AR 201-12981B

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 02/23/2001

Test Substance

Remarks: 95% ethanol

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Chemical Category

Method

>> Method/Guideline followed

Growthinhibition in Chlorella

>> Test Type

static

>> GLP Unknown

>> Year study performed 1996

>> Species

Chlorella vulgaris

>> End Point ,growth,as indicated by chlorophyll(a) content

>> Analytical monitoring None

>> Exposure period 4 days

>> Statistical Method t-test at confidence level of 0.05

Remarks for Method

* Test organisms
- Laboratory culture: Isolated from Lake Geneva in 1980.
- Method of cultivation: Stock cultures were grown in Algal Assay Procedure (1971) medium (500-ml flasks containing 250 ml algal suspension) at 21 deg. C and with continuous illumination at 100 microE/m^2-sec.
- Controls: Controls consisting of algal suspensions without solvent were used in each experiment.

* Test Conditions
- Test temperature range: 21 deg. C +/- 1 deg.

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

- Growth/test medium chemistry (hardness, alkalinity, pH, TOC, TSS, dissolved oxygen, salinity, EDTA): Algal Assay Procedure (1971) medium with 15 mg/l NaHCO3, 12 mg/l K2HPO4.
- Dilution water source: Not specified.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): 20x125-mm test tubes containing about 20 ml of suspension and ethanol. Three tubes per test concentration were used.
- Water chemistry in test (pH) in at least one replicate of each concentration (at start and end of the test): Not described.
- Stock solutions preparation (vehicle, solvent, concentrations): Not described.
- Light levels and quality during exposure: 100 microE/m^2-sec; except that illumination was reduced to 1.5 microE/m^2-sec 20 minutes before and during measurement of chlorophyll content by fluorescence.

* Test design (number of replicates, concentrations): Ethanol was tested three times at each concentration: 0, 0.05%, 0.1%, 0.3%, 0.5%, 1%.

* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Only nominal concentrations were used.

Results

>> Nominal concentration 0, 500, 1000, 2000, 5000, 10,000 mg/l

>> Measured concentration Not measured

>> Precision =

>> Endpoint Type ErC50

>> Endpoint Value 1000 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 96

>> NOEC Precision < **>> NOEC** 500 **>> Unit used** mg/L

>> NOEC Concentration Type Nominal

>> NOEC Effect(s) assesse Growth, as indicated by chlorophyll (a) content.

>> LOEC Precision = **>> LOEC** 500 **>> Unit used** mg/L

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> LOEC Concentration Type Nominal

>> LOEC Effect(s) assesse Growth, as indicated by chlorophyll (a) content.

>> Response of Control Group (was it satisfactory? Yes

>> Statistical results

Growth of Chlorella was statistically significantly inhibited (at p=0.05) at all concentrations of ethanol tested.

Results Remark

* Note whether cells removed prior to measurement: Cells were not removed prior to measurement.
* Biological observations
  - Cell density at each flask at each measuring point: Cell density not given.
  - Growth curves: Growth, as indicated by chlorophyll (a) content, was plotted over time for each concentration, including control.
* Percent biomass/growth rate inhibition per concentration
  Observations: at 500, 1000, 2000, 5000, and 10,000 mg/l, the growth inhibition was, respectively, 37%, 54%, 69%, 86%, and 95%.

Conclusions

Solvents such as ethanol are often used to dissolve test compounds in aquatic toxicity tests, but have not necessarily been tested for toxicity themselves. EPA guidance from 1975 recommended maximum solvent concentrations of 0.05% and 0.01% for acute and chronic tests, respectively, but higher concentrations are often used in practice. Thus, ethanol was tested here at concentrations of 0.05% (500 mg/L) and higher, and was found to cause significant growth inhibition of Chlorella at each concentration after four days. Growth was inhibited by 54% at an ethanol concentration of 1,000 mg/L; this approximates the ErC50.

Data Quality

Reliability

Data Reliability Remarks

Reference

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> Remarks

El Jay, A. (1996). Toxic effects of organic solvents on the growth of Chlorella vulgaris and Selenastrum capricornutum. Bull. Environ. Contam. Toxicol. 57:191-198.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/28/2000

Test Substance

Remarks: 95% ethanol

Chemical Category

Method

>> Method/Guideline followed

Growth inhibition in Selenastrum

>> Test Type

static

>> GLP Unknown

>> Year study performed 1996

>> Species

Selenastrum capricornutum

>> End Point growth, as indicated by chlorophyll (a) content

>> Analytical monitoring None

>> Exposure period 4 days

>> Statistical Method t-test at confidence level of 0.05

Remarks for Method

* Test organisms
- Laboratory culture: Obtained from EPA (Corvallis, OR).
- Method of cultivation: Stock cultures were grown in Algal Assay Procedure (1971) medium (500-ml flasks containing 250 ml algal suspension) at 21 deg. C with continuous illumination at 100 microE/m^2-sec.
- Controls: Controls consisting of algal suspensions without solvent were used in each experiment.

* Test Conditions
- Test temperature range: 21 deg. C +/- 1 deg.

- Growth/test medium chemistry (hardness, alkalinity, pH, TOC, TSS, dissolved oxygen, salinity, EDTA): Algal Assay Procedure (1971) medium with 15 mg/l NaHCO3 and 12 mg/l K2HPO4.
- Dilution water source: Not specified.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): 20x125-mm test tubes containing about 20 ml of suspension and ethanol. Three tubes per test concentration were used.
- Water chemistry in test (pH) in at least one replicate of each concentration (at start and end of the test): Not described.
- Stock solutions preparation (vehicle, solvent, concentrations): Not described.
- Light levels and quality during exposure: 100 microE/m^2-sec; except that illumination was reduced to 1.5 microE/m^2-sec 20 minutes before and during measurement of chlorophyll content by fluorescence.

* Test design (number of replicates, concentrations): Ethanol was tested three times at each concentration: 0, 0.05%, 0.1%, 0.2%, 0.5%, 1%.

* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Only nominal concentrations were used.

Results

>> Nominal concentration 0, 500, 1000, 2000, 5000, 10,000 mg/l

>> Measured concentration Not measured

>> Precision =

>> Endpoint Type ErC50

>> Endpoint Value 10000 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 96

>> NOEC Precision < **>> NOEC** 500 **>> Unit used** mg/L

>> NOEC Concentration Type Nominal

>> NOEC Effect(s) assesse Growth, as indicated by chlorophyll (a) content.

>> LOEC Precision = **>> LOEC** 500 **>> Unit used** mg/L

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> LOEC Concentration Type Nominal

>> LOEC Effect(s) assesse Growth, as indicated by chlorophyll (a) content.

>> Response of Control Group (was it satisfactory? Yes

>> Statistical results

Growth of Selenastrum was statistically significantly inhibited (at p=0.05) at all concentrations of ethanol tested.

Results Remark

* Note whether cells removed prior to measurement: Cells were not removed prior to measurement.
* Biological observations
  - Cell density at each flask at each measuring point: Cell density was not given.
  - Growth curves: Growth, as indicated by chlorophyll (a) content, was plotted over time for each concentration, including control.
* Percent biomass/growth rate inhibition per concentration
  Observations: at 500, 1000, 2000, 5000, and 10,000 mg/l, the growth inhibition was, respectively, 14%, 19%, 26%, 37%, and 48%.

Conclusions

Solvents such as ethanol are often used to dissolve test compounds in aquatic toxicity tests, but have not necessarily been tested for toxicity themselves. EPA guidance from 1975 recommended maximum solvent concentrations of 0.05% and 0.01% for acute and chronic tests, respectively, but higher concentrations are often used in practice. Thus, ethanol was tested here at concentrations of 0.05% (500 mg/L) and higher, and was found to cause significant growth inhibition of Selenastrum at each concentration after four days. Growth was inhibited by 48% at an ethanol concentration of 10,000 mg/L; this approximates the ErC50.

Data Quality

Reliability

Data Reliability Remarks

Reference

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> Remarks

El Jay, A. (1996). Toxic effects of organic solvents on the growth of Chlorella vulgaris and Selenastrum capricornutum. Bull. Environ. Contam. Toxicol. 57:191-198.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/28/2000

Test Substance

Remarks: 100% absolute ethanol, dehydrated, USP

Chemical Category

Method

>> Method/Guideline followed

EPA procedures as described by Holst (1986) and Holst and Ellwanger (1982)

>> Test Type

static

>> GLP Unknown

>> Year study performed 1991

>> Species

Lemna gibba G-3 (duckweed)

>> End Point Biomass (dry wt.) and growth (# of plants/fronds).

>> Analytical monitoring None

>> Exposure period 7 days

>> Statistical Method EC50: regression analysis. NOEL: Dunnett's t-test.

Remarks for Method

* Test organisms
  - Laboratory culture: Obtained from the Smithsonian Institution.
  - Method of cultivation: Maintained at 25 deg. C +/- 2 deg, with 6461 +/- 323 lux continuously. Medium was revised Hoagland's with a pH of 4.6-5.4. Medium was renewed weekly. The acclimation period was 8 weeks.
  - Controls: Controls containing medium and Lemna but no ethanol were used.

* Test Conditions
  - Test temperature range: 25 deg. C +/- 2.

- Growth/test medium chemistry (hardness, alkalinity, pH, TOC, TSS, dissolved oxygen, salinity, EDTA): Hardness: 636 mg/l as CaCO3. Alkalinity: 23 mg/l as CaCO3. Conductivity: 5000 micromhos/cm. pH ranged from 4.5-5.1.
- Dilution water source: Not specified.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): 250-ml vessels; Shimadzu closures covered with paraffin. Each concentration and control was replicated three times.
- Water chemistry in test (pH) in at least one replicate of each concentration (at start and end of the test): Range over exposure period was 4.6-5.1.
- Stock solutions preparation (vehicle, solvent, concentrations): Not described.
- Light levels and quality during exposure: Mean lux 5382 +/- 89 during the exposure period.

* Test design (number of replicates, concentrations): 21 concentrations, ranging from 1.0 to 21,000 mg/l, plus control. Each concentration and control was repeated three times.

* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Only nominal concentrations were used.

Results

>> Nominal concentration 0, 1.0, 1.7, 2.8, 4.7, 7.8, 13, 21, 36 . . . 21000

>> Measured concentration Not measured

>> Precision =

>> Endpoint Type ErC50

>> Endpoint Value 4432 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 168

>> NOEC Precision = **>> NOEC** 280 **>> Unit used** mg/L

>> NOEC Concentration Type Nominal

>> NOEC Effect(s) assesse Growth in # of plants or fronds

>> LOEC Precision > **>> LOEC** 280 **>> Unit used** mg/L

>> LOEC Concentration Type Nominal

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> LOEC Effect(s) assesse Not assessed

>> Response of Control Group (was it satisfactory? Unknown

>> Statistical results

The EC50 for Lemmna gibba plant growth was 4432 mg/l (95% confidence interval 845-8018), and for frond growth was 4816 mg/l (1635-7998). The EC50 for biomass (dry weight) was 5967 mg/l (1640-10,293).

Results Remark

* Note whether cells removed prior to measurement: Unclear. Plants and fronds were counted visually. Biomass was measured by dry weight of plants and fronds.
* Biological observations
  - Cell density at each flask at each measuring point: Not applicable.
  - Growth curves: Not shown.
* Percent biomass/growth rate inhibition per concentration
  Observations: Results were not given for each of the 21 concentrations.

Conclusions

Of eight materials tested in this study, ethanol was the least toxic to Lemna, next to acetone. Confidence intervals for EC50's used inverse estimation and are wider than standard confidence intervals.

Data Quality

Reliability Highly reliable

Data Reliability Remarks

An unusually large number of concentrations of ethanol were tested, ranging over four orders of magnitude. Each concentration was tested in triplicate. The method followed (with one exception, the length of the test) was that given by EPA as described in 1986 and 1982.

Reference

>> Remarks

Cowgill, U., Milazzo, D., and Landenberger, B. (1991). The sensitivity of Lemna gibba G-3 and four clones of Lemna minor to eight common chemicals using a 7-day test. Res. J. Water Pollut. Control Fed. 63:991-998.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/28/2000

Test Substance

Remarks: 100% absolute ethanol, dehydrated, USP

Chemical Category

Method

>> Method/Guideline followed

EPA procedures as described by Holst (1986) and Holst and Ellwanger (1982).

>> Test Type

static

>> GLP Unknown

>> Year study performed 1991

>> Species

Lemna minor 6591 (duckweed)

>> End Point Biomass (dry wt.) and growth (# of plants/fronds).

>> Analytical monitoring None

>> Exposure period 7 days

>> Statistical Method EC50: regression analysis. NOEL: Dunnett's t-test.

Remarks for Method

* Test organisms
- Laboratory culture: Obtained from the Geobotanisches Institut in Zurich, Switzerland.
- Method of cultivation: Maintained at 25 deg. C +/- 2 deg, with 5385 +/- 323 lux continuously. Medium was revised Hoagland's with a pH of 4.6-5.4. Medium was renewed weekly. The acclimation period was 8 weeks.
- Controls: Controls containing medium and Lemna but no ethanol were used.

* Test Conditions
- Test temperature range: 25 deg. C +/- 2.

- Growth/test medium chemistry (hardness, alkalinity, pH, TOC, TSS, dissolved oxygen, salinity, EDTA): Hardness: 636 mg/l as CaCO3. Alkalinity: 23 mg/l as CaCO3. Conductivity: 5000 micromhos/cm. pH ranged from 4.5-5.1.
- Dilution water source: Not specified.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): 250-ml vessels; Shimadzu closures covered with paraffin. Each concentration and control was replicated three times.
- Water chemistry in test (pH) in at least one replicate of each concentration (at start and end of the test): Range over exposure period was 4.6-5.1.
- Stock solutions preparation (vehicle, solvent, concentrations): Not described.
- Light levels and quality during exposure: Mean lux 5382 +/- 89 during the exposure period.

* Test design (number of replicates, concentrations): 21 concentrations, ranging from 1.0 to 21,000 mg/l, plus control. Each concentration and control was repeated three times.

* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Only nominal concentrations were used.

Results

>> Nominal concentration	0, 1.0, 1.7, 2.8, 4.7, 7.8, 13, 21, 36 . . . 21000
>> Measured concentration	Not measured
>> Precision	=
>> Endpoint Type	ErC50
>> Endpoint Value	3690
>> Unit used	mg/L
>> Concentration Type	Nominal
>> Endpoint Time	168
>> NOEC Precision	=
>> NOEC	778
>> Unit used	mg/L
>> NOEC Concentration Type	Nominal
>> NOEC Effect(s) assesse	Growth in # of plants or fronds
>> LOEC Precision	>
>> LOEC	778
>> Unit used	mg/L
>> LOEC Concentration Type	Nominal

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> LOEC Effect(s) assesse Not assessed

>> Response of Control Group (was it satisfactory? Unknown

>> Statistical results

The EC50 for plant growth was 3,690 mg/l (95% confidence interval (81-167,764), and for frond growth was 4,875 mg/l (1,645-8,105). The EC50 for biomass (dry weight) was 6,986 mg/l (3,155-10,817).

Results Remark

* Note whether cells removed prior to measurement: Unclear. Plants and fronds were counted visually. Biomass was measured by dry weight of plants and fronds.
* Biological observations
  - Cell density at each flask at each measuring point: Not applicable.
  - Growth curves: Not shown.
* Percent biomass/growth rate inhibition per concentration
  Observations: Results were not given for each of the 21 concentrations.

Conclusions

Of eight materials tested in this study, ethanol was the least toxic to Lemna, next to acetone. Confidence intervals for EC50's used inverse estimation and are wider than standard confidence intervals. Three other clones of Lemna minor were also tested in this experiment (7101, 7120, and 7136). Clones 7120 and 7136 were generally much more resistant to the effects of ethanol, with EC50's of at least 10,000 mg/l, and NOELs of at least 1000 mg/l.

Data Quality

Reliability Highly reliable

Data Reliability Remarks

An unusually large number of concentrations of ethanol were tested, ranging over four orders of magnitude. Each concentration was tested in triplicate. The method followed (with one exception, the length of the test) was that give by EPA as described in 1986 and 1982.

Reference

>> Remarks

Cowgill, U., Milazzo, D., and Landenberger, B. (1991). The sensitivity of Lemna gibba G-3 and four clones of Lemna minor to eight common chemicals using a 7-day test. Res. J. Water Pollut. Control Fed. 63:991-998.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/28/2000

Test Substance

Remarks: 100% absolute, dehydrated, USP

Chemical Category

Method

>> Method/Guideline followed

Growth inhibition in Skeletonema

>> Test Type

static

>> GLP Unknown

>> Year study performed 1989

>> Species

Skeletonema costatum

>> End Point cell number and volume: by Coulter counter

>> Analytical monitoring none

>> Exposure period 5 days

>> Statistical Method Not described

Remarks for Method

* Test organisms
- Laboratory culture: Obtained from the Bigelow Laboratory for Ocean Sciences in West Boothbay Harbor, Maine.
- Method of cultivation: Cultured in revised ASP12 medium at 20 deg. C +/- 2, with 14 hr of light at 4,304 lux +/- 161 per day. Agitated daily and transferred every 7 days. Acclimated for 4 weeks.
- Controls: Controls consisting of Skeletonema in medium without ethanol were used.

* Test Conditions
- Test temperature range: 19.5-20.6 deg. C.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

- Growth/test medium chemistry (hardness, alkalinity, pH, TOC, TSS, dissolved oxygen, salinity, EDTA): Not described.
- Dilution water source: Not described.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): 100-ml vessels, covered with Parafilm. Each concentration and control was tested in triplicate.
- Water chemistry in test (pH) in at least one replicate of each concentration (at start and end of the test): Range was 7.7-9.0.
- Stock solutions preparation (vehicle, solvent, concentrations): Prepared with double-distilled, sterile water.
- Light levels and quality during exposure: Mean lux 4304 +/- 8.2 with a 14 h light/10 h dark cycle.

* Test design (number of replicates, concentrations): Five or more concentrations, plus control, each repeated three times.

* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Only nominal concentrations were used.

Results

>> Nominal concentration	Not listed
>> Measured concentration	Not measured
>> Precision	=
>> Endpoint Type	ErC50
>> Endpoint Value	11619
>> Unit used	mg/L
>> Concentration Type	Nominal
>> Endpoint Time	120
>> NOEC Precision	=
>> NOEC	5400
>> Unit used	mg/L
>> NOEC Concentration Type	Nominal
>> NOEC Effect(s) assesse	Total cell count
>> LOEC Precision	>
>> LOEC	5400
>> Unit used	mg/L
>> LOEC Concentration Type	Nominal

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> LOEC Effect(s) assesse Not assessed

>> Response of Control Group (was it satisfactory? Unknown

>> Statistical results

The EC50's for total cell count and total cell volume, and their 95% confidence intervals, are: 11,619 mg/l (7923-15,314) and 10,943 mg/l (7061-14,826), respectively.

Results Remark

* Note whether cells removed prior to measurement: Not stated.
* Biological observations
  - Cell density at each flask at each measuring point: Not given.
  - Growth curves: Not given. However, growth was stimulated before inhibition began.
* Percent biomass/growth rate inhibition per concentration
  Observations: Not given.

Conclusions

The authors state that, using EPA criteria, ethanol can be judged "practically nontoxic" by this test. Ethanol was a carbon source for Skeletonema, stimulating growth before inhibition began at higher concentrations.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Cowgill, U., Milazzo, D., and Landenberger, B. (1989). Toxicity of nine benchmark chemicals to Skeletonema costatum, a marine diatom. Environ. Toxicol. Chem. 8:451-455.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

Revision Date: 12/05/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Growth inhibition in Dunaliella

>> Test Type

static

>> GLP Unknown

>> Year study performed 1988

>> Species

Dunaliella bioculata

>> End Point Growth rate: optical density at 48 hours

>> Analytical monitoring Not discussed

>> Exposure period 48 hours

>> Statistical Method Not discussed

Remarks for Method

* Test organisms: Bacteria-free Dunaliella bioculata from the University of Gottingen, Germany.
- Laboratory culture: A 200-ml culture was prepared by inoculating media, incubating at 24 deg. C under continuous light (30 microE/m^2-sec). When optical density at 600 nm reached 0.6, a sample was transferred to start 600 ml of main culture. In the large cultures, air containing 5% CO2 was bubbled through.
- Method of cultivation: As above. In tests, flasks were shaken continuously at 120 rpm.
- Controls: Untreated controls were used.

* Test Conditions

- Test temperature range: 24 deg. C.
- Growth/test medium chemistry (hardness, alkalinity, pH, TOC, TSS, dissolved oxygen, salinity, EDTA): The media formulation is given, but not these parameters.
- Dilution water source: Not discussed. All media were autoclaved.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): 100-ml flasks.
- Water chemistry in test (pH) in at least one replicate of each concentration (at start and end of the test): Not discussed.
- Stock solutions preparation (vehicle, solvent, concentrations): Not discussed.
- Light levels and quality during exposure: Continuous illumination at 30 microE/(m^2-sec).

* Test design (number of replicates, concentrations): Not discussed.

* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Not discussed.

Results

>> Nominal concentration 500, 1,000 mg/l

>> Measured concentration Not measured

>> Precision =

>> Endpoint Type EC10-CD

>> Endpoint Value 1000 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 48

>> NOEC Precision **>> NOEC** 0 **>> Unit used**

>> NOEC Concentration Type

>> NOEC Effect(s) assesse Not determined

>> LOEC Precision **>> LOEC** 0 **>> Unit used**

>> LOEC Concentration Type

>> LOEC Effect(s) assesse Not determined

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

>> Response of Control Group (was it satisfactory? Unknown

>> Statistical results

None given.

