

# MPDIOL Glycol

(2-Methyl-1,3-Propanediol)

Toxicological Data Supplement

## Description

*MPDIOL* glycol is of low toxicity as determined by oral and dermal routes of exposure. It has low skin and eye irritation potential and is not a dermal sensitizer. Studies in humans confirm that *MPDIOL* glycol has low potential to cause irritation or sensitization following topical application. Based on studies in bacteria and mammalian cells, *MPDIOL* glycol is not a genetic toxicant. The weight of evidence indicates that *MPDIOL* glycol showed no reproductive or developmental effects in animal studies even at repeated, high level oral exposures. Although *MPDIOL* glycol has not been tested for carcinogenicity, the available data and consideration of structure activity relationships, suggests that it would be unlikely to present a carcinogenic hazard.

For additional guidance refer to the material safety data sheet (MSDS), other product literature, or call 1-888-777-0232 for technical service assistance.

## Acute Toxicity

The acute oral toxicity of *MPDIOL* glycol was investigated in five male and five female albino rats. The LD50 was greater than 5000 mg/kg body weight.

Male and female albino rabbits (five per sex) were used to investigate the acute toxicity of *MPDIOL* glycol following skin contact. The dermal LD50 was greater than 2000 mg/kg body weight.

An acute inhalation toxicity test was carried out using nose-only exposure in five male and five female albino rats. All animals survived a four-hour aerosol exposure to 5.1 mg/l *MPDIOL* glycol. No adverse effects were seen during a 14 day follow-up period, and it was concluded that the inhalation LC50 for *MPDIOL* glycol was in excess of 5.1 mg/l in both sexes.

## Eye Irritation

The eye irritation potential of *MPDIOL* glycol was tested in New Zealand albino rabbits. Neat *MPDIOL* glycol (0.1 ml) was administered into one eye of each of nine animals, the other eye serving as control. The treated eyes of six rabbits remained unwashed with warm water for 20-30 seconds one minute after dosing with test substance. All six unwashed eyes of treated animals appeared normal during the study.

There was no corneal opacity, iritis or moderate conjunctival irritation noted in the three washed eyes during this study. Slight conjunctival irritation was noted in one of three eyes. This cleared by day two, and two eyes appeared normal during the study.

## Skin Irritation

The skin irritation potential of *MPDIOL* glycol was tested in six albino rabbits. Neat *MPDIOL* glycol (0.5 ml) was applied to two intact and two abraded areas of skin at a total dose of 2.0 ml/rabbit. The torso was wrapped loosely with an airtight plastic dressing during the exposure period. The test article remained in contact with the skin for four hours, after which time the wrappings were removed and dermal reactions scored at 4, 24, 48 and 72 hours. There was no erythema or edema at any site on any animal at any of the observation points. In this study, *MPDIOL* glycol was found not to be a skin irritant.

## Skin Sensitization

The dermal sensitization potential of *MPDIOL* glycol was tested in the guinea pig "maximization" test (Magnusson and Kligman.)

Female Himalayan albino guinea pigs were used in this study, 20 animals were used in the test group and 10 animals in the control group.

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A preliminary study was carried out, in order to determine the irritation potential of the test material and to assist with dose selection for the induction/challenge phase of the main study. On day one in the main study, experimental animals were treated dorsally in the scapular region with three pairs of intradermal injections (0.1 ml per site), comprising of; test material (10% solution), adjuvant (50:50 with distilled water) and 20% solution of test substance (emulsified in 50:50 adjuvant). At day seven, animals were administered 0.5 ml of undiluted test substance epidermally (48 hr occlusion) in the interscapular region after pretreatment on day six with 10% sodium dodecyl sulfate in petrolatum. Control animals were similarly treated, but with the vehicle only. Skin irritation was scored immediately after the epidermal exposure. Two weeks after the epidermal application, all animals were challenged on their flanks with test substance at concentrations of 100%, 50% and 25% and vehicle (distilled water), applied on patches (0.05 ml) for 24 hours. The challenge reactions were assessed at 24 and 48 hours.

The epidermal exposure of *MPDIOL* glycol in the induction phase resulted in no skin irritation. Epidermal exposure *MPDIOL* glycol in the challenge phase resulted in one animal showing a response (grade 1) to undiluted test substance, three animals showing an exposure (grade 1) to the 50% solution and to one animal showing a response (grade 1) to the 25% solution.

The results in the above study lead to a sensitization rate of 15% for the 50% test substance concentration. It was concluded that *MPDIOL* glycol has a low potential to cause skin sensitization and does not require classification as a skin sensitizer according to EC criteria for classification and labeling.

