

Frequency of Treatment: 5 days per week, 6 hours a day

Post-Exposure Period: Rat – 3 days
Rabbit – 11 days

Method/Guideline and Test Condition Remarks: Exposure period: 12 days
Recovery period: Rat – 3 days; Rabbit – 11 days
Control group: None
Method: OECD 412 (OECD 1981)
5 males, 5 pregnant females (rat) and 5 pregnant females (rabbit) were used per group (whole body exposure). Animals were observed for mortality and clinical symptoms once before each exposure, several times during exposure, once after each exposure and daily during the recovery period. Body weights were recorded before treatment (females) and weekly during the study (females), food consumption was determined weekly. Haematological examination (haemoglobin concentration, reticulocyte count, haematocrit, erythrocyte count, leukocyte count, thrombocyte count, differential blood count and clotting time) was performed in females 3 days before the first exposure and 3 days after the last exposure. The rats were sacrificed 3 days (21 days post copulationem) after the last treatment, the rabbits 11 days (day 29 of gestation) after the last exposure and examined for gross macroscopic changes. Foetuses were removed by Caesarean section. Testes and epididymis of the treated male rats were examined histopathologically.
Ethylene glycol dimethyl ether was applied to a vaporizer and continuously evaporated at 80°C. The resulting test substance/air mixture was carried to the inhalation chambers using an air stream of 800 L/h. The Ethylene glycol dimethyl ether concentration was determined by a Miran 80 photometer every 15 min. CO, CO₂ (Uras 2 T Infrared-Gasanalyser) and O₂ (Magnos 3 magnetic Oxygen-Analysator) concentration as well as humidity (Transmitter HMT 12) and temperature (CMR-Meßumformer TEU 320) were determined continuously.

Test Results – Repeated-Dose Toxicity

Concentration (LOAEL/LOAEC/NOAEL/NOAEC): NOAEL < 100 ppm (0.374 mg/L)

Results Remarks: **Mortality/Viability:** All animals survived and no clinical signs were noted at 100 ppm. No deaths or clinical signs

occurred in the rats of the 500 ppm dose group. All rabbits of the 500 ppm dose group died (one female died after the 7th exposition, one on the first day after the last application, two on the second day after the last application and one was found dead 8 days after the last application).

Body weight: Body weight gain of the rats at 100 ppm exposure was unaffected. Four of five rabbits in the 100 ppm dose group had a slightly decreased body weight gain. The body weight of the male rats of the 500 ppm dose group was unaffected; the body weight of three female rats and all rabbits was decreased.

Food consumption: There were no effects upon the mean daily food consumption observed in the 100 ppm dose group. Food consumption of all females (rats and rabbits) in the 500 ppm dose group was decreased.

Haematology: There were no changes noted at 100 ppm. At 500 ppm the leukocyte count was decreased in all animals; the lymphocyte count and reticulocyte count was decreased in the rabbits.

Macroscopic/microscopic findings: The rabbits of the 500 ppm exposure group showed enlarged livers. No changes occurred in the 100 ppm dose group and in all rats. The microscopic examination of the testes and epididymis showed oligospermia at 100 ppm and severe lesions of the seminiferous epithelium at 500 ppm exposure.

Maternal/developmental toxicity:

Rat: At 100 ppm retardation of foetal development was observed. At 500 ppm an increase of resorptions occurred.

Rabbit: Exposure to 100 ppm of the test substance resulted in the resorption of all embryos. At 500 ppm no rabbit survived.

Conclusion: Based on the observed oligospermia in rats and the retardation of foetal development and resorption of embryos in rats and rabbits, respectively, the NOAEL is considered to be lower than 100 ppm (0.374 mg/L).

Reliability/Data Quality – Repeated-Dose Toxicity

Reliability: 2 (valid with restrictions)

Reference – Repeated-Dose Toxicity

Reference: H. Hollander and W. Weigand, Orientierende Prüfung auf embryotoxische Wirkung an Kaninchen und Ratten (1985); Hoechst Study Report No. 85.0477

Repeated-Dose Toxicity

Test Substance – Repeated-Dose Toxicity

Category Chemical: (110-71-4) Ethylene glycol dimethyl ether (EGDME)

Test Substance: (110-71-4) Ethylene glycol dimethyl ether (EGDME)