Results Remark

* Note whether cells removed prior to measurement: Not discussed
* Biological observations
  - Cell density at each flask at each measuring point: At 500 mg/l, 94% of control. At 1,000 mg/l, 91% of control.
  - Growth curves: Not shown.
* Percent biomass/growth rate inhibition per concentration: At 500 mg/l, 6% inhibition. At 1,000 mg/l, 9% inhibition.
  Observations: None reported.

Conclusions

This study examined the effects of several herbicides on Dunaliella, and secondarily examined the effects of some solvents and formulation components (including ethanol) sometimes included in the herbicide mixtures. Apparently, only two concentrations of ethanol were tested. Ethanol reduced growth of this alga by about 10% at a concentration of 0.1% (1,000 mg/l) after 48 hours. The NOEC and LOEC for ethanol were not determined.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Felix, H., Chollet, R., and Harr, J. (1988). Use of the cell wall-less alga Dunaliella bioculata in herbicide screening tests. Ann. Appl. Biol. 113:55-60.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

Revision Date: 01/02/2001

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Growth inhibition in Chlamydomonas

>> Test Type

semi-static

>> GLP Unknown

>> Year study performed 1980

>> Species

Chlamydomonas eugametos

>> End Point Growth rate (number of cells)

>> Analytical monitoring None

>> Exposure period 48 hr

>> Statistical Method Duncan's multiple range test

Remarks for Method

* Test organisms
- Laboratory culture: Bacteria-free Chlamydomonas eugametos (from Indiana culture collection No. 9).
- Method of cultivation: Stocks grown on agar slants; liquid cultures made 3-4 days before assay. Liquid cultures grown at 25 deg. C with continuous aeration and diurnal light cycle of 12 hr.
- Controls: Controls were used (and used as benchmarks for cell growth) but are not specifically discussed. Tests of ethanol and other solvents were controls for tests of herbicides dissolved in these solvents.

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Test Conditions
- Test temperature range: 25 deg. C.
- Growth/test medium chemistry (hardness, alkalinity, pH, TOC, TSS, dissolved oxygen, salinity, EDTA): Chemistry not described. Cultures grown in nutrient medium.
- Dilution water source: Not described.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): Parent cultures were 150 ml in 250-ml erlenmeyer flasks, aerated. For bioassays, 1 x 10^6 cells suspended in 20 ml nutrient medium were added to 50-ml flasks. These test cultures were not aerated. Tests were at least duplicated.
- Water chemistry in test (pH) in at least one replicate of each concentration (at start and end of the test): Not described.
- Stock solutions preparation (vehicle, solvent, concentrations): Not described.
- Light levels and quality during exposure: Assumed to be the same as for parent cultures: 12-hr diurnal cycle at 200 microEm^2/s PPFD.

* Test design (number of replicates, concentrations): Solvents (including ethanol) were tested at four concentrations; each concentration was tested at least twice.

* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Not described. Nominal concentrations likely used.

Results

>> Nominal concentration 0.5, 1.0. 2.5, 5.0 % v/v

>> Measured concentration Not measured.

>> Precision <

>> Endpoint Type EC50-CD

>> Endpoint Value 2 **>> Unit used** % v/v

>> Concentration Type Nominal **>> Endpoint Time** 48

>> NOEC Precision = **>> NOEC** 1 **>> Unit used** % v/v

>> NOEC Concentration Type Nominal

>> NOEC Effect(s) assesse Increase in cell number

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> LOEC Precision = **>> LOEC** 2 **>> Unit used** % v/v

>> LOEC Concentration Type Nominal

>> LOEC Effect(s) assesse Increase in cell number

>> Response of Control Group (was it satisfactory? Unknown

>> Statistical results

A statistically significant inhibition of growth in cell number occurred at 2.5 % v/v ethanol ($p<0.05$).

Results Remark

* Note whether cells removed prior to measurement: Before counting, 5% glutaraldehyde was added to test systems. One-ml samples were analyzed with a hemocytometer or Coulter counter.
* Biological observations
  - Cell density at each flask at each measuring point: Absolute measurements were not given.
  - Growth curves: Not given.
* Percent biomass/growth rate inhibition per concentration: No inhibition at ethanol concentrations of 0.5 or 1.0 %. At 2.5%, cell number was 57% of control. At 5.0%, growth was completely inhibited. Observations: None described.

Conclusions

This paper describes the development of a algal bioassay for testing herbicides. Ethanol and other solvents were tested as controls for solvent effects on herbicides. Growth inhibition by ethanol in this 48-hour test began at concentrations between 1.0 and 2.5% v/v and was complete by 5%.

Data Quality

Reliability

Data Reliability Remarks

Reference

EPA High Production Volume (HPV) Track

Ecotoxicity End Point :
Toxicity to Aquatic Plants

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> Remarks

Hess, F. (1980). A Chlamydomonas algal bioassay for detecting growth inhibitor herbicides. Weed Sci. 28(5):515-520.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 02/23/2001

Test Substance

Remarks: USP-grade, 95% ethanol

Chemical Category

Method

>> Method/Guideline followed

Acute toxicity in Daphnia

>> Test Type

static

>> GLP Unknown

>> Year study performed 1981

>> Species

Daphnia pulex

>> Analytical monitoring No monitoring: defined volumes of EtOH added.

>> Exposure period 18 hr

>> Statistical Method Probit

Remarks for Method

* Test organisms
- Source, supplier, any pretreatment, breeding method: Captured from a nearby pond; maintained on an enriched broth and fed yeast every other day.
- Age at study initiation: Organisms less than 24 hours old were used.
- Control group: None mentioned.

* Test conditions
- Stock solutions preparation (vehicle, solvent, concentrations) and stability: Not discussed.
- Test temperature range: 23 deg. C. +/- 1 deg.

Results

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): 50-ml culture tubes were used, containing a total volume of 25 ml test medium. Tubes were loosely capped, and not aerated. Each concentration was tested in duplicate.
- Dilution water source: Aerated, deionized deep well water.
- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio): Not measured.
- Lighting (quality, intensity and periodicity): 1 hr of typical fluorescent illumination, 15.5 hr at 10% normal illumination, then 1.5 hr typical illumination.
- Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed: Not measured.

* Endpoints assessed (i.e. immobilization): Organisms were considered dead if they did not move after being swirled under a light.
* Test design (number of replicates, individuals per replicate, concentrations): Ten organisms per tube, two tubes per concentration, at least four concentrations of ethanol.
* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Not described.

>> Nominal concentration Range from 1% v/v to 2% v/v according to graph

>> Measured concentration Not measured

>> Precision =

>> Endpoint Type LC50

>> Endpoint Value 2 **>> Unit used** % v/v

>> Concentration Type Nominal **>> Endpoint Time** 18

>> Statistical results

p value not given. 95% confidence interval is 1.17-1.80 % v/v

Results Remark

* Biological observations
- Number immobilized as compared to the number exposed: Mortality ranged from 0 to 100%.
- Concentration response with 95% confidence limits: LC50 (confidence interval): 1.53 % v/v (1.17-1.80)
- Cumulative immobilization: Not discussed.
- Was control response satisfactory (yes/no/unknown): Unknown.

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Conclusions

Ethanol was more toxic than dimethylsulfoxide but less toxic than acetonitrile or acetone in this static LC50 determination using the water flea Daphnia pulex. The 18-hr LC50 for ethanol was 1.53 %v/v.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Bowman, M., Oller, W., and Cairns, T. (1981). Stressed bioassay systems for rapid screening of pesticide residues: Part 1: Evaluation of bioassay systems. Arch. Environ. Contam. Toxicol. 10:9-24.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/10/2000

Test Substance

Remarks: USP-grade, 95% ethanol

Chemical Category

Method

>> Method/Guideline followed

Acute toxicity in Hyalella

>> Test Type

static

>> GLP Unknown

>> Year study performed 1981

>> Species

Hyalella azteca

>> Analytical monitoring No monitoring: defined volumes of EtOH added.

>> Exposure period 18 hr

>> Statistical Method Probit

Remarks for Method

* Test organisms
- source, supplier, any pretreatment, breeding method: Captured from a nearby slough; maintained in aquaria with added aerated water and aeration.
- Age at study initiation: Used juveniles with 14-16 antenna segments.
- Control group: None mentioned.

* Test conditions
- Stock solutions preparation (vehicle, solvent, concentrations) and stability: Not discussed.
- Test temperature range: 23 deg. C. +/1 1 deg.

Results

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): 400-ml beakers were used, containing a total volume of 100 ml test medium. Beakers were covered with aluminum foil. Each concentration was tested in duplicate.
- Dilution water source: Aerated, deionized deep well water.
- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio): Not measured.
- Lighting (quality, intensity and periodicity): 1 hr of typical fluorescent illumination, 15.5 hr at 10% normal illumination, the 1.5 hr typical illumination.
- Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed: Not measured.

* Endpoints assessed (i.e. immobilization): Organisms were considered dead if they did not move in response to light, sound vibration, or gentle probing.
* Test design (number of replicates, individuals per replicate, concentrations): Ten organisms per beaker, two beakers per concentration, at least five concentrations of ethanol.
* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Not described.

>> Nominal concentration Range from about 0.8 to 2% v/v according to graph

>> Measured concentration Not measured

>> Precision =

>> Endpoint Type LC50

>> Endpoint Value 1 **>> Unit used** % v/v

>> Concentration Type Nominal **>> Endpoint Time** 18

>> Statistical results

p value not given. 95% confidence interval is 0.761-1.28 % v/v

Results Remark

* Biological observations
- Number immobilized as compared to the number exposed: Mortality ranged from 20 to 100%.
- Concentration response with 95% confidence limits: LC50 (confidence interval): 1.04 % v/v (0.761-1.28 % v/v)
- Cumulative immobilization: Not discussed.

- Was control response satisfactory (yes/no/unknown): Unknown.

Conclusions

Ethanol was more toxic than dimethylsulfoxide and methanol in this static LC50 determination using the scud Hyalella, but less toxic than acetonitrile and acetone. The 18-hr LC50 for ethanol was 1.04 %v/v.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Bowman, M., Oller, W., and Cairns, T. (1981). Stressed bioassay systems for rapid screening of pesticide residues: Part 1: Evaluation of bioassay systems. Arch. Environ. Contam. Toxicol. 10:9-24.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/10/2000

Test Substance

Remarks: USP-grade, 95% ethanol

Chemical Category

Method

>> Method/Guideline followed

Acute toxicity in Palaemonetes

>> Test Type

static

>> GLP Unknown

>> Year study performed 1981

>> Species

Palaemonetes kadiakensis

>> Analytical monitoring No monitoring: defined volumes of EtOH added.

>> Exposure period 18 hr

>> Statistical Method Probit

Remarks for Method

* Test organisms
- Source, supplier, any pretreatment, breeding method: Captured from a nearby lake; maintained in aquaria with aerated water.
- Age at study initiation: Juvenile organisms were used.
- Control group: None mentioned.

* Test conditions
- Stock solutions preparation (vehicle, solvent, concentrations) and stability: Not discussed.
- Test temperature range: 23 deg. C +/- 1 deg.

Results

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): 2-l beakers were used, containing a total volume of 100 ml test medium. Each concentration was tested in duplicate.
- Dilution water source: Aerated, deionized deep well water.
- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio): Not measured.
- Lighting (quality, intensity and periodicity): 1 hr of typical fluorescent illumination, 15.5 hr at 10% normal illumination, then 1.5 hr typical illumination.
- Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed: Not measured.

* Endpoints assessed (i.e. immobilization): Organisms were considered dead if they did not move in response to light, sound vibration, or gentle probing.
* Test design (number of replicates, individuals per replicate, concentrations): Five organisms per beaker, two beakers per concentration, at least five concentrations of ethanol.
* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Not described.

>> Nominal concentration Range from about 1% v/v to 1.5 % v/v, per graph

>> Measured concentration Not measured

>> Precision =

>> Endpoint Type LC50

>> Endpoint Value 1 **>> Unit used** % v/v

>> Concentration Type Nominal **>> Endpoint Time** 18

>> Statistical results

p value not given. 95% confidence interval is 1.18-1.38% v/v

Results Remark

* Biological observations
- Number immobilized as compared to the number exposed: Mortality ranged from 0 to 100%.
- Concentration response with 95% confidence limits : LC50 (confidence interval): 1.28 % v/v (1.18-1.38)
- Cumulative immobilization: Not discussed.
- Was control response satisfactory (yes/no/unknown): Unknown.

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Conclusions

Ethanol was more toxic than dimethylsulfoxide and methanol to Palaemonetes in this static LC50 test, but less toxic than acetone or acetonitrile. The LC50 for ethanol was 1.28 %v/v.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Bowman, M., Oller, W., and Cairns, T. (1981). Stressed bioassay systems for rapid screening of pesticide residues: Part 1: Evaluation of bioassay systems. Arch. Environ. Contam. Toxicol. 10:9-24.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/10/2000

Test Substance

Remarks: Ethanol, obtained from Merck.

Chemical Category

Method

>> Method/Guideline followed

Acute toxicity in Artemia

>> Test Type

static

>> GLP Unknown

>> Year study performed 1994

>> Species

Artemia salina

>> Analytical monitoring No monitoring; defined volumes of EtOH added

>> Exposure period 24 hr

>> Statistical Method Litchfield and Wilcoxon

Remarks for Method

* Test organisms
- Source, supplier, any pretreatment, breeding method: Dry eggs purchased from San Francisco Bay Brand were hydrated in distilled water to release cysts. Cysts were incubated in synthetic sea water for 24 hours at 25 deg. C with continuous side illumination and slight aeration.
- Age at study initiation: 24-hour-old nauplius larvae.
- Control group: Appropriate controls were used (test systems without ethanol) but not described.

Results

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Test conditions
- Stock solutions preparation (vehicle, solvent, concentrations) and stability: Ethanol was not described. Synthetic seawater was prepared using 35% Synthetica sea salt and distilled, deionized water.
- Test temperature range: 25 deg. C.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): Plastic 16-mm petri dishes.
- Dilution water source: See above.
- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio): Not described.
- Lighting (quality, intensity and periodicity): Larvae were incubated with ethanol in the dark.
- Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed: Not discussed.

* Endpoints assessed (i.e. immobilization): Organisms were considered dead if they did not move during 10 seconds of observation.
* Test design (number of replicates, individuals per replicate, concentrations): Ten larvae per dish, three to five replicates per concentration per experiment, experiment repeated five times. Concentration range not given.
* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Nominal concentrations only.

>> Nominal concentration Concentrations not stated

>> Measured concentration Concentrations not stated

>> Precision =

>> Endpoint Type LC50

>> Endpoint Value 1833 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 24

>> Statistical results

p value not given. 95% confidence interval is 1,325-2,538 mg/L.

Results Remark

* Biological observations
- Number immobilized as compared to the number exposed: Not discussed.
- Concentration response with 95% confidence limits: LC50 (confidence interval) 1,834 mg/L (1,324-2,538)
- Cumulative immobilization: Not discussed.
- Was control response satisfactory (yes/no/unknown): Unknown

Conclusions

Ethanol (LC50, 1,833 mg/L) was less toxic to 24-hour-old brine shrimp larvae in this static 24-hour test than acetonitrile or methanol, but more toxic than dimethylsulfoxide. Larvae of different ages displayed differing sensitivities to ethanol, as described in other study summaries.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Barahona-Gomariz, M., Sanz-Barrera, F., and Sanchez-Fortun, S. (1994). Acute toxicity of organic solvents on Artemia salina. Bull. Environ. Contam. Toxicol. 52:766-771.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/10/2000

Test Substance

Remarks: Ethanol, obtained from Merck.

Chemical Category

Method

>> Method/Guideline followed

Acute toxicity in Artemia

>> Test Type

static

>> GLP Unknown

>> Year study performed 1994

>> Species

Artemia salina

>> Analytical monitoring No monitoring: defined volumes of EtOH added

>> Exposure period 24 hr

>> Statistical Method Litchfield and Wilcoxon

Remarks for Method

* Test organisms
- Source, supplier, any pretreatment, breeding method: Dry eggs purchased from San Francisco Bay Brand were hydrated in distilled water to release cysts. Cysts were incubated in synthetic sea water for 24 hours at 25 deg. C. with continuous side illumination and slight aeration.
- Age at study initiation: 48-hour-old nauplius larvae.
- Control group: Appropriate controls were used (tests systems without ethanol) but not described.

Results

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Test conditions
- Stock solutions preparation (vehicle, solvent, concentrations) and stability: Ethanol was not described. Synthetic sea water was prepared using 35% Synthetica sea salt and distilled, deionized water.
- Test temperature range: 25 deg. C.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): Plastic 16-mm petri dishes.
- Dilution water source: See above.
- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio): Not described.
- Lighting (quality, intensity and periodicity): Larvae were incubated with ethanol in the dark.
- Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed: Not discussed.

* Endpoints assessed (i.e. immobilization): Organisms were considered dead if they did not move during 10 seconds of observation.
* Test design (number of replicates, individuals per replicate, concentrations): Ten larvae per dish, three to five replicates per concentration per experiment, experiment repeated five times. Concentration range not given.
* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Nominal concentrations only.

>> Nominal concentration Concentrations not stated

>> Measured concentration Concentrations not stated

>> Precision =

>> Endpoint Type LC50

>> Endpoint Value 858 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 24

>> Statistical results

p value not given. 95% confidence interval is 726-1,014 mg/L.

Results Remark

* Biological observations
- Number immobilized as compared to the number exposed: Not discussed.
- Concentration response with 95% confidence limits: LC50 (confidence interval) 858 mg/L (726-1,014)
- Cumulative immobilization: Not discussed.
- Was control response satisfactory (yes/no/unknown): Unknown

Conclusions

Ethanol (LC50, 858 mg/L) was less toxic to 48-hour-old brine shrimp larvae in this static 24-hour test than acetonitrile, but more toxic than methanol or dimethylsulfoxide. Larvae of different ages displayed differing sensitivities to ethanol, as described in other study summaries.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Barahona-Gomariz, M., Sanz-Barrera, F., and Sanchez-Fortun, S. (1994). Acute toxicity of organic solvents on Artemia salina. Bull. Environ. Contam. Toxicol. 52:766-771.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/10/2000

Test Substance

Remarks: Ethanol, obtained from Merck.

Chemical Category

Method

>> Method/Guideline followed

Acute toxicity in Artemia

>> Test Type

static

>> GLP Unknown

>> Year study performed 1994

>> Species

Artemia salina

>> Analytical monitoring No monitoring: defined volumes of EtOH added

>> Exposure period 24 hr

>> Statistical Method Litchfield and Wilcoxon

Remarks for Method

* Test organisms
- Source, supplier, any pretreatment, breeding method: Dry eggs purchased from San Francisco Bay Brand were hydrated in distilled water to release cysts. Cysts were incubated in synthetic sea water for 24 hours at 25 deg. C with continuous side illumination and slight aeration.
- Age at study initiation: 72-hour-old nauplius larvae.
- Control group: Appropriate controls were used (test systems without ethanol) but not described.

Results

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Test conditions
- Stock solutions preparation (vehicle, solvent, concentrations) and stability: Ethanol was not described. Synthetic sea water was prepared using 35% Synthetica sea salt and distilled, deionized water.
- Test temperature range: 25 deg. C.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): Plastic 16-mm petri dishes.
- Dilution water source: See above.
- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio): Not described.
- Lighting (quality, intensity and periodicity): Larvae were incubated with ethanol in the dark.
- Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed: Not discussed.

* Endpoints assessed (i.e. immobilization): Organisms were considered dead if they did not move during 10 seconds of observation.
* Test design (number of replicates, individuals per replicate, concentrations): Ten larvae per dish, three to five replicates per concentration per experiment, experiment repeated five times. Concentration range not given.
* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Nominal concentrations only.

>> Nominal concentration Concentration not stated

>> Measured concentration Concentration not stated

>> Precision =

>> Endpoint Type LC50

>> Endpoint Value 695 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 24

>> Statistical results

p value not given. 95% confidence interval is 589-821 mg/L.

Results Remark

* Biological observations
- Number immobilized as compared to the number exposed: Not discussed.
- Concentration response with 95% confidence limits: LC50 (confidence interval) 695 mg/L (589-821)
- Cumulative immobilization: Not discussed.
- Was control response satisfactory (yes/no/unknown): Unknown

Conclusions

Ethanol (LC50, 695 mg/L) was less toxic to 72-hour-old brine shrimp larvae in this static 24-hour test than acetonitrile, but more toxic than methanol or dimethylsulfoxide. 72-hour-old larvae were more sensitive to ethanol than younger larvae.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Barahona-Gomariz, M., Sanz-Barrera, F., and Sanchez-Fortun, S. (1994). Acute toxicity of organic solvents on Artemia salina. Bull. Environ. Contam. Toxicol. 52:766-771.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/10/2000

Test Substance

Remarks: Absolute ethanol (dehydrated, USP)

Chemical Category

Method

>> Method/Guideline followed

ASTM

>> Test Type

static

>> GLP Unknown

>> Year study performed 1984

>> Species

Daphnia magna

>> Analytical monitoring None

>> Exposure period 48 hr

>> Statistical Method Thompson method of moving averages

Remarks for Method

* Test organisms
- Source, supplier, any pretreatment, breeding method: Source not specified. Daphnia stocks had been maintained in adjusted, autoclaved, aerated Lake Huron water for three years before the study began. Neonates hatched by isolated gravid females were gathered by sieving.
- Age at study initiation: Neonates.
- Control group: Dilution water controls were included.

Results

* Test conditions
- Stock solutions preparation (vehicle, solvent, concentrations) and stability: Ethanol not

discussed.
- Test temperature range: 20 deg. C.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): Covered beakers, not aerated; triplicates for each concentration.
- Dilution water source: Lake Huron.
- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio): Detailed data are given. Hardness: 160 mg/L as CaCO3. pH: 8.0. TOC: 5,520 ug/L. TDS: 289,550 ug/L. Ca/Mg: 5.7. Na/K: 4.5.
- Lighting (quality, intensity and periodicity): 1916 lux +/- 75; 16 hr light, 8 hr dark.
- Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed: Test conditions: DO 7.6-8.9 mg/L. pH 7.8-8.4.