## Human Skin-Compatibility Testing

The potential of *MPDIOL* glycol to cause irritation or allergy after repeated skin contact was investigated in a group of 102 normal male and female volunteers, using a standard repeat insult patch test protocol. The test sample was applied on nine occasions to the mid-scapular region of the back (24 hr skin contact period) under occlusive or semi-occlusive conditions. This was followed two weeks later by a 'challenge' application on an adjacent skin site. Two separate production batches of *MPDIOL* glycol were evaluated in the study.

Responses to both samples were very mild, generally consisting of barely perceptible or mild skin redness in a few subjects, while the majority was unaffected. Overall, under the conditions of the study, no evidence was found to suggest that *MPDIOL* glycol was a skin irritant or dermal sensitizer in humans.

## Repeat Dose Oral Toxicity

The oral toxicity of *MPDIOL* glycol was assessed following repeated administration to male and female Wistar rats over 14 days (sub-acute) and 90 days (sub-chronic).

In the sub-acute study, *MPDIOL* glycol was given by gavage at dose levels of 0 (distilled water), 300, 600 or 1000 mg/kg/day to Wistar rats (five animals per sex per treatment level). During the study period, the animals were observed at least daily for clinical signs and mortality, and weekly details of body weight and food consumption recorded. An ophthalmoscopic examination was conducted during the second week of treatment. Clinical chemistry and haematological analyses were performed on a sample of blood collected immediately prior to post-mortem examination. At necropsy, the animals were subject to a post-mortem examination, and the major organs (adrenal glands, heart, kidneys, liver, spleen, testes) examined, weighed and a sample retained for subsequent histopathological examination.

There were no signs of clinical toxicity or evidence of mortality during the study period, nor did treatment *MPDIOL* glycol have any effect on body weight, body weight gain or food consumption. Occasional differences were evident in some hematological or clinical chemistry parameters, but

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these were invariably minor and appeared unrelated to treatment. Ophthalmoscopic examination of the eyes and macroscopic examination of the major internal organs at post-mortem did not reveal any treatment-related changes, nor was there any effect on organ weights. No abnormalities were apparent in the tissues upon microscopic examination. Overall, based on the results of this study, it was concluded that the sub-acute oral No Observed Adverse Effect Level (NOAEL) for *MPDIOL* glycol in the rat was 1000 mg/kg/day.

The same dose levels and general experimental protocol was followed in the sub-chronic study, which used 10 male and 10 female Wistar rats per treatment. An extensive range of tissues was sampled at necropsy and fixed in neutral phosphate buffered 4% formaldehyde solution. Those from the controls (0 mg/kg/day) and the high dose (1000 mg/kg/day) groups were subsequently examined by light microscopy.

No treatment-related changes in clinical appearance and behavior of the animals, mortality, body weight and body weight gain, food consumption or ophthalmoscopic findings were apparent. There were occasional differences in some hematological or clinical chemistry parameters, but these were minor and unrelated to treatment. No treatment-related macroscopic abnormalities or organ weight changes were found post-mortem, and no unusual findings were apparent when tissue sections from the high dose group animals were examined by light microscopy. It was concluded that the sub-chronic oral NOAEL for *MPDIOL* glycol in the rat was 1000 mg/kg/day.

## Effects During Reproduction

The effects of *MPDIOL* glycol on reproduction were investigated in a two-generation study using male and female Sprague Dawley rats. This included an assessment of the effect of *MPDIOL* glycol on parental reproductive processes in the F0 generation, as well as its effect on the neonatal growth and development of the F1 generation pups. When sexually mature, selected young F1 generation adults were themselves mated to produce a F2 generation, with parental and pup parameters evaluated as described above.

*MPDIOL* glycol was administered by gavage to parental animals of both sexes at dose levels of 0 (water), 100, 300 and 1000 mg/kg body weight/day for at least 70 days prior to mating.

Clinical observations, body weights and food consumption were recorded at intervals in the adults throughout the study period. Tissues from some of the control and high dose adult animals were processed and examined by light microscopy. Sperm and ovarian parameters were recorded in F0 and F1 adults from the control and high dose groups.

Developmental milestones were recorded in selected F1 pups, and selected F1 and F2 pups were subjected to a necropsy examination.

No treatment-related mortalities or clinical findings were noted in the adult F0 or F1 generation, and body weight and food consumption were highly comparable to the controls. Reproductive parameters and spermatogenic and ovarian endpoints were unaffected by *MPDIOL* glycol administration. No macroscopic or microscopic internal abnormalities were observed in adults of either generation, and absolute and relative organ weights were unaffected by treatment.