Test Substance Purity/Composition and Other Test

Substance Comments: Ethylene glycol dimethyl ether, 99.8 % with 0.2 % 2-Methyl-1.3 Dioxolane, 140 ppm Dioxane

Method – Repeated-Dose Toxicity

Route of Administration: Inhalation

Type of Exposure: Vapor

Species: Rat

Mammalian Strain: Rat – Hoe: WISKf (SPF 71)

Gender: Both M/F

Number of Animals per Dose: 20

Dose: 0; 10; 50; 250 ppm (0; 0.037; 0.187; 0.935 mg/L)

Year Study Performed: 1986

Method/Guideline Followed: OECD Guideline for Testing of Chemicals 412 (Repeated Dose Inhalation Toxicity: 28-day or 14-day Study)

GLP: Yes

Exposure Period: 14 days

Frequency of Treatment:

5 days per week, 6 hours a day

Post-Exposure Period:

36 days

Method/Guideline and Test Condition Remarks:

Exposure period: 14 days

Recovery period: 36 days

Control group: Yes, concurrent to treatment (air)

Method: OECD 412 (OECD 1981)

10 males and 10 females were used per group (whole body exposure). Animals were observed for mortality and clinical symptoms once before each exposure, several times during exposure, once after each exposure and daily during the recovery period. Body weights were recorded before treatment and weekly during the study, food and water consumption were determined weekly. Haematological examination (haemoglobin concentration, reticulocyte count, haematocrit, erythrocyte count, leukocyte count, thrombocyte count, differential blood count, thromboplastin time, Heinz body count, activated partial thromboplastin time and clotting time) and clinical biochemistry (sodium, potassium, bilirubin, creatinine, glucose, urea nitrogen, calcium, chloride, glutamic-pyruvic transaminase, glutamic-oxaloacetic transaminase, cholesterol, total serum protein, meth-haemoglobin, lactate dehydrogenase, phosphorus, lipids, electrophoresis) were performed in 10 animals per group (5 males and 5 females) one day after the last exposure and in the remaining animals 36 days after the last exposure. 10 rats of each dose group (5 males and 5 females) were sacrificed 1 day after the last treatment and the remaining animals 36 days after the last exposure and examined for gross macroscopic changes. Heart, spleen, lung, liver, kidney, brain, testis, ovary, seminal vesicle, adrenal, pituitary gland and thyroid gland were weighed and the relative organ weight was calculated. Full histopathology was carried out on numerous organs and tissues.

Ethylene glycol dimethyl ether was applied to a vaporizer and continuously evaporated at 80°C. The resulting test substance/air mixture was carried to the inhalation chambers (2.25 m³) using an air stream of 800 L/h. The Ethylene glycol dimethyl ether concentration was determined by a Miran 80 photometer every 30 min. CO, CO₂ (Uras 2 T Infrared-Gasanalyser) and O₂ (Magnos 3 magnetic Oxygen-Analyser) concentration as well as humidity (Transmitter HMT 12) and temperature (CMR-Meßumformer TEU 320) were determined continuously.

Test Results – Repeated-Dose Toxicity

**Concentration
(LOAEL/LOAEC/
NOAEL/NOAEC):**

NOEL = 50 ppm (0.187 mg/L)

Results Remarks:

Mortality/Viability: All animals survived and no clinical signs were noted at any dose level. No neurological or ophthalmological effects or changes in mucosa were noted.

Body weight: Body weight gain of all animals was not affected.

Food/water consumption: There were no effects upon the mean daily food consumption observed at all dose levels. Water consumption of all females of the 50 ppm dose group was decreased from day 29 until termination of the study. Water consumption of all females of the 250 ppm dose group was decreased on study day 22 and 50.

Haematology: There were no changes noted at any dose level.

Clinical biochemistry: All determined parameters were within the control range.

Organ weights: Relative organ weights were within the control range.

Macroscopic/microscopic findings: No changes occurred at any dose level with the exception of the reduction of cell layers of seminiferous epithelium in male rats of the 250 ppm dose group. This effect was reversible. There were no such findings in the recovery group.

Conclusion:

Based on the observed slight changes in the seminiferous epithelium in male rats of the 250 ppm dose group, the NOEL is considered to be 50 ppm (0.187 mg/L).