* Endpoints assessed (i.e. immobilization): Mortality assessed microscopically.
* Test design (number of replicates, individuals per replicate, concentrations): 10 individuals/test, three replicates per concentration. Number of concentrations not specified.
* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Not discussed. Geometric means of LC50s were determined.

>> Nominal concentration Concentrations not given

>> Measured concentration Concentrations not given

>> Precision =

>> Endpoint Type LC50

>> Endpoint Value 12340 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 48

>> Statistical results

p value not given. 95% confidence interval for geometric mean LC50: 11,065-13,948 mg/L

Results Remark

* Biological observations
- Number immobilized as compared to the number exposed: Not discussed.
- Concentration response with 95% confidence limits: LC50 (confidence interval) 12,340 mg/L (11,065-13,948)
- Cumulative immobilization: Not discussed.
- Was control response satisfactory (yes/no/unknown): Unknown

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Conclusions

The 48-hour LC50 for ethanol towards Daphnia magna was 12,340 mg/L at 20 deg. C. The experiment was repeated at 24 deg. C, yielding an LC50 that was not statistically different (12,318 mg/L). The ASTM method for acute toxicity testing of 1980 was used.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Takahashi, I., Cowgill, U., and Murphy, P. (1987). Comparison of ethanol toxicity to Daphnia magna and Ceriodaphnia dubia tested at two different temperatures: static acute toxicity test results. Bull. Environ. Contam. Toxicol. 39:229-236.

Similar results were obtained by Kuhn, R., Pattard, M., Pernakk, K. and Winter, A. (1989). Wat. Res. 23(4):495-499. In that test, the 24- and 48-hour EC50s (based on ability to swim) for ethanol toward Daphnia magna were >10,000 mg/L.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Aquatic Invertebrates

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	8
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/13/2000

Test Substance

Remarks: Absolute ethanol (dehydratd, USP)

Chemical Category

Method

>> Method/Guideline followed

ASTM

>> Test Type

static

>> GLP Unknown

>> Year study performed 1984

>> Species

Ceriodaphnia dubia

>> Analytical monitoring None

>> Exposure period 48 hr

>> Statistical Method Thompson method of moving averages

Remarks for Method

* Test organisms
- Source, supplier, any pretreatment, breeding method: Source not specified. Organisms were mass cultured and acclimated to temperature for at least 10 weeks, and maintained in filtered, autoclaved Lake Huron water. Neonates hatched by isolated gravid females were gathered by sieving.
- Age at study initiation: Neonates.
- Control group: Dilution water controls were included.

* Test conditions

Results

- Stock solutions preparation (vehicle, solvent, concentrations) and stability: Ethanol not discussed.
- Test temperature range: 24 deg. C.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): Covered vials, not aerated; triplicates for each concentration.
- Dilution water source: Lake Huron.
- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio): Detailed data are given. Hardness: 90 mg/L as CaCO3. Alkalinity: 70 mg CaCO3/L. pH: 8.8. TOC:5,280 ug/L. TDS: 140,000 ug/L. Ca/Mg: 2.8. Na/K: 4.3.
- Lighting (quality, intensity and periodicity): 646 lux +/- 85; 16 hr light, 8 hr dark.
- Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed: Test conditions: DO 8.4-10.3 mg/L +/- 0.2. pH 8.2-8.4.

* Endpoints assessed (i.e. immobilization) : Mortality assessed microscopically.
* Test design (number of replicates, individuals per replicate, concentrations): 10 individuals/test, three replicates per concentration. Number of concentrations not specified.
* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Not discussed. Geometric means of LC50s were determined.

>> Nominal concentration Concentrations not given

>> Measured concentration concentrations not given

>> Precision =

>> Endpoint Type LC50

>> Endpoint Value 5012 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 48

>> Statistical results

p value not given. 95% confidence interval for geometric mean LC50: 4,233-5,913 mg/L

Results Remark

* Biological observations
- Number immobilized as compared to the number exposed: Not discussed.
- Concentration response with 95% confidence limits: LC50 (confidence interval) 5,012 mg/L (4,233-5,913).
- Cumulative immobilization: Not discussed.
- Was control response satisfactory (yes/no/unknown): Unknown.

Conclusions

The 48-hour LC50 for ethanol toward Ceriodaphnia dubia was 5,012 mg/L at 24 deg. C. The experiment was repeated at 20 deg. C., yielding an LC50 of 6,492 mg/L, which differed with statistical significance from the LC50 at 24 deg. C. The ASTM method for acute toxicity testing of 1980 was used.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Takahashi, I., Cowgill, U., and Murphy, P. (1987). Comparison of ethanol toxicity to Daphnia magna and Ceriodaphnia dubia tested at two different temperatures: static acute toxicity test results. Bull. Environ. Contam. Toxicol. 39:229-236.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Fish

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date
02/23/2001

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Acute lethality in trout

>> Test Type

flow-through

>> GLP Unknown

>> Year study performed 1978

>> Species

Salmo gairdneri

>> Analytical monitoring Not described

>> Exposure period 24 hr

>> Statistical Method Litchfield (1949) and APHA (1971)

Remarks for Method

* Parameters about organism:
 - age: Fingerlings.
 - length: 9.2 cm +/- 1.1
 - weight: 9.5 g +/- 3.8
 - loading: One fish/liter.
 - pretreatment: Acclimated for at least two weeks to temperature and light:dark pattern.
* Parameters of Test system, e.g.:
 - Dilution water source: Dechlorinated city tap water.
 - Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity): $CaCO_3$, 90 mg/l.

Conductivity, 190 uS/cm. pH, 8.0.
- Stock and test solution and how they are prepared: Not described.
- Flow-through rate: In holding tanks, 95% replacement time of 17 hr.
- Vehicle/solvent and concentrations: None besides water.
- Stability of the test chemical solutions: Not described.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, lighting, # per treatment): Holding tanks were PET-lined, 20-l vessels. 12-hr light, 12-hr dark pattern.
- Number of replicates, fish per replicate: Ten fish/concentration.
- Water chemistry in test (D.O., pH) in the control and one concentration where effects were observed: Not described for particular test concentrations.

* Test temperature range: 10 deg. C +/- 0.5
* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Nominal concentrations were used.

Results

>> Nominal concentration Six concentrations, up to 30,000 mg/l

>> Measured concentration Nominal concentrations only

>> Precision =

>> Endpoint Type LC50

>> Endpoint Value 11200 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 24

>> Statistical results

Median survival time calculated using Litchfield (1949) and LC50 using graphical interpolation of APHA (1971). No p values given.

Results Remark

* Biological observations
* Table showing cumulative mortality: Not presented.
* Lowest test substance concentration causing 100% mortality: In static tests, 25,000 mg/l caused 100% mortality in 3 hr.
* Mortality of controls: Not discussed.
* Abnormal responses: Not discussed.

* Reference substances (if used) - results: None used. However, acetone was also tested and found to have a 24-hr LC50 of 6,100 mg/L.
* Any observations, such as precipitation that might cause a difference between measured and nominal values: None.

Conclusions

The LC50 for ethanol toward trout in this assay was 11,200 mg/L.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Majewski, H., Klaverkamp, J., and Scott, D. (1978). Acute lethality, and sub-lethal effects of acetone, ethanol, and propylene glycol on the cardiovascular and respiratory systems of rainbow trout (Salmo gairdneri). Water Res. 13:217-221.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Fish

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date
12/01/2000

Test Substance

Remarks: Reagent-grade ethanol

Chemical Category

Method

>> Method/Guideline followed

Acute lethality in minnows

>> Test Type

static

>> GLP Unknown

>> Year study performed 1986

>> Species

Pimephales promelas

>> Analytical monitoring None

>> Exposure period 96 hr

>> Statistical Method ASTM method: interpolation using log concentration

Remarks for Method

* Parameters about organism:
  - age: Juvenile.
  - length: Not specified.
  - weight: 0.2-0.5 g
  - loading: <0.5 g wet weight/liter.
  - pretreatment: Acclimated; food witheld for 24 hr before the start of test.
* Parameters of Test system, e.g.:
  - Dilution water source: Activated carbon-filtered, dechlorinated and tempered Lake Ontario industrial service water.

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Fish

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity): Hardness: 130 mg/l as CaCO3. Alkalinity: 93 mg/l as CaCO3. pH: 7.4. TOC: 1.8 mg/l. TSS: total dissolved solids, 180 mg/l. Salinity: 26 mg/l Cl-. Concentrations of metals and ions are also provided.
- Stock and test solution and how they are prepared: Soluble test chemicals, such as ethanol, were added directly to the test solutions.
- Flow-through rate: Not applicable.
- Vehicle/solvent and concentrations: Not applicable.
- Stability of the test chemical solutions: Not applicable.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, lighting, # per treatment): Seamless glass 30.5-cm cuboidal Pyrex chromatography jars, containing 20 l of test solution. Not sealed. Aerated if dissolved oxygen fell below 40% of the starting level, but whether this was needed was not stated. The surface of the water received 50 ft-c of cool-white fluorescent light, 16 h per day.
- Number of replicates, fish per replicate: 10 minnows/test concentration, one replicate each.
- Water chemistry in test (D.O., pH) in the control and one concentration where effects were observed: Parameter values during the test were not stated, but were measured daily in test and control vesses and corrected to pH 7.0 if necessary, or aerated in the DO fell below 40% of the starting value.

* Test temperature range: 20 deg. C +/- 0.1
* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Only nominal concentrations were used.

Results

>> Nominal concentration 0.1, 1, 10, 100 mg/l

>> Measured concentration Not measured

>> Precision >

>> Endpoint Type LC50

>> Endpoint Value 100 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 96

>> Statistical results

The LC50 was not achieved.

Results Remark

* Biological observations: Not discussed. Minnows were considered dead if they were motionless and failed to respond to prodding.
* Table showing cumulative mortality: None given.
* Lowest test substance concentration causing 100% mortality: 100% mortality not attained with the concentrations used.
* Mortality of controls: Not discussed.
* Abnormal responses: None mentioned.
* Reference substances (if used) - results : None; however, numerous other chemicals were tested in the same assay.
* Any observations, such as precipitation that might cause a difference between measured and nominal values: None.

Conclusions

The 96-hour LC50 for ethanol towards minnows is greater than 100 mg/l, the maximum concentration tested in this study. The investigation also demonstrated the feasibility of testing lethality towards several organisms simultaneously in the same chamber.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Ewell, W., Gorsuch, J., Kringle, R., et al. (1986). Simultaneous evaluation of the acute effects of chemicals on seven aquatic species. Environ. Toxicol. Chem. 5:831-840.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Fish

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date
12/06/2000

Test Substance

Remarks: Reagent-grade ethanol

Chemical Category

Method

>> Method/Guideline followed

Acute lethality in minnows, presumably using an EPA method.

>> Test Type

static

>> GLP Unknown

>> Year study performed 1974

>> Species

Pimephales promelas

>> Analytical monitoring None

>> Exposure period 96 hr

>> Statistical Method Standard graphical procedures

Remarks for Method

* Parameters about organism:
- age: Juveniles, 4-8 wks.
- length: 1.1-3.1 cm
- weight: Not stated.
- loading: In tests, 20 fish per jar in 2 l of test water.
- pretreatment: Acclimated for at least 48 hr in a holding trough with flowing water at 18-22 deg. C.

* Parameters of Test system, e.g.:
- Dilution water source: Lake Superior water.

- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity): Not stated.
- Stock and test solution and how they are prepared: Weighed amounts of ethanol were mixed in 4 l of Lake Superior water and shaken.
- Flow-through rate: Static tests only.
- Vehicle/solvent and concentrations: Not applicable.
- Stability of the test chemical solutions: Not measured.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, lighting, # per treatment): 3-l cylindrical glass battery jars containing 2 l of test water, maintained at 18-22 deg. C. Glass covers were placed over each jar. No aeration.
- Number of replicates, fish per replicate: 10 fish per concentration; two replicates per concentration.
- Water chemistry in test (D.O., pH) in the control and one concentration where effects were observed: Dissolved oxygen and pH were made at the beginning of and once or twice during the test, but the results are not given. However, dissolved oxygen was < or = 4 mg/l during at least some tests.

* Test temperature range: 18-22 deg. C.
* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Concentrations were not measured.

Results

>> Nominal concentration Not given.

>> Measured concentration Not measured: nominal concentrations only.

>> Precision =

>> Endpoint Type LC50

>> Endpoint Value 13480 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 96

>> Statistical results

Statistical results not given.

Results Remark

* Biological observations: Not given for ethanol specifically. In response to at least some test compounds, fish lost equilibrium.
* Table showing cumulative mortality: Not given.
* Lowest test substance concentration causing 100% mortality: Not stated.
* Mortality of controls: Not described.
* Abnormal responses: None mentioned.
* Reference substances (if used) - results: Not applicable.
* Any observations, such as precipitation that might cause a difference between measured and nominal values.: Not applicable.

Conclusions

The 96-hr LC50 for ethanol towards juveline fathead minnows in this static test was 13,480 mg/l. This result was said to be within 50% of LC50's previously reported. LC50's for shorter time periods were also calculated: For 1-hr, >18,000 mg/l. For 24-hr, >18,000 mg/l. For 48-hr, 13,480 mg/l. For 72-hr, 13,480 mg/l. Ethanol was the least lethal compound of the 26 organic chemicals tested in this lab.

Data Quality

Reliability Probably reliable

Data Reliability Remarks

These data were collected by the EPA's Environmental Research Lab in Duluth, Minnesota, a lab likely to have significant experience with acute toxicity testing of this kind.

Reference

>> Remarks

Mattson, V., Arthur, J., and Walbridge, C. (1976). Acute Toxicity of Selected Organic Compounds to Fathead Minnows. U.S. EPA Environmental Research Laboratory: Duluth, Minnesota. EPA 600/3-76-097.

General

EPA High Production Volume (HPV) Track

Ecotoxicity End Point:
Acute Toxicity to Fish

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date

Test Substance

12/06/2000

Remarks: Purity not stated, but LC50 is based on the active ingredient.

Chemical Category

Method

>> Method/Guideline followed

Acute lethality in trout

>> Test Type

static

>> GLP Unknown

>> Year study performed 1978

>> Species

Rainbow trout

>> Analytical monitoring Not discussed

>> Exposure period 96 hr

>> Statistical Method Litchfield and Wilcoxon (1949)

Remarks for Method

* Parameters about organism:
- age: Not stated; fingerlings.
- length: Not stated.
- weight: 0.8 g.
- loading: < or = 0.8 g/l.
- pretreatment: Acclimated to dilution water over a 1-3-day period.

* Parameters of Test system, e.g.:
- Dilution water source: Reconstituted deionized water containing reagent-grade chemicals.
- Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity): Hardness: 40-50 mg/l

as $CaCO_3$. Alkalinity: 30-35 mg/l. pH: 7.2-7.5. Other parameters not given.
- Stock and test solution and how they are prepared: Not described.
- Flow-through rate: Static tests.
- Vehicle/solvent and concentrations: Not relevant.
- Stability of the test chemical solutions: Not discussed.
- Exposure vessel type (e.g., size, headspace, sealed, aeration, lighting, # per treatment): 18.9-l wide-mouthed jars containing 15 l test solution. Not aerated.
- Number of replicates, fish per replicate: At least 10 fish per concentration; number of replicates not stated.
- Water chemistry in test (D.O., pH) in the control and one concentration where effects were observed: Not described.

* Test temperature range: 12 deg. C. +/- 1 deg.
* Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Not discussed.

Results

>> Nominal concentration Not given. At least six concentrations.

>> Measured concentration Not measured.

>> Precision =

>> Endpoint Type LC50

>> Endpoint Value 13000 **>> Unit used** mg/L

>> Concentration Type Nominal **>> Endpoint Time** 96

>> Statistical results

P-value not given. 95% confidence interval: 12,000-16,000 mg/l.

Results Remark

* Biological observations: Not described.
* Table showing cumulative mortality: Not given.
* Lowest test substance concentration causing 100% mortality: Not stated.
* Mortality of controls: Not discussed.
* Abnormal responses: None mentioned.
* Reference substances (if used) - results: Not applicable.

* Any observations, such as precipitation that might cause a difference between measured and nominal values.: Not discussed.

Conclusions

The Columbia National Fisheries Research Laboratory presents in this document results of tests of scores of chemicals conducted from 1965-1978. Results for ethanol are given in summary form only.

Data Quality

Reliability Highly reliable

Data Reliability Remarks

The Columbia National Fisheries Research Laboratory conducted aquatic toxicity tests of more than 400 chemicals during 1965-1978; this is a major research area for the Lab. The Lab also particiapted in the development of the standard acute toxicity test methodology. Only test meeting acceptable procedures were included in this compilation.

Reference

>> Remarks

Johnson, W. and Finley, M. (1980). Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. U.S. Dept. of Interior, Fish and Wildlife Service: Washington, DC. Resource Publication 137.

General

EPA High Production Volume (HPV) Track

Environmental Fate and Pathway End Point: Biodegradation

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 02/28/2001

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Biodegradation microcosms

>> Test Type

anaerobic

>> GLP Unknown

>> Year study performed 1993

>> Contact Time 30

>> Inoculum

Not stated

Remarks for Method

* Inoculum (concentration and source):
 - Other: Sediment and groundwater from a methanogenic portion of a shallow anoxic aquifer contaminated by landfill leachate.

* Concentration of test chemical, vehicle used, pre-acclimation conditions: 50 ppm C as ethanol. Ethanol was added to slurries of 50 g sediment and 75 ml groundwater in 160-ml bottles.
* Temperature of incubation °C: Room temperature.
* Dosing procedure: Not described.
* Sampling frequency: Not described. Ethanol concentrations do not appear to have been measured. At the end of incubation, methane formation, the indicator of ethanol consumption, was measured using gas chromatography with a flame ionization detector.
* Were appropriate controls and blank system used?: Yes, autoclaved controls were used.
* Analytical method used to measure biodegradation: Methane formation, measured by gas chromatography.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Method of calculating measured concentrations (i.e., arithmetic mean, geometric mean, etc.) Degradation rate was calculated as the mean of three tests.

Results

>> Precision =

>> Degradation Value 91

>> Upper value 0

>> Time Frame 30

>> Time Units Days

>> Breakdown products Yes

Results Remarks

* Lag time: The acclimation period was estimated as 25-30 days.
* Observed inhibition: Not discussed.
* Excessive biodegradation: Not discussed.
* Excessive standard deviation: Not discussed.
* Time required for 10% degradation: Not discussed. The degradation rate was calculated as 17.9 ppm C/day.
* Total degradation at the end of the test: 91% of theoretical methane production was recovered.

Conclusions

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Production of methane by ethanol-containing sediment was monitored by an automated pressure transducer system. The acclimation period was 25-30 days, and the rate of biodegradation was calculated to be 17.9 ppm C/day (s.d. 0.6). Total methane recovery was 91% of the theoretical limit. The actual incubation time (days during which methane was produced) was not stated.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Suflita, J. and Mormile, M. (1993). Anaerobic biodegradation of known and potential gasoline oxygenates in the terrestrial subsurface. Environ. Sci. Technol. 27:976-978.

The rapidity and completeness of ethanol biodegradation is supported by the work of Corseuil et al. (Wat. Res. 32(7):2065-2072, 1998) and by Yeh and Novak (Wat. Environ. Res. 66(5):744-752, 1994). Corseuil et al. assessed the influence of ethanol on degradation of BTX (benzene, toluene, and xylene) in aerobic and anaerobic microcosms. In the presence of BTX, ethanol was degraded preferentially in aerobic microcosms, with complete mineralization of 100 mg/l ethanol within 6 days. In various anaerobic microcosms, ethanol in the presence of BTX was completely degraded, but over incubation periods ranging from 3 days to more than 20 days. Yeh and Novak, studying the degradation of TBA (tertiary butyl alcohol) in denitrifying conditions, found that 100 mg/l ethanol (in the presence of TBA) was completely degraded in less than 14 days.

General

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 10/16/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Biological oxygen demand protocol.

>> Test Type

aerobic

>> GLP: Unknown

>> Year study performed: 1974

>> Contact Time: 20

>> Inoculum

Unknown

Remarks for Method

* Inoculum (concentration and source):
- Other: This was a test of biodegradation in fresh water. Filtered, settled domestic wastewater was used as seed material.

* Concentration of test chemical, vehicle used, pre-acclimation conditions: 3, 7, and 10 mg/l ethanol was added, using 0.1% stock solution.
* Temperature of incubation °C: Not specified.
* Dosing procedure: Not discussed. Domestic wastewater was placed in bottles, to which was then added aerated dilution water and test chemical.
* Sampling frequency: Biological oxygen demand was measured every 5 days. Ethanol concentrations were not measured during the experiment.
* Were appropriate controls and blank system used? Yes. Blanks containing the same amount of seed but no test chemical were used.
* Analytical method used to measure biodegradation: Cumulative oxygen uptake in ethanol-amended and control samples was measured with a dissolved oxygen meter.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Method of calculating measured concentrations (i.e., arithmetic mean, geometric mean, etc.) Ethanol concentrations were not measured. Extent of biodegradation was calculated as percentage of the theoretical oxygen demand utilized.

Results

>> Precision =

>> Degradation Value 84

>> Upper value 0

>> Time Frame 20

>> Time Units Days

>> Breakdown products Unknown

Results Remarks

* Lag time: Not measured.
* Observed inhibition: Not measured.
* Excessive biodegradation: Not discussed.
* Excessive standard deviation: Not discussed.
* Time required for 10% degradation: Not calculated. Af 5 days, 74% of ethanol had been degraded.
* Total degradation at the end of the test: 84%.