Pup body weight, sex ratios, litter sizes and viability indices were unaffected by *MPDIOL* glycol treatment, and there were no effects on physical development or behavioral responses in the F1 pups. No treatment-related internal findings occurred in the F1 or F2 pups.

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Based on these findings, a NOAEL for parental, neonatal and reproductive toxicity of 1000 mg/kg body weight/day was established.

## Effects During Pregnancy

The effect on the fetus of maternal exposure to *MPDIOL* glycol during pregnancy has been thoroughly investigated in two developmental / teratogenicity studies.

In the first investigation, female Wistar rats were administered a daily treatment of *MPDIOL* glycol at dose levels of 0 (water), 300, 600 or 1000 mg/kg body weight/day on days 0 to 20 of pregnancy. Gestational parameters were assessed on day 21, which included enumeration of corpora lutea, weight of gravid uterus, the number and distribution of live and dead fetuses, the number and distribution of embryo-fetal deaths and the sex of each live fetus. In addition, each fetus was examined for any unusual external features, and then preserved for an assessment of visceral and skeletal abnormalities.

In the second study, pregnant female Wistar rats were given *MPDIOL* glycol on days 0 to 19 of pregnancy at dose levels of 0 (water), 100, 300 and 1000 mg/kg body weight/day. In this instance, gestational parameters were evaluated on day 20 of pregnancy, and the fetuses examined for external, soft tissue, and skeletal malformations and variations.

*MPDIOL* glycol treatment was without effect on the mothers, with no differences in clinical observation, food consumption or body weight in either study. There were also no treatment-related internal findings.

Examination of the uterine contents revealed an apparent slight increase in embryonic resorptions in mothers from one study given 600 and 1000 mg/kg/day during pregnancy, with a corresponding slight decrease in live litter size. However, the magnitude of these effects was small and within the background control range for this strain of rat. The relatively minor nature of the effect suggested it reflected biological variation rather than an adverse effect of *MPDIOL* glycol. This was confirmed in the second investigation, where inter-uterine growth and survival was unaffected up to and including 1000 mg/kg/day. Other gestational parameters were unaffected by *MPDIOL* glycol treatment in both studies.

Fetal parameters were unremarkable, with no treatment-related difference in sex ratios, fetal weight or in the occurrence of external abnormalities. Similarly an examination of the internal structure of the fetuses revealed no soft tissue or skeletal malformations or variations that could be attributed to *MPDIOL* glycol.

These studies establish a NOAEL of 1000 mg/kg body weight/day for both maternal and fetal effects following administration of *MPDIOL* glycol during pregnancy in the rat.

## Mutagenicity Data

### *Bacterial Cell*

*MPDIOL* glycol was not mutagenic when tested in a bacterial mutagenicity assay, utilizing *S. Typhimurium* strains TA1535, TA1537, TA98, and TA100 (Ames test). The study was conducted concentrations of *MPDIOL* glycol up to 5000mg/plate, both with and without metabolic activation.

### *Mammalian Cell*

*MPDIOL* glycol was not mutagenic when tested in an in-vitro mammalian cell gene mutation assay, utilizing V79/HPRT Chinese hamster cells. In this study *MPDIOL* glycol was tested at a concentration of 333-5000mg/ml culture medium both with and without metabolic activation.

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### Chromosomal Aberrations

MPDIOL glycol was found to be non-clastogenic in an in-vitro chromosomal aberration assay, utilizing human lymphocytes. In this study, MPDIOL glycol was tested at concentrations up to and including 500mg/ml culture medium, both with and without metabolic activation.

SUMMARY OF MPDIOL GLYCOL PHYSICAL & CHEMICAL PROPERTIES	
Freezing Point, °C	<-54°. Increased viscosity to -54°C with no clear change to solid.
Boiling Point	212°C @ 760 mm Hg
Water Solubility	Complete at room temperature.
Partition Coefficient	O/W 0.24 @ 20° C
Flash Point	127°C (260°F) Closed Cup
Autoignition Temperature	380°C (716°F)
Fat Solubility	9.4 g/kg
Molecular Weight (g/mole)	90.1
Viscosity (cps @ 25°C)	168
Specific Gravity	1.015
Density	1.01 g/cm <sup>3</sup> @ 20° C
Vapor Pressure (mm Hg @20°C)	<0.1
Surface Tension	72.2 mN/m @ 20° C
Refractive Index	1.445

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