Reliability/Data Quality – Repeated-Dose Toxicity

Reliability:

1 (valid without restrictions)

Reference – Repeated-Dose Toxicity

Reference:

H. Hollander and W. Weigand, Subchronische inhalative Toxizität – 10 Expositionen in 14 Tagen an SPF-Wistar-Ratten (1986); Hoechst Study Report No. 86.0002

Repeated-Dose Toxicity

Test Substance – Repeated-Dose Toxicity

Category Chemical: (110-71-4) Ethylene glycol dimethyl ether (EGDME)

Test Substance: (110-71-4) Ethylene glycol dimethyl ether (EGDME)

Test Substance Purity/Composition and Other Test

Substance Comments: Ethylene glycol dimethyl ether, 99.8 % with 0.2 % 2-Methyl-1,3 Dioxolane, 140 ppm Dioxane

Method – Repeated-Dose Toxicity

Route of Administration: Inhalation

Type of Exposure: Vapor

Species: Rabbit

Mammalian Strain: Rabbit – Hoe: HIMK (SPF Wiga)

Gender: Both M/F

Number of Animals per Dose: 12

Dose: 0; 10; 50; 250 ppm (0; 0.037; 0.187; 0.935 mg/L)

Year Study Performed: 1986

Method/Guideline Followed: OECD Guideline for Testing of Chemicals 412 (Repeated Dose Inhalation Toxicity: 28-day or 14-day Study)

GLP: Yes

Exposure Period: 14 days

Frequency of Treatment:

5 days per week, 6 hours a day

Post-Exposure Period:

36 days

Method/Guideline and Test Condition Remarks:

Exposure period: 14 days

Recovery period: 36 days

Control group: Yes, concurrent to treatment (air)

Method: OECD 412 (OECD 1981)

6 males and 6 females were used per group (whole body exposure). Animals were observed for mortality and clinical symptoms once before each exposure, several times during exposure, once after each exposure and daily during the recovery period. Body weights were recorded before treatment and weekly during the study, food and water consumption were determined weekly. Haematological examination (haemoglobin concentration, reticulocyte count, haematocrit, erythrocyte count, leukocyte count, thrombocyte count, differential blood count, thromboplastin time, Heinz body count, activated partial thromboplastin time and clotting time) and clinical biochemistry (sodium, potassium, bilirubin, creatinine, glucose, urea nitrogen, calcium, chloride, glutamic-pyruvic transaminase, glutamic-oxaloacetic transaminase, cholesterol, total serum protein, meth-haemoglobin, lactate dehydrogenase, phosphorus, lipids, electrophoresis) were performed in 6 animals per group (3 males and 3 females) one day after the last exposure and in the remaining animals 36 days after the last exposure. 6 rabbits of each dose group (3 males and 3 females) were sacrificed 1 day after the last treatment and the remaining animals 36 days after the last exposure and examined for gross macroscopic changes. Heart, spleen, lung, liver, kidney, brain, testis, ovary, adrenal, pituitary gland, thymus, pancreas and thyroid gland were weighed and the relative organ weight was calculated. Full histopathology was carried out on numerous organs and tissues.

Ethylene glycol dimethyl ether was applied to a vaporizer and continuously evaporated at 80°C. The resulting test substance/air mixture was carried to the inhalation chambers (2.25 m³) using an air stream of 800 L/h. The Ethylene glycol dimethyl ether concentration was determined by a Miran 80 photometer every 30 min. CO, CO₂ (Uras 2 T Infrared-Gasanalysator) and O₂ (Magnos 3 magnetic Oxygen-Analysator) concentration as well as humidity (Transmitter HMT 12) and temperature (CMR-Meßumformer TEU 320) were determined continuously.

Test Results – Repeated-Dose Toxicity

**Concentration
(LOAEL/LOAEC/
NOAEL/NOAEC):**

NOEL = 10 ppm (0.037 mg/L)

Results Remarks:

Mortality/Viability: In the control group, one male was found dead on day 10 and in the 10 ppm dose group, one female died on day 11. In the 50 ppm dose group, one male was found dead on day 2 (this animal was replaced by one male of the satellite group) and in the 250 ppm dose group, one female was found dead on day 12. All other animals survived and no clinical signs were noted at any dose level. No neurological or ophthalmological effects or changes in mucosa were noted.

Body weight: Body weight gain of all animals was not affected within the first 15 days of the study. During the 36 days recovery period the body weight gain of the male animals of the 250 ppm dose group was considerably decreased, the body weight gain of the females of this dose group was slightly decreased.