Conclusions

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Ethanol was extensively biodegraded after 20 days in fresh water inoculated with a wastewater sample, as measured by biological oxygen demand.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Price, K., Waggy, G., and Conway, R. (1974). Brine shrimp bioassay and seawater BOD of petrochemicals. J. Water Poll. Control Fed. 46(1):63-77.

In this same study, biodegradation of ethanol was measured in synthetic seawater inoculated with raw settled wastewater. After 20 days, 75% of the ethanol was degraded, as assessed by BOD.

General

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 02/22/2001

Test Substance

Remarks: Analytical-grade ethanol

Chemical Category

Method

>> Method/Guideline followed

Biological oxygen demand protocol

>> Test Type

aerobic

>> GLP: Unknown

>> Year study performed: 1966

>> Contact Time: 1

>> Inoculum

Unknown

Remarks for Method

* Innoculum (concentration and source):
 - Fresh activated sludge: Activated sludges were obtained from municipal treatment plants in Columbus, Hilliard, and Linworth, Ohio.

* Concentration of test chemical, vehicle used, pre-acclimation conditions: 500 mg/l ethanol was added to 125-ml flasks containing 20 ml of blended sludge with a concentration of 2,500 mg/l suspended solids.
* Temperature of incubation °C: 20 deg. C.
* Dosing procedure: see above.
* Sampling frequency: Biological oxygen demand was measured 6, 12, and 24 hours after inoculation. Ethanol concentrations were not measured during the experiment.
* Were appropriate controls and blank system used? Yes, flasks containing sludge suspension but no ethanol were included.
* Analytical method used to measure biodegradation: Oxygen uptake of the sludges was measured in a Warburg respirometer.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Method of calculating measured concentrations (i.e., arithmetic mean, geometric mean, etc.): Not discussed.

Results

>> Precision =

>> Degradation Value 37

>> Upper value 0

>> Time Frame 1

>> Time Units Days

>> Breakdown products Unknown

Results Remarks

* Lag time: Not discussed.
* Observed inhibition: Not discussed.
* Excessive biodegradation: Not discussed.
* Excessive standard deviation: Not discussed.
* Time required for 10% degradation: Not calculated. At 6 hours, oxygen demand was 12.9% of theoretical.
* Total degradation at the end of the test: 37.3% at 24 hours.

Conclusions

All sludges were capable of oxidizing ethanol, as measured by biological oxygen demand. At 24 hours (the end of the experiment), BOD in ethanol-treated samples was 37.3% of maximum, similar to that for other short-chain alcohols.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Gerhold, R. and Malaney, G. (1966). Structural determinants in the oxidation of aliphatic compounds by activated sludge. J. Water Poll. Control Fed. 38:562-579.

General

EPA High Production Volume (HPV) Track

Environmental Fate and Pathway End Point: Photodegradation

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

Revision Date: 02/28/2001

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Unknown

>> Light Source: Unknown

>> Light Source Spectrum in nm: 350

>> Relative Intensity: 700 microW/cm^2

>> Absorption Spectrum of Substance: UV (used for analysis)

>> GLP: Unknown

>> Year study performed: 1977

Remarks for Method

* Test medium (air, water, soil, other - specify): The test system was a 12-cubic-meter smog chamber filled with air, 2 ppmv of ethanol, and 1 ppmv of nitrogen oxides. The air temperature was 30 deg. C and the relative humidity was 55%.
* Duration of test: Five hours. Percent degradation was determined by gas chromatography and UV spectroscopy.
* Positive/Negative Controls - what was used and at what concentration: Unclear.

Results

>> Concentration Value: 2

>> Unit: ppm

>> Temperature: 30

EPA High Production Volume (HPV) Track

Environmental Fate and Pathway End Point: Photodegradation

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

>> Direct Photolysis Precision

>> Direct Photolysis 0

>> Direct Photolysis Upper value 0

>> Direct Photolysis Unit

>> Indirect Photolysis Precision

>> Indirect Photolysis 0

>> Indirect Photolysis Upper value 0

>> Indirect Photolysis Unit

>> Sensitizer

>> Sensitizer Concentration

>> Sensitizer Unit

>> Rate Constant

>> Breakdown products Unknown

Results Remark

* % degradation results other than half lives (e.g., the % degraded after time 't'): A 20% decrease in ethanol concentration was observed after 2 hours.
* quantum yield (e.g., total recovery at end of test as a fraction (0-1.0)): Not discussed.

Conclusions

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

After two hours of irradiation at 345-355 nm, the ethanol concentration decreased by 20% from the starting concentration of 2 ppm. Assuming a first-order reaction, the rate constant for ethanol photolysis in this system was 0.045 hr^-1 and the half-life was 15.4 hr.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

The results reported here come from article summaries provided by the CHEMFATE database of the Syracuse Research Corporation. The database can be found at http://esc.syrres.com/efdb/Chemfate.htm.

Yanagihara, S., et al. (1977). Photochemical reactivities of hydrocarbons. Proc. Int. Clean Air Congr., 4th. Pages 472-7.

Hustert, K. and Parlar, H. (1981). Ein testverhahren zum photochemischer abbau von umweltchemikalien in der gas phase. Chemosphere 10:1045-50. These investigators irradiated a reaction vessel containing air and 100 ppm ethanol with a mercury lamp (230 nm) for two hours and found 35.5% degradation.

General

EPA High Production Volume (HPV) Track

Environmental Fate and Pathway End Point: Stability in Water

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

Revision Date: 02/28/2001

Test Substance

Remarks: 100% ethanol

Chemical Category

Method

>> Method/Guideline followed

Estimation procedure

>> Test Type Estimation procedure

>> GLP No

>> Year study performed 2001

Remarks for Method

* Duration (days) of test: Not relevant.
* Positive/Negative Controls - what was used and what concentration: Not relevant.
* Analytical procedures used to measure test substance loss: Not relevant.

Results

>> Nominal concentration

>> Measured concentration

>> Precision

>> Hydrolysis Resul 0

>> Upper Value 0

>> Unit

EPA High Production Volume (HPV) Track

Environmental Fate and Pathway End Point: Stability in Water

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

>> pHVal 0

>> Temperature

>>Breakdown products

Results Remarks

According to Lyman et al. (1990), both alkanes and alcohols are resistant to hydrolysis. As these are the only functional groups present in ethanol, ethanol is not expected to undergo hydrolysis. Furthermore, if ethanol did undergo hydrolysis, losing its hydroxyl group to water and gaining a water molecule in its place, the final products would be identical to the reactants. Thus, we can safely conclude that the rate of abiotic degradation in water is negligible.

Conclusions

By using first principles, it can be concluded that ethanol does not undergo meaningful hydrolysis.

Data Quality

Reliability

Data Reliability Remarks

Reference

EPA High Production Volume (HPV) Track

Environmental Fate and Pathway End Point: Stability in Water

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

>> Remarks

Lyman, W., Reehl, W., and Rosenblatt, D. (1990). Handbook of Chemical Property Estimation Methods: Environmental Behavior of Organic Compounds. American Chemical Society: Washington, D.C.

General

EPA High Production Volume (HPV) Track

Environmental Fate and Pathway End Point: Transport between Environmental Compartments (Fugacity)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date:
02/28/2001

Test Substance

Remarks: 100% ethanol

Chemical Category

Method

>> Method/Guideline followed

Recommended EQC model

>> Test Type: Level III fugacity model

>> Year study performed: 2001

Remarks for Method

* Model used
- Title: EQC model of Mackay et al. (1996).
- Version: 1.01
- date: May, 1997
* Input parameters
- chemical-specific: Molecular weight, 46.09 g/mol. Data temperature: 25 deg. C. Water solubility: 716,000 g/m^3 (calculated from vapor pressure and Henry's law constant of 5e-06 atm-m^3/mol[Gaffney, 1987]). Vapor pressure: 7870 Pa (59.03 mm). Log Kow: -0.31. Melting point: -114 deg. C. Half-life in air: 203 hr (Graedel, 1978). Half-life in water: 182 hr (from biodegradation data). Half-life in soil or sediment: 210 hr (from biodegradation data).
- environmental conditions: Left at the default values of the model.

Results

>> Media

Air: 13.0%. Water: 44.8%. Soil: 42.1%. Sediment: 0.039%.

>> Distribution Concentration

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Air: 1.60e-8 mol/m^3 (738 ng/m^3).
Water: 2.75e-5 mol/m^3 (1271 ng/l).
Soil: 2.88e-4 mol/m^3 (8.3 ng/g).
Sediment: 9.50e-6 mol/m^3 (0.34 ng/g).

Results Remark

* Adsorption coefficient: Not given.
* Desorption: Not given.
* Volatility: Not given.

Conclusions

Modeling used the EQC model (v. 1.01) of Mackay et al. The model was run in Level III to obtain media-specific concentrations. The chemical-specific parameters required are listed above, and all environmental parameters were left at the default values. At steady state, 67% of additional inputs of ethanol are lost through reactions, and 33% are lost through advection.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Model obtained at http://www.trentu.ca/academic/aminss/envmodel/EQCD.html.

Mackay, D., DiGuardo, A., Paterson, S. and Cowan, C. (1996). Evaluating the environmental fate of a variety of types of chemicals using the EQC model. Environ. Toxicol. Chem. 15(9):1627-1637.

Gaffney, J. et al. (1978). Environ. Sci. Technol. 21:519-523 as cited by HSDB.

EPA High Production Volume (HPV) Track

Environmental Fate and Pathway End Point: Transport between Environmental Compartments (Fugacity)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

General

Graedel, T (1978). Chemical Compounds in the Atmosphere. Academic Press: New York.

EPA High Production Volume (HPV) Track

Physical-Chemical End Point:
Boiling Point

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 10/16/2000

Test Substance

Remarks: Absolute ethanol

Chemical Category

Method

>> Method/Guideline followed

Unknown

>> GLP Unknown

>> Year study performed 1951

Results

Remarks for Method

Test method is not described.

>> Precision =

>> Boiling Point Value 78

>> Upper Value 0

>> Unit °C

EPA High Production Volume (HPV) Track

Physical-Chemical End Point:
Boiling Point

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> Pressure 760

>> Pressure Unit mm Hg

>> Decomposition No

Results Remark

Conclusions

Data Quality

Reliability

Data Reliability Remarks

EPA High Production Volume (HPV) Track

Physical-Chemical End Point:
Boiling Point

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Reference

>> Remarks

McKenna, F., Tartar, H., and Lingfelter, S. (1953). Studies of hemiacetal formation in alcohol-aldehyde systems: refraction studies. J. Amer. Chem. Soc. 75:604-607.

Budavari, S., editor. (1996). The Merck Index, 12th edition. Merck & Co.: Whitehouse Station, NJ.

Lide, D.R., editor. (1991). CRC Handbook of Chemistry and Physics, 72nd edition. CRC Press: Boca Raton, FL.

General

EPA High Production Volume (HPV) Track

Physical-Chemical End Point:
Melting Point

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date:
10/16/2000

Test Substance

Remarks: U.S.I. absolute ethanol

Chemical Category

Method

>> Method/Guideline followed

See below

>> GLP Unknown

>> Year study performed 1953

Remarks for Method

Melting point was determined in a cell that protected the contents from contact with the atmosphere. Temperature in the cell was measured with a copper-constantan thermocouple inserted into a thermocouple well containing n-propanol as a thermal conducting medium. The copper-constantan thermocouple was calibrated in the cell by measuring the freezing point of purified materials. Cooling was accomplished with dry ice-acetone baths or liquid nitrogen, according to the temperature required.

Results

>> Precision =

>> Melting Point Value -114

>> Upper Value 0

>> Unit °C

EPA High Production Volume (HPV) Track

Physical-Chemical End Point: Melting Point

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> Decomposition No

>> Sublimation No

Results Remark

Conclusions

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Corcoran, J., Kruse, H., and Skolnik, S. (1953). Thermal analysis of the systems hydrazine-methanol and hydrazine-ethanol. J. Phys. Chem. 57:435-437.

Budavari, S., editor. (1996). The Merck Index, 12th edition. Merck & Co.: Whitehouse Station, NJ.

The CRC Handbook cites a value of -114.1 deg. C. Lide, D.R., editor. (1991). CRC Handbook of Chemistry and Physics, 72nd edition. CRC Press: Boca Raton, FL.

EPA High Production Volume (HPV) Track

Physical-Chemical End Point:
Melting Point

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

General

EPA High Production Volume (HPV) Track

Physical-Chemical End Point:
Partition Coefficient

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date:
10/16/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Unknown

>> GLP Unknown

>> Year study performed 1900

Remarks for Method

Test method and date are unknown.

Results

>> Precision =

>> Value of Log Pow -0.31

>> Upper Value 0

>> Temperature 25 deg. C

EPA High Production Volume (HPV) Track

Physical-Chemical End Point: Partition Coefficient

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Results Remark

* Surface active
* Dissociative
* What is the water solubility?

Conclusions

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Howard, P. (1991). Handbook of Environmental Fate and Exposure Data for Organic Chemicals, volume II. Solvents. Lewis Publishers: Chelsea, MI.

Hansch, C., Leo, A., and Hoekman, D. (1995). Exploring QSAR: Hydrophobic, Electronic, and Steric Constants. American Chemical Society: Washington, DC. As cited by HSDB.

General

EPA High Production Volume (HPV) Track

Physical-Chemical End Point:
Partition Coefficient

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

EPA High Production Volume (HPV) Track

Physical-Chemical End Point:
Vapor Pressure

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date:
10/16/2000

Test Substance

Remarks: Commercial absolute ethanol was fractionated in a 5-foot column packed with glass helices and then treated with magnesium ethylate. The final product of d (sup 25) (sub 4) 0.78506 was kept under its own vapor pressure in a sealed container over magnesium ethylate and samples were withdrawn by vacuum distillation.

Chemical Category

Method

>> Method/Guideline followed

Equilibrium still of Scatchard et al.

>> GLP Unknown

>> Year study performed 1948

Remarks for Method

The equilibrium still of Scatchard and co-workers was used (see J. Amer. Chem. Soc. 60:1275 and 1278; 61:3206; 62:712, and 68:1957 and 1960), although a water bath was substituted for the vapor jacket. A recently calibrated platinum resistance thermometer and Mueller bridge were used for temperature measurement. Vapor pressure was measured in two ways. First, vapor pressure was measured during still operation using an inverted U-tube manometer of 12 mm inner diamter tubing. The manometer was read with a Model M901 Gaertner cathetometer at a distance of 250 m. Second, static measurements of vapor pressure were made by use of a vapor-pressure cell connected directly to the manometer. Agreement between the methods was within 0.2 mm Hg.

Results

>> Precision =

>> Vapor Pressure Value 59.03

EPA High Production Volume (HPV) Track

Physical-Chemical End Point:
Vapor Pressure

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> Upper Value 0

>> Unit mm Hg

>> Temperature 25 deg. C

>> Decomposition No

Results Remark

Conclusions

Data Quality

Reliability

Data Reliability Remarks

Reference

EPA High Production Volume (HPV) Track

Physical-Chemical End Point: Vapor Pressure

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> Remarks

Kretschmer, C., Nowakowska, J., and Wiebe, R. (1948). Densities and liquid-vapor equilibria of the system ethanol-isooctance (2,2,4-trimethylpentane) between) and 50 deg. J. Amer. Chem. Soc. 70:1785-1790.

Howard, P. (1991). Handbook of Environmental Fate and Exposure Data for Organic Chemicals, volume II. Solvents. Lewis Publishers: Chelsea, MI.

General

EPA High Production Volume (HPV) Track

Physical-Chemical End Point:
Water Solubility

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

Revision Date:
10/16/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Unknown

>> GLP Unknown

>> Year study performed 1900

Remarks for Method

Test method and date are unknown.

Results

>> Precision >

>> Water Solubility Value 10000

>> Upper Value 0

EPA High Production Volume (HPV) Track

Physical-Chemical End Point:
Water Solubility

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

>> Unit mg/L

>> Temperature 25 deg. C

>> Solubility Category Very soluble

>> pH Value 0

>> pKa Value 16

Results Remark

Conclusions

Data Quality

Reliability

Data Reliability Remarks

EPA High Production Volume (HPV) Track

Physical-Chemical End Point:
Water Solubility

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

Reference

>> Remarks

Howard, P. (1991). Handbook of Environmental Fate and Exposure Data for Organic Chemicals, volume II. Solvents. Lewis Publishers: Chelsea, MI.

Riddick, J., Bunger, W., and Sakano, T. (1985). Techniques of Chemistry, 4th edition, volume II. Organic Solvents. John Wiley and Sons: New York, NY. As cited by HSDB.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Acute Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date:
02/23/2001

Test Substance

Remarks: Analytical-grade ethanol.

Chemical Category

Method

>> Method/Guideline followed

Acute oral toxicity

>> GLP Unknown

>> Year study performed 1976

>> Species

mouse

>> Strain SPF-NMRI

>> Sex Both

>> Number of males per dose 5

>> Number of females per dose 5

>> Vehicle 0.9% saline; 20 ml/kg

>> Route of Administration

Oral

Remarks for Method

Sponsor ID	9999999	Sponsor Named In Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age of animals used: Not given. Animals were housed in polycarbonate cages in air-conditioned rooms at a temperature of 22 deg. C. and relative humidity of 55%. Food and water were available ad lib.
* Doses (OECD guidelines 420, 423, and 425 do not provide dose levels, so these must be described in detail): Not stated. However, at least three doses lying between the LD16 and LD84 were used.
* Doses per time period: One.
* Volume administered or concentration: 20 ml/kg total volume.
* Post dose observation period: 7 days.
* Exposure duration (for inhalation studies): Not applicable.

Results

>> Precision =

>>Acute Lethal Value 10

>> Unit ml/kg

>> Deaths per Dose

Data not given.

Results Remark

* Time of death (provide individual animal time if less than 24 hours after dosing): All deaths occurred within 24 hours. Individual times were not given.
* Description, severity, time of onset and duration of clinical signs at each dose level: Not described.
* Necropsy findings, included doses affected, severity and number of animals affected: Not done.
* Potential target organs (if identified in the report): Not discussed.
* If both sexes tested, results should be compared: LD50 given for both sexes combined.

Conclusions

The oral LD50 for ethanol in SPF-NMRI mice, calculated using Finney's programmed probit analysis, was 10.5 ml/kg, with a 95% confidence interval of 9.8-11.6. In terms of g/kg, the LD50 would be 8.3 g/kg.

Data Quality

Reliability

EPA High Production Volume (HPV) Track

Toxicity End Point:
Acute Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Reliability Remarks

Reference

>> Remarks

Bartsch, W., Sponer, G., Dietmann, K., and Fuchs, G. (1976). Acute toxicity of various solvents in the mouse and rat. Arzneim.-Forsch. 26(8):1581-1583.

General

In the same experiment, LD50's were determined for intravenous and intraperitoneal routes. The LD50's for these exposure routes were 2.8 ml/kg and 4.0 ml/kg, respectively.

EPA High Production Volume (HPV) Track

Toxicity End Point:
Acute Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date:
10/24/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Acute intraperitoneal toxicity

>> GLP Unknown

>> Year study performed 1995

>> Species

mouse

>> Strain HS

>> Sex Both

>> Number of males per dose 10

>> Number of females per dose 10

>> Vehicle 0.9% saline (presumed)

>> Route of Administration

Intraperitoneal

Remarks for Method

* Age of animals used: 25-30 days. Animals were housed in Plexiglas cages with aspen shavings in a climate-controlled room with 12 hr light and 12 hr dark. Food and water were provided ad lib.
* Doses (OECD guidelines 420, 423, and 425 do not provide dose levels, so these must be described in detail): 6, 8, and 10 g/kg.
* Doses per time period: One.
* Volume administered or concentration: 10 ml/kg volume administered, using a 20% w/v solution.
* Post dose observation period: 24 hr.
* Exposure duration (for inhalation studies): Not applicable.

Results

>> Precision =

>>Acute Lethal Value 10

>> Unit g/kg

>> Deaths per Dose

As read from graph: Males, 0, 2, 6; females, 0, 1, 6 at low, mid, and high doses, respectively.

Results Remark

* Time of death (provide individual animal time if less than 24 hours after dosing): All deaths occurred within 30 minutes. Individual data were not given.
* Description, severity, time of onset and duration of clinical signs at each dose level: Not described.
* Necropsy findings, included doses affected, severity and number of animals affected: Not done.
* Potential target organs (if identified in the report): Not discussed.
* If both sexes tested, results should be compared: LD50 in males, 9.71 g/kg. LD50 in females, 9.45 g/kg.

Conclusions

The LD50 for ethanol in HS mice, after i.p. dosing, was 9.71 g/kg in males (8.38-11.27) and 9.45 g/kg in females (8.45-10.49), as calculated using the Litchfield-Wilcoxon analysis.

Data Quality

Reliability

EPA High Production Volume (HPV) Track

Toxicity End Point:
Acute Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Reliability Remarks

Reference

>> Remarks

Schechter, M. and Meehan, S. (1995). The lethal effects of ethanol and cocaine and their combination in mice: implications for cocaethylene formation. Pharmacol. Biochem. Behav. 52(1):245-248.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Acute Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date:
10/24/2000

Test Substance

Remarks: 95% ethanol USP

Chemical Category

Method

>> Method/Guideline followed

Acute inhalation toxicity

>> GLP Unknown

>> Year study performed 1985

>> Species

mouse

>> Strain CD-1

>> Sex Both

>> Number of males per dose 6

>> Number of females per dose 6

>> Vehicle None

>> Route of Administration

Inhalation

Remarks for Method

* Age of animals used: Not stated, but they weighted 25-30 g. Animals were maintained in cages with wood-chip bedding in a room with temperature of 22-24 deg. C. and 12 hr of light, 12 hr of dark.
* Doses (OECD guidelines 420, 423, and 425 do not provide dose levels, so these must be described in detail): maxima of 40,000, 50,000, and 60,000 ppm (pure ethanol) for different exposure durations.
* Doses per time period: One exposure period per exposure level.
* Volume administered or concentration: Not applicable.
* Post dose observation period: 72 hours.
* Exposure duration (for inhalation studies): 60, 30, and 10 minutes at the low, medium, and high concentrations, respectively.

