial (TB) region is 100 mg/m^3 (34 ppm), based on observation of pathological changes (tracheal epithelial proliferation and single cell necrosis, bronchopneumonia and bronchial and bronchiolar epithelial proliferation). The TB NOAEL is 19.9 mg/m^3 (6.8 ppm).

This subchronic toxicity study is **Acceptable but does not satisfy** the guideline requirement for a subchronic inhalation study (82-4) in the rat. The study duration was too short and the number of animals used were inadequate to satisfy the Guideline requirement. Detailed tables of the clinical signs were not provided in the study report.

DATA FOR ENTRY INTO ISIS

Subchronic Inhalation Study - rodents (870.3200)

PC code	MRID	Study	Species	Duration	Route	Admin	Dose range µg/L	Doses µg/L	NOAEL µg/L	LOAEL µg/L	Target organ	Comments
068103	4531480 2	subchronic	rat	4 weeks	inhalation	inhalation	0-100	0, 5, 20, 100	5	20	Nose	irritation

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