Food/water consumption: With one exception there were no effects upon the mean daily food consumption observed at all dose levels. The food consumption of the animals of the 250 ppm dose level was decreased during the exposure period. Water consumption of all males of the 250 ppm dose group was increased during the recovery period. In case of all other animals the water consumption was not affected.

Haematology: The reticulocyte count of all animals of the 250 ppm dose group and of the females of the 50 ppm dose group was decreased one day after the last exposure. The leukocyte count of the females in the 250 ppm dose group was slightly decreased. These effects were reversible within the recovery period.

Clinical biochemistry: All determined parameters were within the control range.

Organ weights: Relative organ weights were within the control range with the exception of a decreased testis weight of the males in the high dose group after the recovery period.

Macroscopic/microscopic findings: No changes occurred at any dose level with the exception of changes of the seminiferous epithelium in male rabbits of the 250 ppm dose group which caused aspermia. This effect was irreversible within the recovery period of 36 days

Conclusion:

Based on the decreased reticulocyte count in female rabbits exposed to 50 ppm and the observed changes in the seminiferous epithelium in male rabbits of the 250 ppm dose group, the NOEL is considered to be 10 ppm (0.037 mg/L).

Reliability/Data Quality – Repeated-Dose Toxicity

Reliability: 1 (valid without restrictions)

Reference – Repeated-Dose Toxicity

Reference: H. Hollander et al., Subchronische inhalative Toxizität – 10 Expositionen in 14 Tagen an SPF-HIMK-Kaninchen (1986); Hoechst Study Report No. 86.0426

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Clariant Corp
625 East Catawba Ave



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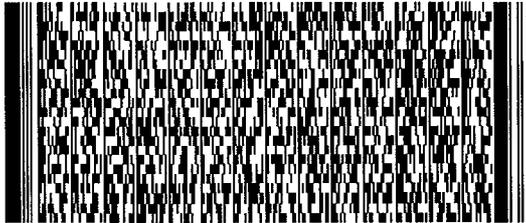
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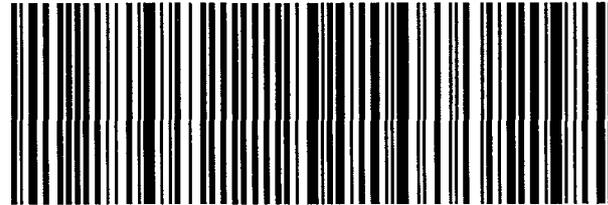
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Clariant Corporation

625 East Catawba Avenue
Mount Holly, NC 28120
704.822.2100

Tel: (704) 822-2245
Fax: (704) 330-1551
Email: US FUN PS@clariant.com

October 3, 2008

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RE: TSCA Section 8(e) report of a series of repeated dose and reproductive and developmental studies in rats and rabbits with Monoglyme (CAS No. 110-71-4)

To: TSCA 8(e)Staff:

Clariant Corp. (US) has recently obtained the attached robust summary reports from a Clariant affiliate in Europe. We are submitting these results under TSCA section 8(e) based on organ-specific, reproductive and developmental effects seen in both rats and rabbits following inhalation exposures. The study titles are listed below, with the robust summaries following as Attachments 1 through 5.

1. 14 d-Inhalation toxicity study in rat (1985), Höchst Corp., Report No. 1985.0477, GLP / OECD; reliability: 2
2. 14 d-Inhalation toxicity study in rat (1986), Höchst Corp., Report No. 1986.0002, GLP / OECD; reliability: 1
3. 14 d-Inhalation toxicity study in rabbit (1986), Höchst Corp., Report No. 1986.0426, GLP / OECD reliability: 1
4. Developmental toxicity study in rabbit (1988, inhalation), Höchst Corp., Report No. 1988.0003, GLP / OECD; reliability: 1
5. Developmental toxicity study in rat (1988, inhalation), Höchst Corp., Report No. 1988.0110, GLP / OECD; reliability: 1

These summaries are also being submitted to EPA under the CHAMP program. Clariant Corp. (US), was not provided with full copies of the studies described above, as they are in German. If you need further information or would like for us to obtain a copies of the full studies, please contact me at the number listed above.