Results

>> Precision >

>>Acute Lethal Value 40000

>> Unit ppm(air)

>> Deaths per Dose

No deaths occurred at any exposure concentration.

Results Remark

* Time of death (provide individual animal time if less than 24 hours after dosing): Not applicable, as there were no deaths.
* Description, severity, time of onset and duration of clinical signs at each dose level: Not described in detail. Slight to moderate ataxia occurred, and recovery time (time to adequate performance on the inverted screen test) was more than 4 hours at all exposure levels.
* Necropsy findings, included doses affected, severity and number of animals affected: Not applicable.
* Potential target organs (if identified in the report): Not applicable.
* If both sexes tested, results should be compared

Conclusions

No LC50 for ethanol was determined in CD-1 mice, as no deaths occurred at the exposure concentrations of 40,000-60,000 ppm ethanol.

EPA High Production Volume (HPV) Track

Toxicity End Point:
Acute Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Moser, V. and Balster, R. (1985). Acute motor and lethal effects of inhaled toluene, 1,1,1,-trichloroethane, halothane, and ethanol in mice: effects of exposure duration. Toxicol. Appl. Pharmacol. 77:285-291.

General

The sexes of the animals were not specified: the numbers given above are estimates, as 12 animals per exposure concentration were used.

EPA High Production Volume (HPV) Track

Toxicity End Point:
Acute Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date:
10/26/2000

Test Substance

Remarks: 95% ethanol

Chemical Category

Method

>> Method/Guideline followed

Acute intraperitoneal toxicity

>> GLP Unknown

>> Year study performed 1979

>> Species

mouse

>> Strain Swiss Webster

>> Sex M

>> Number of males per dose 8

>> Number of females per dose 0

>> Vehicle Distilled water

>> Route of Administration

Intraperitoneal

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age of animals used: Not stated, but they weighed 25-30 g. Animals were housed in plastic cages in a temperature- and humidity-controlled room with a 12-hr light, 12-hr dark cycle. Food and water were given ad lib.
* Doses (OECD guidelines 420, 423, and 425 do not provide dose levels, so these must be described in detail): Not stated, but at least six doses ranging from 5.0 to 11.0 g/kg.
* Doses per time period: Single dose.
* Volume administered or concentration: 0.2-0.25 ml using 20% ethanol diluted in distilled water.
* Post dose observation period: 7 days.
* Exposure duration (for inhalation studies): Not applicable.

Results

>> Precision =

>>Acute Lethal Value 9

>> Unit g/kg

>> Deaths per Dose

Not specified

Results Remark

* Time of death (provide individual animal time if less than 24 hours after dosing): Not reported.
* Description, severity, time of onset and duration of clinical signs at each dose level: Not reported.
* Necropsy findings, included doses affected, severity and number of animals affected: Not reported.
* Potential target organs (if identified in the report): Not discussed.
* If both sexes tested, results should be compared: Not applicable.

Conclusions

The LD50 (i.p.) for ethanol in male mice was calculated using the Litchfield-Wilcoxon method, and found to be 9.2 g/kg with a 95% confidence interval of 8.9-9.4 g/kg.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Ho, A. and Ho, C. (1979). Toxic interactions of ethanol with other central depressants: antagonism by naloxone to narcosis and lethality. Pharmacol. Biochem. Behav. 11:111-114.

General

Revision Date:
10/26/2000

Test Substance

Remarks: Absolute ethanol with 0.1% methanol

Chemical Category

Method

>> Method/Guideline followed

Acute oral toxicity

>> GLP Unknown

>> Year study performed 1992

>> Species

rat

>> Strain albino

>> Sex F

>> Number of males per dose 0

>> Number of females per dose 8

>> Vehicle None, but gavaged after given 5% gum acacia.

>> Route of Administration

Oral (gavage)

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age of animals used: Adults weighing approximately 180 g. Animals received food and water ad lib, and were maintained at 22-26 deg. C on a 12-hr light, 12-hr dark cycle.
* Doses (OECD guidelines 420, 423, and 425 do not provide dose levels, so these must be described in detail): 16, 17, 18, 19, 20, 21, and 22 ml/kg.
* Doses per time period: One.
* Volume administered or concentration: See list of doses.
* Post dose observation period: 24 hours.
* Exposure duration (for inhalation studies): Not applicable.

Results

>> Precision =

>>Acute Lethal Value 19

>> Unit ml/kg

>> Deaths per Dose

0/8, 0/8, 2/8, 4/8, 6/8, 8/8, 8/8

Results Remark

* Time of death (provide individual animal time if less than 24 hours after dosing): Times not given.
* Description, severity, time of onset and duration of clinical signs at each dose level: Clinical observations ranged from inebriation to gait disturbance, to dose-related decrease in response to painful stimuli, respiratory depression, and coma. Deaths were due to cardiorespiratory failure.
* Necropsy findings, included doses affected, severity and number of animals affected: Diffuse congestion of the gastric mucosa, without gross hemorrhage or ulceration, was seen. All other tissues examined (liver, kidney, heart, lungs, spleen, eye, and CNS) were normal.
* Potential target organs (if identified in the report): Not discussed.
* If both sexes tested, results should be compared: Not applicable.

Conclusions

Albino rats were fasted for 16 hours before gavage with ethanol. The dosing protocol followed the Litchfield-Wilcoxon scheme, and the statistical method was maximum likelihood, as described by Cox. The LD50 for ethanol towards female rats was 19 ml/kg.

Data Quality

Reliability

EPA High Production Volume (HPV) Track

Toxicity End Point:
Acute Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Reliability Remarks

Reference

>> Remarks

Youssef, A., Madkour, K., Cox, C., and Weiss, B. (1992). Comparative lethality of methanol, ethanol and mixtures in female rats. J. Appl. Toxicol. 12(3):193-197.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Acute Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date:
11/02/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Acute oral toxicity

>> GLP: Unknown

>> Year study performed: 1970

>> Species

rat

>> Strain: Wistar

>> Sex: M

>> Number of males per dose: 10

>> Number of females per dose: 0

>> Vehicle: water

>> Route of Administration

Oral

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age of animals used: About 100 days. They received food and water ad lib.
* Doses (OECD guidelines 420, 423, and 425 do not provide dose levels, so these must be described in detail): Doses are not stated, but are shown in the graphs. Six to eight dose levels were used, with a dose interval of 1.1.
* Doses per time period: One.
* Volume administered or concentration: Administered as a 40% w/v solution.
* Post dose observation period: 24 hours.
* Exposure duration (for inhalation studies): Not applicable.

Results

>> Precision =

>>Acute Lethal Value 11

>> Unit g/kg

>> Deaths per Dose

Not stated, but can be gleaned from the graph: 10% to 90% for the doses shown.

Results Remark

* Time of death (provide individual animal time if less than 24 hours after dosing): All deaths counted occurred within 24 hours, but individual times are not given.
* Description, severity, time of onset and duration of clinical signs at each dose level: Not described.
* Necropsy findings, included doses affected, severity and number of animals affected: Not conducted.
* Potential target organs (if identified in the report): Cause of death was respiratory failure.
* If both sexes tested, results should be compared: Not applicable.

Conclusions

In "young" rats, the oral LD50 for ethanol was 10.6 g/kg with a 95% confidence interval of 10.0-11.2 g/kg. This result can be compared to that for "old" rats, separately summarized. The LD50 value was estimated by the moving-average method of Weil or the graphical method of Litchfield and Wilcoxon.

Data Quality

Reliability

Data Reliability Remarks

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Reference

>> Remarks

Wiberg, G., Trenholm, H., and Coldwell, B. (1970). Increased ethanol toxicity in old rats: changes in LD50, in vivo and in vitro metabolism, and liver alcohol dehydrogenase activity. Toxicol. Appl. Pharmacol. 16:718-727.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Acute Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date:
11/02/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Acute oral toxicity

>> GLP: Unknown

>> Year study performed: 1970

>> Species

rat

>> Strain: Wistar

>> Sex: M

>> Number of males per dose: 10

>> Number of females per dose: 0

>> Vehicle: water

>> Route of Administration

Oral

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age of animals used: 10-12 months. They received food and water ad lib.
* Doses (OECD guidelines 420, 423, and 425 do not provide dose levels, so these must be described in detail): Doses are not stated, but are shown in the graph. Six to eight dose levels were used, with a dose interval of 1.1.
* Doses per time period: One.
* Volume administered or concentration: Administered as a 40% w/v solution.
* Post dose observation period: 24 hours.
* Exposure duration (for inhalation studies): Not applicable.

Results

>> Precision =

>>Acute Lethal Value 7

>> Unit g/kg

>> Deaths per Dose

Not stated, but can be gleaned from the graph: 10 to 90% for the doses shown.

Results Remark

* Time of death (provide individual animal time if less than 24 hours after dosing): All deaths counted occurred within 24 hours, but individual times are not given.
* Description, severity, time of onset and duration of clinical signs at each dose level: Not described.
* Necropsy findings, included doses affected, severity and number of animals affected: Not conducted.
* Potential target organs (if identified in the report): Cause of death was respiratory failure.
* If both sexes tested, results should be compared: Not applicable.

Conclusions

In "old" rats, the oral LD50 for ethanol was 7.06 g/kg with a 95% confidence intervale of 6.67-7.46 g/kg. This result can be compared to that for "young" rats, separately summarized. Old rats are considerably more senstive than young rats, in this experiment. The LD50 value was estimated by the moving-average method of Weil or the graphical method of Litchfield and Wilcoxon.

Data Quality

Reliability

Data Reliability Remarks

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Reference

>> Remarks

Wiberg, G., Trenholm, H., and Coldwell, B. (1970). Increased ethanol toxicity in old rats: changes in LD50, in vivo and in vitro metabolism, and liver alcohol dehydrogenase activity. Toxicol. Appl. Pharmacol. 16:718-727.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Acute Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	8
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date:
11/02/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Acute intraperitoneal toxicity

>> GLP Unknown

>> Year study performed 1970

>> Species

rat

>> Strain Wistar

>> Sex M

>> Number of males per dose 10

>> Number of females per dose 0

>> Vehicle water

>> Route of Administration

Intraperitoneal

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	8
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age of animals used: About 100 days. They received food and water ad lib.
* Doses (OECD guidelines 420, 423, and 425 do not provide dose levels, so these must be described in detail): Doses are not stated, but are shown in the graph. Six to eight dose levels were used, with a dose interval of 1.05.
* Doses per time period: One.
* Volume administered or concentration: Administered as a 15% w/v solution.
* Post dose observation period: 24 hours.
* Exposure duration (for inhalation studies): Not applicable.

Results

>> Precision =

>>Acute Lethal Value 7

>> Unit g/kg

>> Deaths per Dose

Not stated, but can be gleaned from the graph: 10% to 100% for the doses shown.

Results Remark

* Time of death (provide individual animal time if less than 24 hours after dosing): All deaths counted occurred within 24 hours, but individual times are not given.
* Description, severity, time of onset and duration of clinical signs at each dose level: Not described.
* Necropsy findings, included doses affected, severity and number of animals affected: Not conducted.
* Potential target organs (if identified in the report): Cause of death was respiratory failure.
* If both sexes tested, results should be compared: Not applicable.

Conclusions

In "young" rats, the I.p. LD50 for ethanol was 6.71 g/kg, with a 95% confidence interval of 6.31-7/13 g/kg. This result can be compared to that for "old" rats, separately summarized.The LD50 value was estimated by the moving-average method of Weil or the graphical method of Litchfield and Wilcoxon.

Data Quality

Reliability

Data Reliability Remarks

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	8
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Reference

>> Remarks

Wiberg, G., Trenholm, H., and Coldwell, B. (1970). Increased ethanol toxicity in old rats: changes in LD50, in vivo and in vitro metabolism, and liver alcohol dehydrogenase activity. Toxicol. Appl. Pharmacol. 16:718-727.

General

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	9
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/02/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Acute intraperitoneal toxicity

>> GLP Unknown

>> Year study performed 1970

>> Species

rat

>> Strain Wistar

>> Sex M

>> Number of males per dose 10

>> Number of females per dose 0

>> Vehicle water

>> Route of Administration

Intraperitoneal

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	9
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age of animals used: About 10-12 months. They received food and water ad lib.
* Doses (OECD guidelines 420, 423, and 425 do not provide dose levels, so these must be described in detail): Doses are not stated, but are shown in the graphs. Six to eight dose levels were used, with a dose interval of 1.05.
* Doses per time period: One.
* Volume administered or concentration: Administered as a 15% w/v solution.
* Post dose observation period: 24 hours.
* Exposure duration (for inhalation studies): Not applicable.

Results

>> Precision =

>>Acute Lethal Value 5

>> Unit g/kg

>> Deaths per Dose

Not stated, but can be gleaned from the graph: 10% to 100% for the doses shown.

Results Remark

* Time of death (provide individual animal time if less than 24 hours after dosing): All deaths counted occurred within 24 hours, but individual times are not given.
* Description, severity, time of onset and duration of clinical signs at each dose level: Not described.
* Necropsy findings, included doses affected, severity and number of animals affected: Not conducted.
* Potential target organs (if identified in the report): Cause of death was respiratory failure.
* If both sexes tested, results should be compared: Not applicable.

Conclusions

In "old" rats, the I.p. LD50 for ethanol was 5.10 g/kg, with a 95% confidence interval of 5.01-5.14 g/kg. This result can be compared to that for "young" rats, separately summarized. The LD50 value was estimated by the moving-average method of Weil or the graphical method of Litchfield and Wilcoxon.

Data Quality

Reliability

Data Reliability Remarks

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	9
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Reference

>> Remarks

Wiberg, G., Trenholm, H., and Coldwell, B. (1970). Increased ethanol toxicity in old rats: changes in LD50, in vivo and in vitro metabolism, and liver alcohol dehydrogenase activity. Toxicol. Appl. Pharmacol. 16:718-727.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Developmental Toxicity/Teratogenicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

Revision Date: 02/23/2001

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Developmental toxicity study

>> GLP Unknown

>> Year study performed 1979

>> Species

mouse

>> Strain Mammal strain C57BL/6J

>> Sex F

>> Number of males per dose 0

>> Number of females per dose 16

>> Route of Administration Diet

>> Days of Gestation 4-9

>> Frequency of treatment Ad lib

>> Doses 17%, 25%, and 30% ethanol-derived calories

>> Control Group Yes Concurrent controls

>> Statistical Method

Student's t-tests or chi-square tests. Probabilities of 0.05 or less were considered statistically significant.

Remarks for Method

Sponsor ID	9999999	Sponsor Named In Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

* Age at study initiation: 4-5 months.
* Number of animals per dose per sex: Not explicitly stated, but approximately 16.
* Note whether vehicle used and concentration/volume: Ethanol or sucrose was added to diet to supply the desired calories. Doses (in calories) given above are approximately equal to the following concentrations of ethanol in the liquid diets: 33,000 ppm, 54,000 ppm, and 66,000 ppm. Given stated consumption rates and body weights, daily doses of ethanol were approximately 17, 29, and 28 g/kg.
* Clinical observations performed and frequency: None other than weighing.
* Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): Females housed singly with proven studs until vaginal plugs were found.
* Parameters assessed during study (maternal and fetal): Dams were weighed on days 0, 4, 10, and 18 (sacrifice). Fetuses were examined externally and internally for malformations. The numbers of implants and resorptions were recorded, as was litter weight.
* Organs examined at necropsy (macroscopic and microscopic): No maternal organs were examined. Fetuses were examined for external and visceral malformations.

Results

>> Maternal Precision/NOAEL =

>> Maternal NOAEL dose 17 **>> Unit used** % EtOH-derived cal.

>> Maternal NOAEL effect Body weight change; fetal resorptions

>> Maternal Precision/LOAEL =

>> Maternal LOAEL dose 25 **>> Unit used** % EtOH-derived cal.

>> Maternal LOAEL effect Increased percentage of resorptions.

>> Developmental Precision/NOAEL =

>> Developmental NOAEL dose 17 **>> Unit used** % EtOH-derived cal.

>> Developmental NOAEL effect Percentage of malformed fetuses; litter weight.

>> Developmental Precision/NOAEL =

>> Developmental LOAEL dose 25 **>> Unit used** % EtOH-derived cal.

>> Developmental LOAEL effect Increased percentage of malformed fetuses.

>> Actual dose

Approximately 17, 29, and 28 g/kg.

>> Maternal data with dose level (with NOAEL value).

Diets containing at least 25% ethanol-derived calories caused higher rates of fetal resorption. Body weights were not significantly affected by ethanol-containing diets.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

>> Fetal data with dose level (with NOAEL value).

Litter weight was not affected by ethanol-containing diets, but malformations were significantly increased by maternal diets containing 25% or more ethanol-derived calories.

>> Statistical results

Exact p-values were not given. LOAELs given above were based on statistical significance at the 0.05 level.

Results Remark

Maternal data:
* Mortality and day of death: No mortality occurred.
* Number pregnant per dose level: Pregnancy rates were not given.
* Number aborting: Not reported.
* Number of resorptions, early/late if available: Not distinguished. On average, one resorption/litter at the two lower doses and two/litter at the higher dose (gleaned from table).
* Number of implantations: 7.3/litter in all ethanol-treated groups (gleaned from table).
* Pre and post implantation loss, if available: Not reported.
* Number of corpora lutea (recommended): Not reported.
* Duration of Pregnancy: Not relevant; dams were sacrificed on gestation day 18.
* Body weight: Maternal weight gains were not affected by ethanol treatments.
* Food/water consumption: Rates of liquid diet consumption in the three ethanol-dosed groups were 12.02 ml/d, 12.86 ml/d, and 10.31 ml/d (standard deviations were also given).
* Description, severity, time of onset and duration of clinical signs: Slight tremulousness was observed in the high-dose group when the ethanol-containing diet was removed.
* Hematological findings incidence and severity: Not measured. However, in concurrent, non-pregnant, ethanol-treated aninals, blood alcohol levels were measured during gestation, and ranged from 3 mg% to 384 mg% across the three treatment groups.
* Clinical biochemistry findings incidence and severity: Not measured.
* Gross pathology incidence and severity: Dams not examined.
* Organ weight changes, particularly effects on total uterine weight: Not examined.
* Histopathology incidence and severity: Not examined.

Fetal data:
* Litter size and weights: Litter size was not reported, although implants and percent resorptions were. Litter weights were not statistically significantly affected by ethanol treatments.
* Number viable (number alive and number dead): Numbers not reported.
* Sex ratio: Not reported.
* Postnatal growth (depending on protocol): Not applicable.
* Postnatal survival (depending on protocol): Not applicable.
* Grossly visible abnormalities, external, soft tissue and skeletal abnormalities: The following organs or structures were malformed in fetuses of ethanol-treated dams: limb, eye, brain, heart, urogenital tract, and abdomen.

Conclusions

EPA High Production Volume (HPV) Track

Toxicity End Point:
Developmental Toxicity/Teratogenicity

Sponsor ID	9999999	Sponsor Named In Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

In this study of the developmental toxicity of ethanol towards mice, fetal malformations were increased in litters of dams feeding on 25% ethanol-derived calories. Two controls were used: controls fed standard lab chow, and controls pair-fed with sucrose-containing diets equivalent in calories to the diet consumed by the experimental animals. Equivalent weight gains across treatment and control groups suggests ethanol-treated dams were not malnourished, and that ethanol per se, and not nutritional deprivation, was responsible for the developmental toxicity. As many concurrent, non-pregnant females given the lowest concentration of ethanol in the liquid diet had undectable levels of blood ethanol, and this same diet did not produce statistically significant adverse developmental outcomes, the blood alcohol level may be critical to induction of malformations and fetal loss.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Randall, C. and Taylor, W. (1979). Prenatal ethanol exposure in mice: teratogenic effects. Teratol. 19:305-312.

General

The teratogenicity of ethanol to laboratory mammals has been extensively investigated in an effort to better understand the human fetal alcohol syndrome. Becker et al. (1996; Pharmacol. Biochem. Behav. 55(4):501-513) review 32 studies using acute exposure regimens and 19 using chronic exposure regimens. Additional studies undoubtedly exist. Acute exposure studies generally use I.p. injection, while the chronic studies generally use intragastric administration or liquid diets. These many studies are not individually summarized in this submission.

EPA High Production Volume (HPV) Track

Toxicity End Point:
Developmental Toxicity/Teratogenicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

Revision Date: 10/16/2000

Test Substance

Remarks: Ethanol was 96.5% pure, as checked by gas chromatography with flame ionization detection.

Chemical Category

Method

>> Method/Guideline followed

Developmental toxicity study

>> GLP: Unknown

>> Year study performed: 1985

>> Species

rat

>> Strain: Mammal strain — Sprague-Dawley

>> Sex: F

>> Number of males per dose: 0

>> Number of females per dose: 16

>> Route of Administration: Inhalation

>> Days of Gestation: 1-19

>> Frequency of treatment: 7 hr/d, 7 d/wk

>> Doses: 10,000, 16,000, and 20,000 ppm

>> Control Group: Yes — Concurrent controls

>> Statistical Method

Multivariate analysis, Kruskal-Wallis test, analysis of variance, and Fisher's exact test.

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

* Age at study initiation: Not stated.
* Number of animals per dose per sex: Approximately 16.
* Note whether vehicle used and concentration/volume: Not applicable.
* Clinical observations performed and frequency: Not described.
* Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): Virgin females were caged individually with breeder males; vaginal smears were taken.
* Parameters assessed during study (maternal and fetal): See below.
* Organs examined at necropsy (macroscopic and microscopic): None in dams; fetuses were examined for visceral malformations.

