

**2-(2-(2-Methoxyethoxy)ethoxy)ethanol
(CAS-NR.: 112-35-6)**

Mutagenicity:

TEGME was not mutagenic in vitro (Ames-Test, test with E.coli and HPGRT assay on CHO cells). Also an in vivo micronucleus test on Swiss CD-1 mice with gavage application of max. 5000 mg/kg bw yielded a negative result. According to the EC classification criteria there is no classification warranted (M: -).

Carcinogenicity:

There are no data available. Therefore according to the EC classification criteria there is no classification possible (C: -).

Reproductive Toxicity/Fertility:

There is no specific study on fertility available.

From studies with repeated dosing in rats (13 weeks dermal application of max. 4000 mg/kg bw/d) and in rabbits (21 day dermal study with 1000 mg/kg bw/d) respectively there are no evidences for substance-related effects on the gonades.

During a 13 weeks study on rats with TEGME-application via drinking water (effective dosages: 400; 1300 and 4200 mg/kg bw/d) testicular damage was found in males of the 4200 mg/kg group: 12/15 showed degeneration and 5/15 atrophy of seminiferous tubules. At the lower dosage of 1300 mg/kg there was only 1/15 males showing a severe seminiferous tubule atrophy and there were no cases of degenerations.

Since clear effects on the gonades which might lead to decreased fertility appear only at very high oral doses (4000 mg/kg bw) and since at 1300 mg/kg bw there are practically no effects, according to the EC classification criteria there is no classification warranted (R_F: -).

Reproductive Toxicity/Development:

There are four teratology studies available, 3 on rats and 1 on rabbits.

Wistar rats 10 w/group	gavage g.d. 7-16	0; 250 and 1000 mg/kg/d Maternal Toxicity: NOAEL Fetal Effects: NOAEL	[Leber et al. 1990] > 1000 mg/kg bw/d > 1000 mg/kg bw/d
SD-rats 25 w/group	gavage gd. 6-15 sacrifice gd 20	0; 625; 1250; 2500; 5000 mg/kg/d Maternal Toxicity: NOEL 625 mg/kg bw/d NOAEL 1250 mg/kg bw/d at 1250 mg/kg: food consumption (↓) from 2500 mg/kg: food consumption ↓ (significant) at 5000 mg/kg: mortality (1/25), body weight ↓, gravid uterine weight ↓, clinical signs Fetal Effects: NOEL 625 mg/kg bw/d At 1250 mg/kg: delayed ossification ↑, skeletal variations (↑), fetal weight (↓) From 2500 mg/kg: delayed ossification ↑, skeletal variations ↑, fetal weight ↓ At 5000 mg/kg: resorption rate ↑ (slight but significant)	[Hoberman et al.96]
SD-rats 64 w/group	gavage gd. 6 – pnd. 21	0; 300; 1650; 3000 mg/kg bw/d Maternal Toxicity: NOAEL 1650 mg/kg bw/d at 3000 mg/kg: gestation time ↑ and kidney weight ↑(?) Fetal Effects: NOAEL 300 mg/kg bw/d From 1650 mg/kg: pup weight (pnd 4-21) ↓, age of testes descent ↓	[RTI-Report 1992]
NZW-rabbits 20 w/group sacrifice gd 29	gavage gd. 6-18	0; 250; 500; 10; 1500 mg/kg/d Maternal Toxicity: NOEL 250 mg/kg bw/d NOAEL 500 mg/kg bw/d, at 500 mg/kg: food consumption (↑) in postdosing period at 1000 mg/kg: food consumption ↑ in postdosing period, mortality ↑ (1/20) at 1500 mg/kg: mortality ↑ (8/20), gross lesions, bw gain ↓, food consumption ↓, gravid uterine weight ↓, motor activity ↓, abortions ↑ (3/20) Fetal Effects: NOEL 1000 mg/kg bw/d NOAEL 1500 mg/kg bw/d At 1500 mg/kg bw/d: incidences of angulated hyoid alae and of delayed ossification of xiphoid process ↑	[Hoberman et al.96]

In summary there is some experimental evidence for foetotoxic effects of the substance in rats and rabbits above the limit dose of 1000 mg/kg bw/d and in presence of maternal toxicity. Based on these data and according to the EC classification criteria no classification is warranted (R_E: -).

Stand: November 2001