Sincerely,

Terry L. Wells
Product Safety Manager
Functional Chemicals



CONTAINS NO CBI

CC: Mary Dominiak (for Champ program)
Diane Sheridan

Contains No CBI

314536

Pre-natal developmental Toxicity

Test Substance – Pre-natal developmental Toxicity

Category Chemical: (110-71-4) Ethylene glycol dimethyl ether (EGDME)

Test Substance: (110-71-4) Ethylene glycol dimethyl ether (EGDME)

Test Substance Purity/Composition and Other Test

Substance Comments: Ethylene glycol dimethyl ether, 99.8 % with 0.2 % 2-Methyl-1.3 Dioxolane, 140 ppm Dioxane

Method – Pre-natal developmental Toxicity

Route of Administration: Inhalation

Type of Exposure: Vapor

Species: Rabbit

Mammalian Strain: Russian Rabbit

Gender: F (pregnant)

Number of Animals per Dose: 15

Dose: 0; 5; 16; 50 ppm (0; 0.019; 0.06; 0.187 mg/L)

Year Study Performed: 1988

Method/Guideline Followed: OECD Guideline for Testing of Chemicals 412 (Repeated Dose Inhalation Toxicity: 28-day or 14-day Study) and 414 (Teratogenicity)

GLP: Yes

Exposure Period: Days 6 – 18 of gestation

Frequency of Treatment: daily, 6 hours a day

Post-Exposure Period: 10 days

Method/Guideline and Test Condition Remarks: Exposure period: days 6 – 18 of gestation
Recovery period: 10 days
Control group: Yes, concurrent to treatment (air)
Method: OECD 412 and 414 (OECD 1981)
15 pregnant females were used per group (whole body exposure). Animals were observed for mortality and clinical symptoms daily during treatment and the recovery period. Body weights and food consumption were determined weekly. The rabbits were sacrificed 10 days (29 days post copulationem) after the last treatment. Post mortem examination included uterine contents, uterus weight, number of resorptions and corpora lutea. Foetuses were removed by Caesarean section, weighed and examined for gross external abnormalities. After incubation at 32°C for 24 hours, the viability of the foetuses was determined. Foetuses were sacrificed and sexed. One half of all foetuses and all foetuses that were found dead in the uterus were fixed and stained with Alizerinred S for skeletal examination. The remaining foetuses were fixed in Bouin's fixative and examined by a combination of serial sections of the body. The dams were subjected to a macroscopic examination. Heart, spleen, liver and kidneys were weighed.
Ethylene glycol dimethyl ether was applied to a vaporizer and continuously evaporated at 80°C. The resulting test substance/air mixture was carried to the inhalation chambers (2.25 m³) using an air stream of 800 L/h. The Ethylene glycol dimethyl ether concentration was determined by a Miran 80 photometer every 30 min. CO, CO₂ (Uras 2 T Infrared-Gasanalysator) and O₂ concentration (Magnos 3 magnetic Oxygen-Analysator) as well as humidity (Transmitter HMT 12) and temperature (CMR-Meßumformer TEU 320) were determined continuously.

Test Results – Pre-natal developmental Toxicity

Concentration (LOAEL/LOAEC/NOAEL/NOAEC):

NOEL (maternal) = 5 ppm (0.019 mg/L)
NOEL (developmental) = 16 ppm (0.06 mg/L)

Results Remarks:

Mortality/Viability: All animals survived. With the exception of one abortion in the 16 ppm dose group no serious

clinical signs were noted at any dose level. The urine of one rabbit at the 16 ppm level was stained red on day 9 of gestation.

Body weight (dams): Body weight gain of all animals in the 0, 5 and 16 ppm dose group was not affected. During the first week of treatment the body weight of the animals of the 50 ppm dose group was decreased. Within the second week of treatment this effect disappeared.

Food consumption (dams): There were no effects upon the mean daily food consumption observed at the 5 ppm dose level. The food consumption of the animals of the 50 ppm and 16 ppm dose level was slightly decreased during the exposure period. The effect diminished after the last treatment.

Organ weights (dams): The organ weights were within the control range.

Macroscopic/microscopic findings (dams): No changes occurred at any dose level with the exception of one abortion in the 16 ppm dose group. Grey areas on the kidney surface were found in one control animal, 4 animals of the 5 ppm dose group, 2 animals of 16 ppm dose group and 1 animal of the high dose group.

Examination of litters: There was no effect on foetal development and body weight observed at any dose level. Sex ratio was regular. The vitality of the litters within the first 24 hours after Caesarean section at 50 ppm exposure was considerably decreased.