Results

>> Maternal Precision/NOAEL =

>> Maternal NOAEL dose 16000 **>> Unit used** ppm(air)

>> Maternal NOAEL effect Narcosis; food consumption

>> Maternal Precision/LOAEL =

>> Maternal LOAEL dose 20000 **>> Unit used** ppm(air)

>> Maternal LOAEL effect Narcosis; decreased food consumption

>> Developmental Precision/NOAEL >=

>> Developmental NOAEL dose 20000 **>> Unit used** ppm(air)

>> Developmental NOAEL effect Visceral or skeletal malformations or variations

>> Developmental Precision/NOAEL >

>> Developmental LOAEL dose 20000 **>> Unit used** ppm(air)

>> Developmental LOAEL effect No developmental effects seen.

>> Actual dose

10,013, 12,975, and 20,197 ppm

>> Maternal data with dose level (with NOAEL value).

The lower two concentrations of ethanol seemed to cause hyperactivity after exposure, while the high dose caused complete narcosis by the end of the exposure. Food intake was decreased at the highest.

>> Fetal data with dose level (with NOAEL value).

Sex ratios and fetal weights were unaffected by ethanol exposures of dams. There were no significant differences among groups in incidences of visceral or skeletal malformations or variations.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

>> Statistical results

The only statistically significant finding among treated animals was decreased maternal food consumption during the first week of exposure.

Results Remark

Maternal data:
* Mortality and day of death: No mortality occurred.
* Number pregnant per dose level: 15/15, 15/16, and 14/16 in the low-, medium-, and high-exposure groups, respectively.
* Number aborting: Not stated.
* Number of resorptions, early/late if available: Not distinguished. The percentages of implants resorbed were not affect by ethanol exposures.
* Number of implantations: 14-16/litter, not affected by ethanol exposure.
* Pre and post implantation loss, if available: Not given.
* Number of corpora lutea (recommended): 14-16/litter, not affected by ethanol exposure.
* Duration of Pregnancy: Not applicable; sacrificed on gestation day 20.
* Body weight: Not presented, but weights were said to be unaffected by ethanol treatment.
* Food/water consumption: Food consumption was decreased in the high-dose group during the first week of exposure only.
* Description, severity, time of onset and duration of clinical signs: As described above, the highest concentration of ethanol induced complete narcosis. Lower doses did not induce narcosis, but seemed to cause some hyperactivity afterwards.
* Hematological findings incidence and severity: Not measured. However, blood ethanol levels were measured in non-pregnant, concurrently exposed animals. These ranged from approximately 0.02 to 1.7 mg/ml across the low- to high-dose groups. Ranges and standard deviations were given.
* Clinical biochemistry findings incidence and severity: Not measured.
* Gross pathology incidence and severity: Not studied.
* Organ weight changes, particularly effects on total uterine weight: Not measured.
* Histopathology incidence and severity: Not investigated.

Fetal data:
* Litter size and weights: Litter sizes were not given, but averaged 6.0-7.1 fetuses/litter across the ethanol-exposed and control groups (gleaned from table). Male and female fetal weights did not differ significantly from control values at a p of 0.05.
* Number viable (number alive and number dead): Not given.
* Sex ratio: Sex ratios did not differ significantly from control values at a p of 0.05.
* Postnatal growth (depending on protocol): Not applicable.
* Postnatal survival (depending on protocol): Not applicable.
* Grossly visible abnormalities, external, soft tissue and skeletal abnormalities: Skeletal and visceral malformations and variations are given in detail. There were no statistically signficant differences in the frequencies of malformations or variations in ethanol-exposed groups. However, more litters contained abnormal fetuses in the 20,000-ppm group, compared to controls.

Conclusions

EPA High Production Volume (HPV) Track

Toxicity End Point:
Developmental Toxicity/Teratogenicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

In this investigation, pregnant rats were exposed for 19 days to ethanol in air at concentrations up to 20,000 ppm. The authors concluded there was no definite evidence of malformations due to ethanol exposure, although the incidence at the highest concentration was of "borderline significance."

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Nelson, B., Brightwell, W., MacKenzie, D., et al. (1985). Teratological assessment of methanol and ethanol at high inhalation levels in rats. Fundam. Appl. Toxicol. 5:727-736.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Developmental Toxicity/Teratogenicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

Revision Date: 10/17/2000

Test Substance

Remarks: U.S.P.-grade ethanol

Chemical Category

Method

>> Method/Guideline followed

Male-mediated developmental toxicity study

>> GLP: Unknown

>> Year study performed: 1981

>> Species

mouse

>> Strain: Mammal strain: Swiss Webster

>> Sex: M

>> Number of males per dose: 1

>> Number of females per dose: 0

>> Route of Administration: Diet

>> Days of Gestation: N/A

>> Frequency of treatment: ad lib for 28 d

>> Doses: 6.3% ethanol in liquid diet (32% EtOH-derived cal)

>> Control Group: Yes — Concurrent controls

>> Statistical Method

Chi-square and t-tests.

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

* Age at study initiation: 190 days.
* Number of animals per dose per sex: Not stated. "1" is entered above because a number is demanded.
* Note whether vehicle used and concentration/volume: Ethanol was added to a total liquid nutriment diet. Control diets contained an isocaloric amount of sucrose.
* Clinical observations performed and frequency: Body weights were measured every two days. Blood ethanol levels were determined at an unstated frequency.
* Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): Forty-eight hours after ethanol or sucrose diets were removed, males were mated with nulliparous females (two females per cage). Females were caged with males for up to five days; if no vaginal plugs were found, new females were offered. Mating lasted until 11 days after the last ethanol treatment.
* Parameters assessed during study (maternal and fetal): No maternal parameters were measured other than pregnancy rate and resorptions. (Females were untreated.)
* Organs examined at necropsy (macroscopic and microscopic): Corpora lutea were counted, although the data were not presented. There was no examination of the treated males.

Results

>> Maternal Precision/NOAEL	<		
>> Maternal NOAEL dose	32	**>> Unit used**	% EtOH-derived cal.
>> Maternal NOAEL effect	Fertilization rate		
>> Maternal Precision/LOAEL	=		
>> Maternal LOAEL dose	32	**>> Unit used**	% EtOH-derived cal.
>> Maternal LOAEL effect	Fertilization pregnancy rate		
>> Developmental Precision/NOAEL	<		
>> Developmental NOAEL dose	32	**>> Unit used**	% EtOH-derived cal.
>> Developmental NOAEL effect	Crown-rump length		
>> Developmental Precision/NOAEL	=		
>> Developmental LOAEL dose	32	**>> Unit used**	% EtOH-derived cal.
>> Developmental LOAEL effect	Decreased crown-rump length		

>> Actual dose

31 +/- 4 g/kg

>> Maternal data with dose level (with NOAEL value).

These are the paternal NOAEL and LOAEL, not maternal. Paternal body weight was unaffected by ethanol treatment. Fertilization rate was decreased (1/9) among matings 3-5 days after treatment.

>> Fetal data with dose level (with NOAEL value).

Crown-rump length was reduced in the one litter produced by mating 3-5 days after paternal ethanol treatment ended.

>> Statistical results

Fertilization rate was statistically significantly decreased (1/9; $p<0.001$) in matings 3-5 days post-treatment. Fetal crown-rump length in the one mating from this period was reduced ($p<0.001$).

Results Remark

Maternal data:
* Mortality and day of death: No mortality was reported.
* Number pregnant per dose level: 9
* Number aborting: None. However, pregnancy rates were reduced.
* Number of resorptions, early/late if available: Percent resorptions did not differ from control values, and ranged from 0 to 27% across mating intervals.
* Number of implantations: Not reported.
* Pre and post implantation loss, if available: Not reported.
* Number of corpora lutea (recommended): Counted, but data not reported.
* Duration of Pregnancy: Females were sacrificed on gestation day 18.
* Body weight: Paternal but not maternal body weights were measured. They were unaffected by ethanol treatment.
* Food/water consumption: Controls were given diets isocaloric to paternal ethanol diet consumption.
* Description, severity, time of onset and duration of clinical signs: Not reported.
* Hematological findings incidence and severity: Not measured. Paternal blood ethanol levels reached 296 +/- 19 mg%.
* Clinical biochemistry findings incidence and severity: Not measured.
* Gross pathology incidence and severity: Not studied in dams or sires.
* Organ weight changes, particularly effects on total uterine weight: Not measured.
* Histopathology incidence and severity: Not studied.

Fetal data:
* Litter size and weights: Litter size and weight was not affected by ethanol treatment.
* Number viable (number alive and number dead): Percentage of live fetuses was not affected by ethanol treatment.
* Sex ratio: Not affected by ethanol treatment.
* Postnatal growth (depending on protocol): Not applicable.
* Postnatal survival (depending on protocol): Not applicable.
* Grossly visible abnormalities, external, soft tissue and skeletal abnormalities: Only 2 anomalies occurred in 95 pups sired by treated males: undescended testes and body asymmetry. Skeletons were not examined.

Conclusions

EPA High Production Volume (HPV) Track

Toxicity End Point:
Developmental Toxicity/Teratogenicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

This investigation was undertaken to determine whether anomalies seen in fetal alcohol syndrome might be mediated by paternal alcohol intake. Only a single dietary dose of ethanol was studied, but it produced very high peak blood ethanol levels. Only one of nine matings of treated males mated to untreated females 3-5 days post-treatment resulted in a litter, but fertilization rates in matings 6-11 days post-treatment did not differ from control values. The reason for pregnancy failure in the eight other early matings (confirmed by vaginal plugs) was not determined. No fetal effects were observed, except for decreased crown-rump length in the single litter produced from matings 3-5 days post-treatment; this effect awaits confirmation.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Anderson, R., Furby, J., Oswald, C., and Zaneveld, L. (1981). Teratological evaluation of mouse fetuses after paternal alcohol ingestion. Neurobehav. Toxicol. Teratol. 3:117-120.

The authors cite nine other studies of paternally mediated effects of ethanol on offspring; these studies variously report perinatal mortality, stillbirths, decreased viability, altered weight, altered sex ratio, and decreased litter size.

General

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

Revision Date: 10/24/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Developmental toxicity study

>> GLP: Unknown

>> Year study performed: 1977

>> Species

mouse

>> Strain: Mammal strain: CBA/J

>> Sex: F

>> Number of males per dose: 0

>> Number of females per dose: 10

>> Route of Administration: Oral (liquid diet)

>> Days of Gestation: -31-17

>> Frequency of treatment: Ad lib

>> Doses: 15, 20, 25, and 30% ethanol-derived calories

>> Control Group: Yes — Concurrent controls

>> Statistical Method

Not described in any detail, although ANOVA is mentioned.

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

* Age at study initiation: 60-100 days.
* Number of animals per dose per sex: At least 8 per group.
* Note whether vehicle used and concentration/volume: Ethanol was provided in a nutritionally balanced, liquid diet. Females received specific diets for 10 days before graduating to the next higher concentration of ethanol until there were 10 females in each diet group. Thus, depending on dose group, females had been exposed to ethanol for 30 to 80 days before mating. Both lab chow and liquid diet control groups were used.
* Clinical observations performed and frequency: Blood ethanol was measured before mating.
* Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): Mated in pairs during 1.5-hour periods. Copulation plugs were indicative of pregnancy.
* Parameters assessed during study (maternal and fetal): Blood ethanol levels in dams before pregnancy; liver weights in three females sacrificed before mating; fetal weights and anomalies.
* Organs examined at necropsy (macroscopic and microscopic): Adult livers. Fetuses were examined for abnormalities of the skeleton and internal organs.

Results

>> Maternal Precision/NOAEL <

>> Maternal NOAEL dose 15 **>> Unit used** % EtOH-derived cal.

>> Maternal NOAEL effect No NOAEL found.

>> Maternal Precision/LOAEL =

>> Maternal LOAEL dose 15 **>> Unit used** % EtOH-derived cal.

>> Maternal LOAEL effect Resorptions were increased at the lowest dose.

>> Developmental Precision/NOAEL <

>> Developmental NOAEL dose 15 **>> Unit used** % EtOH-derived cal.

>> Developmental NOAEL effect No NOAEL found

>> Developmental Precision/NOAEL =

>> Developmental LOAEL dose 15 **>> Unit used** % EtOH-derived cal.

>> Developmental LOAEL effect Visceral and skeletal anomalies

>> Actual dose

Not reported

>> Maternal data with dose level (with NOAEL value).

At the highest concentration of ethanol in diet, dams resorbed all implants; even at the lowest dose, 57% of implants were resorbed. No other maternal effects were reported.

>> Fetal data with dose level (with NOAEL value).

Fetal weights appeared depressed by maternal ethanol treatment, although no statistical analysis was done. All fetuses examined showed a 100% incidence of skeletal anomalies, chiefly of the skull.

>> Statistical results

Little statistical analysis was conducted. Blood ethanol concentrations increased significantly with dose ($p<0.05$). Daily caloric intakes and relative liver weights did not vary with significance.

Results Remark

Maternal data:
* Mortality and day of death: No early deaths were reported. Pregnant animals were sacrificed on gestation day 17.
* Number pregnant per dose level: 8-10.
* Number aborting: All implants were resorbed at the highest concentration of ethanol in diet.
* Number of resorptions, early/late if available: Early and late resorptions were not distinguished. Resorption rates (as % of all implants at each dose level) were 2% and 0% in lab chow and liquid diet controls, and 57%, 72%, 73%, and 100% in the treatment groups.
* Number of implantations: Implants per litter were 4.8 and 5.6 in the lab chow and liquid diet controls, and 4.0, 5.5, 5.2, and 0 in the treatment groups.
* Pre and post implantation loss, if available: Not specified.
* Number of corpora lutea (recommended): Not measured.
* Duration of Pregnancy: Dams were sacrificed on gestation day 17.
* Body weight: Not given.
* Food/water consumption: Caloric intakes were reported as means of three females per group: 14 and 20 in the lab chow and liquid diet controls, and 20, 18, 15, and 16 in the treatment groups. (Standard errors were given, but no units.)
* Description, severity, time of onset and duration of clinical signs: Not discussed, although dams were described as alcoholic.
* Hematological findings incidence and severity: Not measured. Blood ethanol levels measured before mating in three females per group were 0 and 0 mg/dl in the lab chow and liquid diet controls, and 73, 121, 174, and 315 mg/dl in the treatment groups. (Standard errors were also given.)
* Clinical biochemistry findings incidence and severity: Not measured.
* Gross pathology incidence and severity: Not described.
* Organ weight changes, particularly effects on total uterine weight: Liver weight relative to body weight, measured in three females per group before mating, was not affected by treatment.
* Histopathology incidence and severity: In three females per group sacrificed before mating, no pathology was seen in the liver.

Fetal data:
* Litter size and weights: Litter size was not given. Fetal weights appeared depressed by treatment, with means of 0.97 and 0.95 g in the lab chow and liquid diet controls, and 0.64, 0.33, and 0.51 g in the three lowest ethanol dose groups. (There were no high-dose fetuses.)
* Number viable (number alive and number dead): Not reported.
* Sex ratio: Not reported.
* Postnatal growth (depending on protocol): Not applicable.
* Postnatal survival (depending on protocol): Not applicable.
* Grossly visible abnormalities, external, soft tissue and skeletal abnormalities: Skeletal

abnormalities appeared with 100% incidence in all three ethanol groups yielding fetuses for analysis. The defects were primarily of the occipital bone, but also affected the sternum and ribs. Visceral anomalies affected 0% of fetuses in either control group, and affected 36%, 100%, and 100% of fetuses examined in the three treatment groups yielding fetuses. Dilated brain ventricles were the most prevalent anomaly, but open eyelids, exencephaly, gastroschisis, and heart defects also occurred in the higher dose groups.

Conclusions

This experiment aimed to simulate human chronic alcoholism in CBA mice in order to better understand the fetal alcohol syndrome. Females were fed nutritionally balanced liquid diets containing specified percentages of calories from ethanol; control groups included animals on lab chow and on liquid diet containing sucrose instead of ethanol. Females were started on diets at least 30 days before mating; high-dose females received gradually increasing levels of ethanol in order to avoid weight loss. Blood ethanol levels, measured before mating, showed a significant dose-related increase, but relative liver weight was not affected by ethanol treatment. All implants at the highest dose were resorbed. Fetuses in the three lower dose groups showed 100% incidence of skeletal defects; and high rates (82-100%) of soft-tissue defects.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Chernoff, G. (1977). The fetal alcohol syndrome in mice: an animal model. Teratol. 15:223-230.

General

Revision Date: 10/24/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Developmental toxicity study

>> GLP: Unknown

>> Year study performed: 1977

>> Species

mouse

>> Strain: Mammal strain: C3H/Ig

>> Sex: F

>> Number of males per dose: 0

>> Number of females per dose: 10

>> Route of Administration: Oral (liquid diet)

>> Days of Gestation: -31-17

>> Frequency of treatment: Ad lib

>> Doses: 20, 25, 30, and 35% ethanol-derived calories

>> Control Group: Yes: Concurrent controls

>> Statistical Method

Not described in any detail, although ANOVA is mentioned.

Remarks for Method

* Age at study initiation: 60-100 days.
* Number of animals per dose per sex: At least 8 per goup.
* Note whether vehicle used and concentration/volume: Ethanol was provided in a nutritionally balanced, liquid diet. Females received specific diets for 10 days before graduating to the next higher concentration of ethanol until there were 10 females in each diet group. Thus, depending on dose group, females had been exposed to ethanol for 30 to 80 days before mating. Both lab chow and liquid diet control groups were used.
* Clinical observations performed and frequency : Blood ethanol was measured before mating.
* Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): Mated in pairs during 1.5-hour periods. Copulation plugs were indicative of pregnancy.
* Parameters assessed during study (maternal and fetal): Blood ethanol levels and relative liver weights in females before mating; fetal weights and anomalies.
* Organs examined at necropsy (macroscopic and microscopic): Adult livers. Fetuses were examined for abnormalities of the skeleton and internal organs.

Results

>> Maternal Precision/NOAEL =

>> Maternal NOAEL dose 20 **>> Unit used** % EtOH-derived cal.

>> Maternal NOAEL effect Percentage of implants resorbed.

>> Maternal Precision/LOAEL =

>> Maternal LOAEL dose 25 **>> Unit used** % EtOH-derived cal.

>> Maternal LOAEL effect Increased percentaage of resorptions.

>> Developmental Precision/NOAEL <

>> Developmental NOAEL dose 20 **>> Unit used** % EtOH-derived cal.

>> Developmental NOAEL effect No NOAEL found.

>> Developmental Precision/NOAEL =

>> Developmental LOAEL dose 20 **>> Unit used** % EtOH-derived cal.

>> Developmental LOAEL effect Anomalies and fetal weights.

>> Actual dose

Not reported

>> Maternal data with dose level (with NOAEL value).

At the highest concentration of ethanol in diet, dams resorbed all implants; at the lowest dose, no implants were resorbed. No other maternal effects were reported.

>> Fetal data with dose level (with NOAEL value).

Fetal weights appeared depressed by maternal ethanol treatment, although no statistical analysis was done. Fetuses showed high rates of skeletal and visceral anomalies at all doses yielding fetuses.

>> Statistical results

Little statistical analysis was conducted. Blood ethanol concentrations increased significantly with dose ($p<0.05$). Daily caloric intakes and relative liver weights did not vary with significance.

Results Remark

Maternal data:
* Mortality and day of death: No early deaths were reported. Pregnant animals were sacrificed on gestation day 17.
* Number pregnant per dose level: 8-10.
* Number aborting: All implants were resorbed at the highest concentration of ethanol in diet.
* Number of resorptions, early/late if available: Early and late resorptions were not distinguished. Resorption rates (as % of all implants at each dose level) were 7% and 0% in lab chow and liquid diet controls, and 0%, 30%, 72%, and 100% in the treatment groups.
* Number of implantations: Implants per litter were 11 and 7.3 in the lab chow and liquid diet controls, and 6.8, 6.5, 6.1, and 0 in the treatment groups.
* Pre and post implantation loss, if available: Not specified.
* Number of corpora lutea (recommended): Not measured.
* Duration of Pregnancy: Dams were sacrificed on gestation day 17.
* Body weight: Not given.
* Food/water consumption: Caloric intakes were reported as means of three females per group (before mating): 16 and 20 in the lab chow and liquid diet controls, and 19, 17, 17, and 16 in the treatment groups. (Standard errors were given but no units.)
* Description, severity, time of onset and duration of clinical signs: Not discussed, although dams were described as alcoholic.
* Hematological findings incidence and severity: Not measured. Blood ethanol levels measured before mating in three females per group were 0 and 0 mg/dl in the lab show and liquid diet controls, and 103, 160, 289, and 398 mg/dl in the treatment groups. (Standard errors were also given.)
* Clinical biochemistry findings incidence and severity: Not measured.
* Gross pathology incidence and severity: Not described.
* Organ weight changes, particularly effects on total uterine weight: Liver weight relative to body weight, measured in three females per group before mating, was not affected by treatment.
* Histopathology incidence and severity: In three females per group sacrificed before mating, no pathology was seen in the liver.

Fetal data:
* Litter size and weights: Litter size was not given. Fetal weights appeared depressed by ethanol treatment, with means of 1.14 and 1.27 g in the lab chow and liquid diet controls, and 0.77, 0.50, and 0.58 g in the three lowest ethanol dose groups. (There were no high-dose fetuses.)
* Number viable (number alive and number dead): Not reported.
* Sex ratio: Not reported.
* Postnatal growth (depending on protocol): Not applicable.
* Postnatal survival (depending on protocol): Not applicable.

* Grossly visible abnormalities, external, soft tissue and skeletal abnormalities: Skeletal anomalies affected 6% and 4% of lab chow and liquid diet control fetuses, 82% of the low-dose fetuses, and 100% of fetuses in the next two highest groups. The defects were primarily of the occipital bone, but also affected the sternum and ribs. Visceral anomalies affected 0% and 2% of lab chow and liquid diet control fetuses, 78% of low-dose ethanol fetuses, and 100% of fetuses in the next two highest ethanol dose groups. Defects of the brain (dilated ventricles) and heart were most prevalent.

