

**1,2-Bis(2-methoxyethoxy)ethan
(CAS-NR.: 112-49-2)**

Mutagenicity:

There are no data available.

According to the EC classification criteria there is no classification possible (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 a continuous breeding study on mice available.

Swiss CD-1 Mice 20 pairs/ group	drinking water	0; 440; 830 and 1470 mg/kg/d Parental Toxicity: NOEL: 830 mg/kg bw/d at 1470 mg/kg/d: liver weight ↑, pituitary weight ↓ (w) Fertility Effects: NOAEL: 830 mg/kg bw/d From 440 mg/kg: decrease of fertility index, live pups/ Litter and proportion of pups born alive with statistically significant dose response trend (P < 0.05) 1470 mg/kg/d: mean pup bw ↓, female fertility index ↓, live pups/litter ↓*;proportion of pups born alive ↓*, litters per pair ↓* (* P < 0.05 versus control)	[Bossert et al. 1992]
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In a 28 day subacute oral study on rats (0; 62.5; 250; 1000 mg/kg bw/d) there were at the highest dose clear toxic effects at the male gonades: Decrease in testes weight and testicular degeneration, azoospermia, isolated foci of necrosis of germinal epithelium).

The results of the continuous breeding study show that female fertility is decreasing with a statistically significant dose response trend starting at 440 mg/kg bw/d. In rats the 28 day application of 1000 mg/kg bw/d led to serious effects at the male gonades. According to the EC classification criteria a classification in category 2 (R_F: 2) seems appropriate.

Reproductive Toxicity/Development:

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

CD-1 mice 50 w/group	gavage g.d. 7-14	3500 mg/kg/d Maternal Toxicity: mortality 2/50 Fetal Effects: 100 % resorptions	[Schuler et al. 1984]
CD-1 mice 26-28 w/gr.	gavage g.d. 6-15	0; 250; 500; 1000 mg/kg/d Maternal Toxicity: NOEL 250 mg/kg bw/d from 500 mg/kg: relative liver weight ↑ Fetal Effects: NOEL 250 mg/kg bw/d from 500 mg/kg: fetal bw/litter ↓, % live malformed fetuses/litter ↑ (neural tube, cranio-facial structures, axial skeleton)	[George et al. 1987]
CD-1 mice 20 w/gr.	gavage g.d. 11	713 mg/kg/d Maternal Toxicity: NOEL 713 mg/kg bw/d Fetal Effects: NOEL 713 mg/kg bw/d	[Hardin & Eisenmann, 1987]
NZW- rabbits 22-25 w/gr.	gavage gd. 6-19 sacrifice gd 30	0; 75; 125; 175; 250 mg/kg/d Maternal Toxicity: NOEL 125 mg/kg bw/d from 175 mg/kg: bw gain ↓, gravid uterine weight ↓, at 250 mg/kg: relative liver weight ↑ Fetal Effects: NOEL 125 mg/kg bw/d From 175 mg/kg bw/d: prenatal mortality ↑, incidences of malformations ↑ at 250 mg/kg: preimplantational losses ↑	[Schwetz et al.1992]

In summary there is clear experimental evidence for teratogenic effects of the substance in mice and rabbits. Based on these data and according to the EC classification criteria classification in category 2 (R_E: 2) is proposed.

Stand: November 2001