Skeletal examination (foetuses): One foetus of the control group had an abnormal orientation of the fore-paws and an umbilical hernia. In the 5 ppm dose group 3 foetuses with skull malformations were found. One foetus of the 16 ppm dose level showed a retarded skeletal development and multiple malformations of skull, spine and extremity (left fore-paw almost completely missing). In the 50 ppm dose group 10 foetuses had an abnormal orientation of one or both fore-paws. Two foetuses showed skull malformations. Irregularity of the skull ossification was observed in 2 foetuses of the control group, 1 foetus of the 5 ppm dose group, 3 foetuses of the 16 ppm group and 8 foetuses of the high dose group. There was an increased incidence of rib anomalies combined with an increased dosage (statistically significant). The skeletal development of viable foetuses was not affected by treatment compared to the control group.

Soft tissue examination (foetuses): Cases of lung anomalies and blood within the chest were present in all groups. Enlarged stomachs were observed in the 16 ppm and 50 ppm dose groups as well as in the control group. 2 foetuses of the high dose group had red-bordered spots on the skin (mandible, neck and below the eyes).

Conclusion:

Based on the slightly decreased food consumption of female rabbits exposed to 16 ppm and the decreased viability of

foetuses within the first 24 hours after caesarean section, the NOEL (maternal) is considered to be 5 ppm (0.019 mg/L) and the NOEL (developmental) was set at 16 ppm (0.06 mg/L).

Reliability/Data Quality – Repeated-Dose Toxicity

Reliability: 1 (valid without restrictions)

Reference – Repeated-Dose Toxicity

Reference: Ch. Baeder et al., Monoethylenglykoldimethylether
HOECHST Prüfung auf embryotoxische Wirkung an Russen-
Kanichen bei inhalativer Verabreichung (1988); Hoechst
Study Report No. 88.0003

Pre-natal developmental Toxicity

Test Substance – Pre-natal developmental Toxicity

Category Chemical: (110-71-4) Ethylene glycol dimethyl ether (EGDME)

Test Substance: (110-71-4) Ethylene glycol dimethyl ether (EGDME)

Test Substance Purity/Composition and Other Test

Substance Comments: Ethylene glycol dimethyl ether, 99.8 % with 0.2 % 2-Methyl-1,3 Dioxolane, 140 ppm Dioxane

Method – Pre-natal developmental Toxicity

Route of Administration: Inhalation

Type of Exposure: Vapor

Species: Rat

Mammalian Strain: Wistar

Gender: F (pregnant)

Number of Animals per Dose: 20

Dose: 0; 10; 32; 100 ppm (0; 0.037; 0.12; 0.374 mg/L)

Year Study Performed: 1988

Method/Guideline Followed: OECD Guideline for Testing of Chemicals 412 (Repeated Dose Inhalation Toxicity: 28-day or 14-day Study) and 414 (Teratogenicity)

GLP: Yes

Exposure Period: Days 7 – 16 of gestation

Frequency of Treatment: daily, 6 hours a day

Post-Exposure Period: 10 days

Method/Guideline and Test Condition Remarks: Exposure period: days 7 – 16 of gestation
Recovery period: 5 days
Control group: Yes, concurrent to treatment (air)
Method: OECD 412 and 414 (OECD 1981)
20 pregnant females were used per group (whole body exposure). Animals were observed for mortality and clinical symptoms daily during treatment and the recovery period. Body weights and food consumption were determined weekly. The rats were sacrificed 5 days (21 days post copulation) after the last treatment. Post mortem examination included uterine contents, placenta weight, number of resorptions and corpora lutea. Foetuses were removed by Caesarean section, weighed, examined for gross external abnormalities, sexed and sacrificed. One half of all foetuses and all foetuses that were found dead in the uterus were fixed and stained with Alizerinred S for skeletal examination. The remaining foetuses were fixed in Bouin's fixative and examined by a combination of serial sections of the body. The dams were subjected to a macroscopic examination. Heart, spleen, liver and kidneys were weighed.
Ethylene glycol dimethyl ether was applied to a vaporizer and continuously evaporated at 80°C. The resulting test substance/air mixture was carried to the inhalation chambers (2.25 m³) using an air stream of 800 L/h. The Ethylene glycol dimethyl ether concentration was determined by a Miran 80 photometer every 30 min. CO, CO₂ (Uras 2 T Infrared-Gasanalysator) and O₂ concentration (Magnos 3 magnetic Oxygen-Analysator) as well as humidity (Transmitter HMT 12) and temperature (CMR-Meßumformer TEU 320) were determined continuously.