Conclusions

This experiment aimed to simulate human chronic alcoholism in C3H mice in order to better understand the fetal alcohol syndrome. Females were fed nutritionally balanced iquid diets containing specified percentages of calories from ethanol; control goups included animals on lab chow and on liquid diet containing sucrose instead of ethanol. Females were started on diets at least 30 dyas before mating; high-dose females received gradually increasing levels of ethanol in order to avoid weight loss. Blood ethanol levels, measured before mating, showed a significant dose-related increase, but relative liver weight was not affected by ethanol treatment. All implants at the highest dose were resorbed. Fetuses in the three lower dose groups showed high rates (82-100%) of skeletal defects and high rates (78-100%) of soft-tissue defects.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Chernoff, G. (1977). The fetal alcohol syndrom in mice: an animal model. Teratol. 15:223-230.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Developmental Toxicity/Teratogenicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

Revision Date: 10/24/2000

Test Substance

Remarks: 200-proof ethanol

Chemical Category

Method

>> Method/Guideline followed

Teratology probe

>> GLP: Unknown

>> Year study performed: 1987

>> Species

mouse

>> Strain: Mammal strain: CD-1

>> Sex: F

>> Number of males per dose: 0

>> Number of females per dose: 6

>> Route of Administration: Oral (gavage)

>> Days of Gestation: 8-14

>> Frequency of treatment: Once per day

>> Doses: 2,200, 3,600, 5,000, 6,400, and 7,800 mg/kg

>> Control Group: Yes — Concurrent controls

>> Statistical Method

Bartlett's test for homogeneity of variance, one-way analysis of variance, Dunnett's test, Duncan's test, Kruskal-Wallis test, Dunn's test, nested analysis of variance.

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

* Age at study initiation: 8-10 weeks.
* Number of animals per dose per sex: 6 confirmed pregnant animals/group.
* Note whether vehicle used and concentration/volume: Ethanol was administered in distilled water; gavaged with 10-ml bolus doses.
* Clinical observations performed and frequency: Physical examinations were performed, and weights taken, on six occasions during pregnancy. Animals were checked for viability twice daily.
* Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): Females were paired, 1:1, with males; copulatory plugs were considered indicative of pregnancy.
* Parameters assessed during study (maternal and fetal): Maternal body weights; numbers of implantation sites, resorptions, live and dead fetuses, fetal weights, external abnormalities.
* Organs examined at necropsy (macroscopic and microscopic): None.

Results

>> Maternal Precision/NOAEL =

>> Maternal NOAEL dose 2200 **>> Unit used** mg/kg

>> Maternal NOAEL effect No mortality or clinical signs of toxicity.

>> Maternal Precision/LOAEL =

>> Maternal LOAEL dose 3600 **>> Unit used** mg/kg

>> Maternal LOAEL effect Lethargy, staggered gait, mortality.

>> Developmental Precision/NOAEL >=

>> Developmental NOAEL dose 6400 **>> Unit used** mg/kg

>> Developmental NOAEL effect No changes in developmental parameters.

>> Developmental Precision/NOAEL >

>> Developmental LOAEL dose 6400 **>> Unit used** mg/kg

>> Developmental LOAEL effect No NOAEL found

>> Actual dose

Not reported.

>> Maternal data with dose level (with NOAEL value).

No maternal mortality occurred at 2,200 mg/kg, but 1/6 dams died at 3,600 mg/kg, rising to 6/6 at 7,700 mg/kg. At doses of at least 3,600 mg/kg, dams were lethargic and showed labored breathing.

>> Fetal data with dose level (with NOAEL value).

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

At 5,000 mg/kg, resorptions/litter were increased and live fetuses/litter were decreased, but this did not occur at lower doses or at 6,400 mg/kg (based on 1 litter). No other fetal effects were seen.

>> Statistical results

The two significant litter effects noted above were significant at the 0.05 level.

Results Remark

Maternal data:
* Mortality and day of death: No control animals died. Mortality rates in the treatment groups (low to high) were 0/6, 1/6, 4/6, 5/6, and 6/6. The day of death was not reported.
* Number pregnant per dose level: 6
* Number aborting: Not reported. By inspection, it seems that perhaps 2 litters were aborted at 5,000 mg/kg. The one surviving dam at 6,400 mg/kg delivered a litter.
* Number of resorptions, early/late if available: Not distinguished. Resorptions per litter (means varying from 0.8 to 7.0) did not differ from control except in the 5,000 mg/kg group.
* Number of implantations: Mean implants per litter ranged from 10.5 (control) to 13.83, but no statistically significant effect of treatment was noted.
* Pre and post implantation loss, if available: Not reported.
* Number of corpora lutea (recommended): Not measured.
* Duration of Pregnancy: Dams were sacrificed on gestation day 18.
* Body weight: Not affected by treatment (data not shown).
* Food/water consumption: Not reported.
* Description, severity, time of onset and duration of clinical signs: Timing and duration were not reported. At doses of 3,600 mg/kg or more, dams exhibited lethargy, staggered gait, and/or labored breathing.
* Hematological findings incidence and severity: Not measured.
* Clinical biochemistry findings incidence and severity: Not measured.
* Gross pathology incidence and severity: Not reported.
* Organ weight changes, particularly effects on total uterine weight: Not measured.
* Histopathology incidence and severity: Not reported.

Fetal data:
* Litter size and weights: Litter size was not reported. Group mean litter weights ranged from 1.33 g (control) to 0.99 g, and did not vary with statistical significance.
* Number viable (number alive and number dead): The mean number of dead fetuses per litter did not vary significantly with dose, and ranged from 0 to 0.5. The number of live fetuses differed significantly from control only in the 5,000 mg/kg dose group.
* Sex ratio: Not reported.
* Postnatal growth (depending on protocol): Not applicable.
* Postnatal survival (depending on protocol): Not applicable.
* Grossly visible abnormalities, external, soft tissue and skeletal abnormalities: No externally malformed fetuses were found in the treatment groups. Other types of anomalies were not sought.

Conclusions

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	

This "teratology probe" study of ethanol in CD-1 mice examined a limited number of endpoints. Acute maternal toxicity was clearly produced by oral ethanol doses of 3,600 mg/kg or more (including mortality), but no other maternal effects were reported. No dose-related adverse effects on fetuses were observed: two effects (increased resorptions and decreased live fetuses/litter) seen at 5,000 mg/kg did not occur at 6,400 mg/kg, and no trends were evident. No fetuses in the ethanol groups showed external malformations. Thus, ethanol had no clear effect on fetuses in this study, although dams were definitely affected.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Wier, P., Lewis, S., and Traul, K. (1987). A comparison of developmental toxicity evident at term to postnatal growth and survival using ethylene glycol monoethyl ether, ethylene glycol monobutyl ether, and ethanol. Teratogen. Carcinogen. Mutagen. 7:55-64.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Repeated Dose Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 02/23/2001

Test Substance

Remarks: Ethanol was spectroscopically pure.

Chemical Category

Method

>> Method/Guideline followed

Subchronic toxicity study

>> GLP Unknown

>> Year study performed 1986

>> Species

rat

>> Strain Mammal strain: Sprague-Dawley

>> Sex Both

>> Number of males per dose 20

>> Number of females per dose 20

>> Route of Administration Oral (semisynthetic liquid diet)

>> Exposure Period 90

>> Frequency of treatment Daily

>>Doses 5%, 10% w/w ethanol in liquid diet

>> Control Group Yes

>> Post observation period Not reported.

>> Statistical Method No tests of significance, apparently.

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age at study initiation: 70 days.
* No. of animals per sex per dose: 18-20 per sex, per dose group.
* Note whether vehicle used and concentration/volume: Ethanol was supplied in nutritionally balanced liquid diet at specified % w/w.
* Satellite groups and reasons they were added: None.
* Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Body weight was measured weekly and food consumption was measured daily.
* Organs examined at necropsy (macroscopic and microscopic): Liver and kidney; the spleen was also weighed.

Results

>> NOAEL Precision <

>> NOAEL dose 5 **>> Unit** % w/w EtOH in diet

>> NOAEL Effect

No NOAEL was found.

>> LOAEL Precision =

>> LOAEL dose 5 **>> Unit** % w/w EtOH in diet

>> LOAEL Effect

Hepatic steatosis and necrosis, chiefly in males.

>> Actual dose received by dose level by sex

Not available. See conclusions section.

>> Toxic response

At 5% w/w ethanol in diet, males showed hepatic steatosis, necrosis of hepatic cells, and Mallory bodies. These changes were absent or mild in females at this dose.

>> Statistical results

No significance tests were performed, but means, standard deviations, and group sizes are given.

Results Remark

* Body weight: Animals in the low-dose group gained weight normally. Animals in the high-dose group lost weight overall, with marked decreased during the first 3-4 weeks. Thereafter, they gained weight.
* Food/water consumption: At 5% w/w ethanol in diet, females consumed 169 ml diet/kg-d and males 136 ml diet/kg-d. At 10% w/w ethanol in diet, females consumed 117 ml diet/kg-d and males 101 ml diet/kg-d. Consumption in the 10% group was reduced, relative to controls.

EPA High Production Volume (HPV) Track

Toxicity End Point:
Repeated Dose Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Description, severity, time of onset and duration of clinical signs: No adverse clinical signs were observed in the 5% group, but at 10%, all animals showed anorexia, depression, ruffled fur, and increased sensitivity to noise (sometimes causing convulsions).
* Ophthalmologic findings incidence and severity: Not examined.
* Hematological findings incidence and severity: Not examined.
* Clinical biochemistry findings incidence and severity: Not examined.
* Mortality and time to death: No deaths occurred at 5 or 10% ethanol in diet.
* Gross pathology incidence and severity: Some livers in the 5% and most livers in the 10% ethanol groups appeared yellowish. Bodies of the 10% ethanol groups showed wasting, with loss of fatty tissue and skeletal muscle.
* Organ weight changes: Relative liver, kidney, and spleen weights were normal at 5% ethanol in diet, while relative liver and kidney weights appeared slightly increased at 10% ethanol.
* Histopathology incidence and severity: Minimal periportal hepatic steatosis and centrolobular steatosis ocurred in 4/20 and 14/40 females, respectively, in the 5% ethanol group. In males at 5% ethanol, slight to moderate periportal and centrolobular steatosis was seen in 16/20 and 17/20 rats, respectively. At 10% ethanol, 3/18 females showed moderate periportal steatosis and all showed slight to severe centrolobuloar steatosis. In males, slight to moderate periportal steatosis and severe centrolobular steatosis occurred in 17/18 and 18/18 animals. Females in all groups showed normal frequencies of proliferating RE cells and acidophilic bodies, but increases in both occurred in males at both dose levels. In males of both groups, but only in females given 10% ethanol in diet, necrosis of hepatic cells and Mallory bodies were seen. In kidneys, few calcifications or tubular casts were observed. The incidence and severity of tubular fatty change increased with ethanol exposure, more so in females.

Conclusions

This 90-day study in rats was one of two range-finding studies for a two-year cancer bioassay. Ethanol was supplied as specified percentages (w/w) in a liquid diet. As the density of the diet was not reported, the ethanol doses cannot be accurately determined. However, as the diet was probably at least as dense as water, the ethanol doses were likely greater than 8.45 g/kg-d (females at 5%), 6.8 g/kg-d (males at 5%), 11.7 g/kg-d (females at 10%), and 10.1 g/kg-d (males at 10%). Ten percent ethanol in diet was clearly toxic to both sexes, while 5% caused mild effects in females and more significant effects in males.

Data Quality

Reliability

Data Reliability Remarks

Reference

EPA High Production Volume (HPV) Track

Toxicity End Point:
Repeated Dose Toxicity

Sponsor ID	9999999	Sponsor Named In Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> Remarks

Holmberg, B., Kronevi, T., and Ekner, A. (1986). Subchronoic toxicity investigation of ethyl alcohol: a test for lowest effective dose (led) to be used in a long-term bioassay for carcinogenicity. National Board of Occupational Safety and Health, Solna, Sweden.

General

Two subchronic studies are reported by Holmberg et al., and are separately summarized in this database.

EPA High Production Volume (HPV) Track

Toxicity End Point:
Repeated Dose Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 10/26/2000

Test Substance

Remarks: Ethanol was spectroscopically pure.

Chemical Category

Method

>> Method/Guideline followed

Subchronic toxicity study

>> GLP Unknown

>> Year study performed 1986

>> Species

rat

>> Strain Mammal strain: Sprague-Dawley

>> Sex M

>> Number of males per dose 10

>> Number of females per dose 0

>> Route of Administration Oral (semisynthetic liquid diet)

>> Exposure Period 90

>> Frequency of treatment Daily

>>Doses 1, 2, 3, 4, 5% w/w ethanol in liquid diet

>> Control Group No

>> Post observation period Not reported.

>> Statistical Method No tests of significance, apparently.

Remarks for Method

* Age at study initiation: 43 days.
* No. of animals per sex per dose: 10 per dose group
* Note whether vehicle used and concentration/volume: Ethanol was supplied in nutritionally balanced liquid diet at specified w/w%.
* Satellite groups and reasons they were added: None.
* Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Body weight was measured weekly and food consumption was measured daily. At study termination, blood samples were taken for measurement of aspartate aminotransferase and alanine aminotransferase.
* Organs examined at necropsy (macroscopic and microscopic): Liver and kidney; the spleen was also weighed.

Results

>> NOAEL Precision =

>> NOAEL dose 2 **>> Unit** % w/w EtOH in diet

>> NOAEL Effect

Very mild and infrequent liver lesions

>> LOAEL Precision =

>> LOAEL dose 3 **>> Unit** % w/w EtOH in diet

>> LOAEL Effect

Mild liver lesions

>> Actual dose received by dose level by sex

Not available. See conclusions section.

>> Toxic response

Body weights and serum liver enzymes were not affected by treatment, and kidney findings were minimal. Hepatic centrolobular steatosis increased in severity with dose, as did the frequency and severity of Mallory bodies (hyaline) and acidophilic degeneration and necrosis. Most liver findings were absent or mild at 2% w/w ethanol in diet, but became more significant at 3% and higher dose.

>> Statistical results

No significance tests were performed, but means, standard deviations, and group sizes are given.

Results Remark

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Body weight: All groups gained weight, though final weights decreased with dose.
* Food/water consumption: At the 1%, 2%, 3%, 4%, and 5% w/w ethanol in liquid diet levels, daily intakes were respectively 201 ml diet/kg-d, 195 ml diet/kg-d, 194 ml diet/kg-d, 188 ml diet/kg-d, and 182 ml diet/kg-d.
* Description, severity, time of onset and duration of clinical signs: No adverse responses were observed.
* Ophthalmologic findings incidence and severity: Not examined.
* Hematological findings incidence and severity: Not examined.
* Clinical biochemistry findings incidence and severity: Liver enzyme activities did not appear to vary regularly with dose.
* Mortality and time to death: No deaths occurred.
* Gross pathology incidence and severity: Livers of the 1% and 2% groups appeared normal, but in the higher dose groups, livers appeared yellowish (true for most animals given 5% ethanol in diet).
* Organ weight changes: No dose-related changes in liver, kidney, or spleen weights (absolute or relative) were seen.
* Histopathology incidence and severity: Periportal and centrolobular hepatic steatosis was seen in all animals, with the severity increasing with dose. Mallory bodies were seen at 3% ethanol and higher concentrations, and acidophilic degeneration and necrosis at 4% and higher. RE cell proliferation was slight at 1% and 2% ethanol in diet. A few kidney tubular casts were noted at doses of 1-3%, and a few calcifications at doses of 3-5%. In all groups, some very slight-slight degree of tubular fatty change occurred.

Conclusions

These results are for the second of two subchronic studies of ethanol in rats reported in the same publication. Concurrent controls were not used in this sub-study, complicating the evaluation of the liver findings. In addition, rats in this sub-study were younger than in the other experiment. The authors identified 3% w/w ethanol in diet as producing a "slight effect" on the liver, and selected it as the maximum dose for a long-term cancer bioassay. As the density of the liquid diet was not reported, the ethanol doses cannot be accurately determined. However, as the diet was probably at least as dense as water, the ethanol doses were likely greater than 2 g/kg-d (at 1%), 3.9 g/kg-d (2%), 5.8 g/kg-d (3%), 7.5 g/kg-d (4%), and 9.1 g/kg-d (5%).

Data Quality

Reliability

Data Reliability Remarks

Reference

EPA High Production Volume (HPV) Track

Toxicity End Point:
Repeated Dose Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> Remarks

Holmberg, B., Kronevi, T., and Ekner, A. (1986). Subchronic toxicity investigation of ethyl alcohol: a test for lowest effective dose (led) to be used in a long-term bioassay for carcinogenicity. National Board of Occupational Safety and Health, Solna, Sweden.

General

Two subchronic studies are reported by Holmberg et al., and are separately summarized in this database.

EPA High Production Volume (HPV) Track

Toxicity End Point:
Repeated Dose Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 10/26/2000

Test Substance

Remarks: 95% ethanol by infrared spectroscopy

Chemical Category

Method

>> Method/Guideline followed

National Toxicity Program 13-week toxicity protocol

>> GLP Yes

>> Year study performed 1991

>> Species

rat

>> Strain Mammal strain: Fischer 344/N

>> Sex M

>> Number of males per dose 10

>> Number of females per dose 0

>> Route of Administration Oral (drinking water)

>> Exposure Period 90

>> Frequency of treatment Ad lib, 7 d/wk

>>Doses 5% w/v ethanol in deionized water

>> Control Group Yes

>> Post observation period None

>> Statistical Method t- and F-tests (used by preparers of this summary)

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age at study initiation: 43-46 days when started on test.
* No. of animals per sex per dose: 10
* Note whether vehicle used and concentration/volume: Ethanol was diluted in deionized water.
* Satellite groups and reasons they were added: Satellite groups of 10 animals were used for hematology and clinical chemistry exams at 3 and 23 days.
* Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Body weights and water consumption were measured weekly, and clinical observations were made weekly. Hematology and clinical chemistry exams at day 3, day 23, and week 13. Sperm motility was evaluated at the end of the study.
* Organs examined at necropsy (macroscopic and microscopic): Complete necropsies were performed.

Results

>> NOAEL Precision <

>> NOAEL dose 5 **>> Unit** % in drinking water

>> NOAEL Effect

No NOAEL found

>> LOAEL Precision =

>> LOAEL dose 5 **>> Unit** % in drinking water

>> LOAEL Effect

Increased concentration of bile acids, decreased thymus weight, increased heart weight.

>> Actual dose received by dose level by sex

About 1 g/d

>> Toxic response

Only one ethanol dose level was used. Absolute and relative thymus weights and reticulocyte count were decreased at termination, while relative heart weight and serum bile acids were increased.

>> Statistical results

Effects mentioned here are significant at the 0.05 level.

Results Remark

* Body weight: Terminal body weight was not affected by treatment.
* Food/water consumption: Drinking water consumption was not affected by treatment.
* Description, severity, time of onset and duration of clinical signs: No adverse signs were noted.
* Ophthalmologic findings incidence and severity: Not examined.
* Hematological findings incidence and severity: Reticulocyte count was decreased at 13 weeks. Some other hematologic paramters were altered at day 3 and/or 23 but not at week 13. Most values differing from control values differed by less than 10%.
* Clinical biochemistry findings incidence and severity: Serum concentrations of total protein and bile acids varied from control values at week 13, while two other parameters differed only at day 23. Total protein was decreased at day 23 but increased at week 13 (by less than 10% in each case), while bile acids at week 13 were increased by 33%.
* Mortality and time to death: No premature deaths occurred.
* Gross pathology incidence and severity: See below. Sperm parameters were unaffected by treatment.
* Organ weight changes: Relative heart weight was increased by about 10%, while absolute and relative thymus weights were decreased.
* Histopathology incidence and severity: Mild cardiomyopathy occurred in all control and 9/10 test animals, and mild nephropathy occurred in all animals.

Conclusions

These data are extracted from an NTP study of urethane in drinking water (at multiple doses) with or without 5% w/v ethanol. NTP did not compare the 0% and 5% ethanol control groups with each other. Compared to animals drinking deionized water only, animals drinking water with 5% ethanol had a decrease in thymus weight of about 20% after 13 weeks. Reticulocyte count was increased, and serum bile acid concentration increased, at 13 weeks, while some other parameters varied from control values at day 3 or 23. Reproductive tissues and sperm counts were not affected by treatment.

Data Quality

Reliability Data are deemed highly reliable.

Data Reliability Remarks

This experiment was sponsored within the last 10 years by the National Toxicology Program and is thus expected to be of high quality.

Reference

EPA High Production Volume (HPV) Track

Toxicity End Point:
Repeated Dose Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> Remarks

National Toxicology Program (1996). NTP Technical Report on Toxicity Studies of Urethane in Drinking Water and Urethane in 5% Ethanol Administered to F344/N Rats and B6C3F1 Mice. NTP: Research Triangle Park, NC.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Repeated Dose Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 10/26/2000

Test Substance

Remarks: 95% ethanol by infrared spectroscopy

Chemical Category

Method

>> Method/Guideline followed

National Toxicology Program 13-week toxicity protocol

>> GLP Yes

>> Year study performed 1991

>> Species

rat

>> Strain Mammal strain: Fischer 344/N

>> Sex F

>> Number of males per dose 0

>> Number of females per dose 10

>> Route of Administration Oral (drinking water)

>> Exposure Period 90

>> Frequency of treatment Ad lib, 7 d/wk

>>Doses 5% w/v ethanol in deionized water.