Test Results – Pre-natal developmental Toxicity

Concentration (LOAEL/LOAEC/NOAEL/NOAEC): NOEL (maternal) = 100 ppm (0.374 mg/L)
NOEL (developmental) = 10 ppm (0.037 mg/L)

Results Remarks: **Mortality/Viability (dams):** All animals survived. No clinical signs were noted at any dose level.
Body weight/food consumption (dams): Body weight gain and food consumption was within the control range.

Organ weights (dams): The organ weights were within the control range.

Macroscopic/microscopic findings (dams): No changes occurred at any dose level with the exception of one dam in which all embryos were found dead in the 100 ppm dose group.

Examination of litters: Body weight of control foetuses and foetuses of the 10 ppm dose group was regular. There was a slight decrease of foetal weight observed in the 32 ppm dose group and the body weight of the foetuses of the 100 ppm dose group was considerably decreased. The foetuses of the high dose group showed a retarded development. Resorptions as well as dead foetuses were found in this dose group.

Resorptions were present in all groups (control and treatment group), but the number of resorptions at the high dose level was increased compared to the others. The number of viable foetuses was considerably decreased in the 100 ppm dose group. Placenta weight was unaffected.

Skeletal examination (foetuses): One foetus of the control group showed anophthalmia and 5 foetuses had malformations of the extremities. 9 foetuses of the control group showed malformations of the sternum and ribs. In the 10 ppm dose group no anomalies were observed; the ossification was not affected. 4 foetuses of the 32 ppm dose level showed anomalies of the extremities (abnormal orientation, malformations and haematoma) and 2 of them had an open eyelid. 2 foetuses of the 32 ppm dose level had a malformation of the scapula. In the 100 ppm dose group 11 foetuses had malformations of the extremities and scapula (crooked, shortened). One foetus of the high dose group had a shortened tail and 4 foetuses showed subcutaneous oedema. The ossification of the foetuses of the 32 ppm and 100 ppm dose group was considerably retarded. In these dose groups fragmented thoracic and lumbar vertebrae were observed. The number of foetuses showing malformations of ribs was significantly increased at exposure to 32 ppm and 100 ppm of the test substance.

Soft tissue examination (foetuses): Blood in the pericardium and enlarged ureter were observed in foetuses of the 32 ppm and 100 ppm dose group.

Conclusion:

Based on no observed effects in female rats exposed to 100 ppm test substance and observed retarded development and increased incidence of malformations of the extremities in foetuses at 32 ppm, the NOEL (maternal) is considered to be 100 ppm (0.374 mg/L) and the NOEL (developmental) was set at 10 ppm (0.037 mg/L).

Reliability/Data Quality – Repeated-Dose Toxicity

Reliability: 1 (valid without restrictions)

Reference – Repeated-Dose Toxicity

Reference: Ch. Baeder et al., Monoethylenglykoldimethylether
HOECHST Prüfung auf embryotoxische Wirkung an Wistar-
Ratten bei inhalativer Verabreichung (1988); Hoechst Study
Report No. 88.0110

Repeated-Dose Toxicity

Test Substance – Repeated-Dose Toxicity

Category Chemical: (110-71-4) Ethylene glycol dimethyl ether (EGDME)

Test Substance: (110-71-4) Ethylene glycol dimethyl ether (EGDME)

Test Substance

Purity/Composition and Other Test

Substance Comments:

Ethylene glycol dimethyl ether, 99.8 % with 0.2 % 2-Methyl-1.3 Dioxolane, 140 ppm Dioxane

Method – Repeated-Dose Toxicity

Route of Administration:

Inhalation

Type of Exposure:

Vapor

Species:

Rat
Rabbit

Mammalian Strain:

Rat – Hoe: WISKf (SPF 71)
Rabbit – Hoe: HIMK (SPF Wiga)

Gender:

Rat – both M/F (pregnant)
Rabbit – F (pregnant)

Number of Animals per Dose:

Rat – 10
Rabbit – 5

Dose:

100; 500 ppm (0.374; 1.87 mg/L)

Year Study Performed:

1985

Method/Guideline Followed:

OECD Guideline for Testing of Chemicals 412 (Repeated
Dose Inhalation Toxicity)

GLP:

Yes

Exposure Period:

12 days