>> Control Group Yes

>> Post observation period None

>> Statistical Method t- and F-tests (used by preparers of this summary)

Remarks for Method

* Age at study initiation: 43-46 days when started on test.
* No. of animals per sex per dose: 10
* Note whether vehicle used and concentration/volume: Ethanol was diluted in deionized water.
* Satellite groups and reasons they were added: Satellite groups of 10 animals were used for hematology and clinical chemistry exams at 3 and 23 days and week 13.
* Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Body weights and water consumption were measured weekly, and clinical observations were made weekly. Hematology and clinical chemistry exams at day 3, 23 and week 13. Vaginal cytology was performed 12 days before study termination.
* Organs examined at necropsy (macroscopic and microscopic): Complete necropsies were performed.

Results

>> NOAEL Precision <

>> NOAEL dose 5 **>> Unit** % in drinking water

>> NOAEL Effect

No NOAEL found

>> LOAEL Precision =

>> LOAEL dose 5 **>> Unit** % in drinking water

>> LOAEL Effect

Increased concentration of bile acids, increased estrous cycle length, hepatodiaphragmatic nodules.

>> Actual dose received by dose level by sex

About 0.8 g/d

>> Toxic response

Only one ethanol dose level was used. Body and organ weights were unaffected by 13 weeks of exposure to 5% ethanol in drinking water, while alanine aminotransferase was decreased and serum bile acids were increased at the end of treatment. Hepatodiaphragmatic nodules were observed only in ethanol-exposed animals.

>> Statistical results

Effects mentioned here are significant at the 0.05 level.

Results Remark

* Body weight: Terminal body weight was not affected by treatment.
* Food/water consumption: Drinking water consumption was not affected by treatment.
* Description, severity, time of onset and duration of clinical signs: No adverse signs were noted.
* Ophthalmologic findings incidence and severity: Not examined.
* Hematological findings incidence and severity: Several parameters were altered at day 3 or 23, but none differed significantly from control values at 13 weeks. Changes were usually very slight.
* Clinical biochemistry findings incidence and severity: The only clinical chemistry parameters differing from control values at week 13 were serum alanine aminotransferase (decreased by about 10%) and bile acid concentration (nearly doubled). Estrous cycle length was increased by a bit less than one day.
* Mortality and time to death: No premature deaths occurred.
* Gross pathology incidence and severity: See below.
* Organ weight changes: No significant changes.
* Histopathology incidence and severity: Minimal nephropathy occurred in 40% of test animals and in 0% of controls. No liver lesions were found in controls, but 40% of test animals had hepatodiaphragmatic nodules.

Conclusions

These data are extracted from an NTP study of urethane in drinking water (at multiple doses) with or without 5% w/v ethanol. NTP did not compare the 0% and 5% ethanol control groups with each other. In the 5% ethanol group, increased concentration of serum bile acids, decreased concentration of alanine aminotransferase, increased estrous cycle length, and hepatodiaphragmatic nodules were observed.

Data Quality

Reliability Data are deemed highly reliable.

Data Reliability Remarks

This experiment was sponsored within the last 10 years by the National Toxicology Program and is thus expected to be of high quality.

Reference

>> Remarks

National Toxicology Program (1996). NTP Technical Report on Toxicity Studies of Urethane in Drinking Water and Urethane in 5% Ethanol Administered to F344/N Rats and B6C3F1 mice. NTP: Research Triangle Park, NC.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Repeated Dose Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

EPA High Production Volume (HPV) Track

Toxicity End Point:
Repeated Dose Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/02/2000

Test Substance

Remarks: 95% ethanol by infrared spectroscopy

Chemical Category

Method

>> Method/Guideline followed

National Toxicology Program 13-week toxicity protocol

>> GLP Yes

>> Year study performed 1991

>> Species

mouse

>> Strain Mammal strain B6C3F1

>> Sex M

>> Number of males per dose 10

>> Number of females per dose 0

>> Route of Administration Oral (drinking water)

>> Exposure Period 90

>> Frequency of treatment Ad lib, 7 d/wk

>>Doses 5% w/v ethanol in deionized water.

>> Control Group Yes

>> Post observation period None

>> Statistical Method t- and F-tests (used by preparers of this summary)

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age at study initiation: 43-46 days when started on test.
* No. of animals per sex per dose: 10
* Note whether vehicle used and concentration/volume: Ethanol was diluted in deionized water.
* Satellite groups and reasons they were added: None.
* Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Body weights and water consumption were measured weekly, and clinical observations were made weekly. Sperm motility was evaluated at the end of the study.
* Organs examined at necropsy (macroscopic and microscopic): Complete necropsies were performed.

Results

>> NOAEL Precision <

>> NOAEL dose 5 **>> Unit** % in drinking water

>> NOAEL Effect

No NOAEL found

>> LOAEL Precision =

>> LOAEL dose 5 **>> Unit** % in drinking water

>> LOAEL Effect

Body and organ weight increases; decreased sperm concentration.

>> Actual dose received by dose level by sex

About 0.4 g/d

>> Toxic response

Only one ethanol dose level was used. Relative to controls, terminal body weights in ethanol-exposed mice were increased, as were absolute heart, kidney, liver, and lung weights, and relative liver weight. The concentration of sperm in cauda epididymis was decreased by about 30%. Minimal nephropathy occurred in 30% of ethanol-treated animals, compared to 10% of control animals. Fatty change of the liver occurred in 20% and 0% of treated and control animals, respectively.

>> Statistical results

Increases in body and organ weights, and decreases in sperm count, are signficiant at the 0.05 level.

Results Remark

* Body weight: Terminal body weight was increased by an average of 2.5 g by ethanol treatment.
* Food/water consumption: Animals given ethanol in water drank significantly more water than controls.
* Description, severity, time of onset and duration of clinical signs: No adverse signs were noted.
* Ophthalmologic findings incidence and severity: Not examined.
* Hematological findings incidence and severity: Not examined.
* Clinical biochemistry findings incidence and severity: Not examined.
* Mortality and time to death: No premature deaths occurred.
* Gross pathology incidence and severity: See below.
* Organ weight changes: Absolute heart weight was increased by 11%, absolute kidney weight by 12%, absolute liver weight by 18%, and absolute lung weight by 16%. Relative liver weight was increased by 11%.
* Histopathology incidence and severity: Minimal nephropathy occurred in 30% of treated animals and 10% of control animals. Fatty change in the liver occurred in 20% of treated animals and 0% of control animals.

Conclusions

These data are extracted from an NTP study of urethane in drinking water (at multiple doses) with or without 5% w/v ethanol. NTP did not compare the 0% and 5% ethanol groups with each other. Male mice given ethanol in water gained significantly more weight, showed increased relative liver weight, fatty change in the liver, some mild nephropathy, and decreased sperm count.

Data Quality

Reliability Data are deemed highly reliable.

Data Reliability Remarks

This experiment was sponsored within the last 10 years by the National Toxicology Program and is thus expected to be of high quality.

Reference

>> Remarks

National Toxicology Program (1996). NTP Technical Report on Toxicity Studies of Urethane in Drinking Water and Urethane in 5% Ethanol Administered to F344/N Rats and B6C3F1 Mice. NTP: Research Triangle Park, NC.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Repeated Dose Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

EPA High Production Volume (HPV) Track

Toxicity End Point:
Repeated Dose Toxicity

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 11/02/2000

Test Substance

Remarks: 95% ethanol by infrared spectroscopy

Chemical Category

Method

>> Method/Guideline followed

National Toxicology Program 13-week toxicity protocol

>> GLP Yes

>> Year study performed 1991

>> Species

mouse

>> Strain Mammal strain B6C3F1

>> Sex F

>> Number of males per dose 0

>> Number of females per dose 10

>> Route of Administration Oral (drinking water)

>> Exposure Period 90

>> Frequency of treatment Ad lib, 7 d/wk

>>Doses 5% w/v ethanol in deionized water.

>> Control Group Yes

>> Post observation period None

>> Statistical Method t- and F-tests (used by preparers of this summary)

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age at study initiation: 43-46 days when started on test.
* No. of animals per sex per dose: 10
* Note whether vehicle used and concentration/volume: Ethanol was diluted in deionized water.
* Satellite groups and reasons they were added: None.
* Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Body weights and water consumption were measured weekly, and clinical observations were made weekly. Vaginal cytology was performed 12 days before study termination.
* Organs examined at necropsy (macroscopic and microscopic): Complete necropsies were performed.

Results

>> NOAEL Precision =

>> NOAEL dose 5 **>> Unit** % in drinking water

>> NOAEL Effect

Body and organ weights, estrous cycle length.

>> LOAEL Precision >

>> LOAEL dose 5 **>> Unit** % in drinking water

>> LOAEL Effect

No LOAEL found

>> Actual dose received by dose level by sex

About 0.3 g/d

>> Toxic response

Only one ethanol dose was used. Body and organ weights (relative and absolute) were unaffected by ethanol treatment, nor was estrous cycle length. Frequencies of non-neoplastic lesions were not notably different, compared to control animals.

>> Statistical results

No differences between treatment and control groups were significant at the 0.05 level.

Results Remark

* Body weight: Unaffected by treatment.
* Food/water consumption: Water consumption was somewhat decreased in the ethanol group.
* Description, severity, time of onset and duration of clinical signs: No adverse signs were noted.
* Ophthalmologic findings incidence and severity: Not examined.
* Hematological findings incidence and severity: Not examined.

* Clinical biochemistry findings incidence and severity: Not examined.
* Mortality and time to death : No premature deaths occurred.
* Gross pathology incidence and severity: See below.
* Organ weight changes: No organs weights differed significantly from control values.
* Histopathology incidence and severity: Non-neoplastic lesions did not differ notably in type or frequency, compared to control.

Conclusions

These data are extracted from an NTP study of urethane in drinking water (at multiple doses) with or without 5% w/v ethanol. NTP did not compare the 0% and 5% ethanol control groups with each other. Exposure to 5% ethanol in drinking water had little effect on female mice: organ and body weights were unchanged, and frequencies of non-neoplastic lesions were not very different from control values. Estrous cycle length was unchanged. Time spent in diestrus and proestrus was somewhat increased, but it is not clear if these changes were significant.

Data Quality

Reliability Data are deemed highly reliable.

Data Reliability Remarks

This experiment was sponsored within the last 10 years by the National Toxicology Program and is thus expected to be of high quality.

Reference

>> Remarks

National Toxicology Program (1996). NTP Technical Report on Toxicity Studies of Urethane in Drinking Water and Urethane in 5% Ethanol Administered to F344/N Rats and B6C3F1 Mice. NTP: Research Triangle Park, NC.

General

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity to Reproduction

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 02/23/2001

Test Substance

Remarks: 92% pure ethanol

Chemical Category

Method

>> Method/Guideline followed

Fertility assessment by continuous breeding: NTP protocol

>> Test Type

Two generation study

>> GLP Unknown

>> Year study performed 1985

>> Species mouse

>> Strain Mammal strain CD-1

>> Sex Both

>> Number of males per dose 20

>> Number of females per dose 20

>> Route of Administration Oral (drinking water)

>> Exposure period 105

>> Frequency of treatment Ad lib

>> Doses 5, 10, 15% (v/v) ethanol in water

>> Control Group Yes

>> Premating exposure period for female. P: 7 d. F1: 74 d.

>> Premating exposure period for male. P: 7 d. F1: 74 d.

>> Statistical Method Kruskal-Wallis, Mann-Whitney U, Chi-square, ANOVA

Remarks for Method

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity to Reproduction

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Number, age, sex per dose for P, F1 and F2, if appropriate: P generation: approximately 6 weeks old on receipt, 11 weeks old at the start of exposure. About 20 animals/sex/dose group. F1 animals (20; high-dose only) were mated when about 74 days old.
* Note whether vehicle used and concentration/volume. Ethanol was given in deionized, filtered water.
* Dosing schedules and pre and post dosing observations periods for P, F1 and F2, if appropriate: P generation: dosed during a 7-day pre-mating period, then continuously for 98 days. F1 animals (high-dose only) continued on ethanol until mating.

* Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): Animals were mated in pairs. P breeding pairs cohabited for 98 days. Litters were proof of pregnancy. F1 animals were cohabited in pairs for 7 days.
* Standardization of litters (yes/no and if yes, how and when): Not applicable.

* Parameters assessed during study P and F1 as appropriate
- Clinical observations performed and frequency (clinical pathology, functional observations, etc.): None reported.
- Estrous cycle length and pattern (number of days spent in each phase): Not studied.
- Sperm examination (epididymal or vas sperm, concentration, motility, morphology): Assessed in F1 high-dose males only.
- Organ weights: In adult, high-dose F1 animals only. Liver, kidney/adrenal, and male sex organs.

* Parameters assessed during study F1 and F2, as appropriate: F2 parameters were litter data.
- Clinical observations performed and frequency (weight gain, growth rate, etc.): Weight gain of high-dose F1 animals was assessed over 74 days.
- Others, for example anogenital distance, if performed: Not measured.
- Organs examined at necropsy (macroscopic and microscopic): No examination.

Results

>> Parental Precision/NOAEL	=		
>> Parental NOAEL dose	15	**>> Parental NUnit used**	% EtOH in water
>> Parental NOAEL effect assessed	Fertility		
>> Parental Precision/LOAEL	>		
>> Parental LOAEL dose	15	**>> Parental LUnit used**	% EtOH in water
>> Parental LOAEL effect assessed	No LOAEL found		
>> F1 Precision/NOAEL	=		
>> F1 NOAEL dose	10	**>> F1 NUnit used**	% EtOH in water
>> F1 NOAEL effect assesse	Live pups per litter, % live, sex ratio, weight		
>> F1 Precision/LOAEL	=		
>> F1 LOAEL dose	15	**>> F1 LUnit used**	% EtOH in water
>> F1 LOAEL effect assesse	Live pups per litter: male, female, or combined		

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity to Reproduction

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

>> F2 Precision/NOAEL <

>> F2 NOAEL dose 15 **>> F2 NUnit used** % EtOH in water

>> F2 NOAEL effect assesse No NOAEL found

>> F2 Precision/LOAEL =

>> F2 LOAEL dose 15 **>> F2 LUnit used** % EtOH in water

>> F2 LOAEL effect assesse Adjusted live pup weight:male, female, or combined

>> Actual dose received by dose level by sex

Approximately 6.9, 13.8, and 20.7 g/kg-d

>> Parental/ F1 Data

Ethanol treatment had no significant effect on the proportion of breeding pairs producing at least one litter during the continuous breeding phase, or the number of litters per pair.

>>Offspring Data

F1 offspring of the 15% ethanol pairs had fewer live pups/litter. Their F2 offspring weighed less as pups than control pups, males, females, or both sexes.

>> Statistical results

Decreased weights or live pups/litter were significant at the 0.05 level.

Results Remark

* Parental data and F1 as appropriate, provide qualitative descriptions of dose-related observations where dose-related observations were seen:
* Body weight: In the P generation, postpartum body weights of females were not affected by continuous ethanol treatment during at least the first five litters. Body weights of P males were also unaffected. Weights of F1 pups (all litters combined at each dose level) were not affected by parental ethanol exposure. Pups in the final F1 litters exposed to 15% ethanol pre- and postnatally weighed less than controls at birth and days 21 and 74. The F2 offspring of the 15% ethanol group (the only group mated) showed decreased adjusted pup weight.
* Food/water consumption: Water consumption data are given in the appendix, but no comment is made.
* Description, severity, time of onset and duration of clinical signs: None reported, and none was observed in a preliminary range-finding study covering this dose range.
* Fertility index (pregnancies/matings): In the P matings, the fertiilty indices were 97, 100, 100, and 94% in the control, 5%, 10%, and 15% ethanol groups. In the F1 matings, the indices were 85 and 65% in the control and 15% ethanol groups. None of the differences were statistically significant.
* Precoital interval (w/number of days until mating and number of estrous periods until mating): Not reported.
* Duration of gestation (calculated from day 0 of pregnancy): Cumulative days to litter for each pair are reported in the appendix, but not discussed.
* Gestation index (live litters/pregnancies): Not reported.
* Changes in lactation: Not studied.
* Changes in estrus cycles: Not studied.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	110115/	Ethanol HPV Challenge Consortium		Completed:	Y

* Effects on sperm: Only F1 males from the 15% ethanol group were tested. There was a statistically significant decrease in percent motile sperm, but no changes in sperm concentration, percent abnormal sperm, or percent tailless sperm.
* Hematological findings incidence and severity: Not measured.
* Clinical biochemistry findings incidence and severity: Not measured.
* Mortality: Mortality of P animals is reported, but not discussed.
* Gross pathology incidence and severity: Not studied.
* Number of implantations: Not applicable (continuous breeding protocol).
* Number of corpora lutea (recommended): Not applicable.
* Ovarian primordial follicle counts: Not applicable.
* Organ weight changes: F1 males from the 15% ethanol group, sacrificed as adults, showed decreased body weight and decreased weights of the left testis/epididymis, the right epididymis, and the seminal vesicles. When adjusted for body weight, testis, epididymis, and seminal vesicle weights were not different from controls. In F2 females (15%), no absolute changes in organ weights were reported. In these animals (males and females), relative liver weight and kidney/adrenal weight were increased.
* Histopathology incidence and severity: Not studied.

* Offspring toxicity F1 and F2, as appropriate, provide qualitative descriptions of dose-related observations where dose related observations were seen
* Litter size and weights: Not given.
* Sex and sex ratios: Sex ratios in the F1 generation (three ethanol concentrations) and the F2 generation (15% ethanol only) were not affected by treatment.
* Viability index (pups surviving 4 days/total births): Not reported. However, litters born to P exposed to 15% ethanol, the number of live pups per litter was reduced.
* Post natal survival until weaning: Not reported.
* Effects on offspring (grossly visible abnormalities): Not reported.
* Postnatal growth, growth rate: Pups in the final F1 litters exposed to 15% ethanol pre- and postnatally weighed less than controls at birth and days 21 and 74.
* Vaginal opening (F) or preputial separation (M): Not studied.

* Other observations, for instance anogenital distance, if measured: Not studied.
* Organ weights: Described above.
- Gross pathology: Not examined.

Conclusions

In this study, breeding pairs (P) of CD-1 mice were exposed continuously to ethanol in drinking water during a 7-day premating period and the following 98 days of cohabitation. Ethanol had no discernible effect on the fertility of these P animals. Of the F1 generation, only pups from parents exposed to 15% ethanol continued in the study, with continued exposure to 15% ethanol until mating (to exposed animals). In this F1 generation, animals weighed less than controls at birth, day 21, and day 74. The mating and fertility indices of these F1 animals were not statistically different from controls, although the values were lower than at the comparable dose in the P generation. The postpartum weights of the mated F1 females were statistically significantly decreased, compared to controls. In F1 litters (ie., born to P animals), there were fewer live pups at the 15% ethanol dose level, while in F2 litters (15% ethanol), live pup weights were reduced. Other litter endpoints examined were proportion born alive and sex ratio. These data suggest fetotoxicity of ethanol at the 15% level. Changes observed in F1 adults at 15% ethanol included decreased percent motile sperm and relative liver and kidney weights.

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity to Reproduction

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Overall, ethanol in drinking water at concentrations up to 15% had no demonstrable effect on fertility in this two-generation study.

Data Quality

Reliability These data seem highly reliable.

Data Reliability Remarks

This report, conducted on behalf of the National Toxicology Program, used a reproductive toxicity protocol also applied to scores of other chemicals as part of a large research program. The methods seem standardized, and the report includes protocols and results for individual animals as well as a quality assurance statement.

Reference

>> Remarks

George, J., Myers, C., Reel, J., et al. (1985). Ethanol: Reproduction and fertility assessment in CD-2 mice when administered in the drinking water. National Toxicology Program. PB86144979

An abstract of the ethanol is presented by Lamb, J., George, J., Reel, J., et al. (1997). Environ. Health Perspect. 105 Suppl. 1:309-310. Results of all 48 chemical tests, and a review of the continuous breeding protocol, are published by Morrissey, R., Lamb, J., Morris, R., et al. (1989). Fundam. Appl. Toxicol. 13:747-777.

General

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity to Reproduction

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

Revision Date: 12/05/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Male fertility

>> Test Type

Male fertility

>> GLP Unknown

>> Year study performed 1989

>> Species mouse

>> Strain Mammal strain Swiss Webster

>> Sex M

>> Number of males per dose 20

>> Number of females per dose 0

>> Route of Administration Liquid diet

>> Exposure period 49

>> Frequency of treatment ad lib

>> Doses 10% and 25% ethanol-derived calories

>> Control Group Yes

>> Premating exposure period for female. None

>> Premating exposure period for male. Sequential matings until 7 weeks of exposure

>> Statistical Method Fertility: Chi-square. Other: ANOVA

Remarks for Method

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity to Reproduction

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

* Number, age, sex per dose for P, F1 and F2, if appropriate: 20 males per dose and control group. Placed on test at about 75 days of age.
* Note whether vehicle used and concentration/volume: Ethanol was presented ad lib in a nutritionally balanced liquid diet at 10 or 25% of total calories. Two control groups were used, one receiving liquid diet (ad lib) with 0% ethanol-derived calories, and another pair-fed to animals in the 10% ethanol-derived calories group.
* Dosing schedules and pre and post dosing observations periods for P, F1 and F2, if appropriate: Males were given ethanol or control treatments for 7 weeks and were mated periodically to untreated females starting the first week of exposure. Females were allowed to give birth, offspring were weighed, counted, and culled, then re-weighed at 21 days of age.

* Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): Two females per male for four hours. Vaginal plugs were considered proof of pregnancy.
- Standardization of litters (yes/no and if yes, how and when): Litters were culled to a maximum of 8 pups at birth.

* Parameters assessed during study P and F1 as appropriate: Sires were examined for diet consumption, weight, and fertility. Litter size, sex ratio, and pup weight at birth and at day 21 were measured.
- Clinical observations performed and frequency (clinical pathology, functional observations, etc.): None mentioned.
- Estrous cycle length and pattern (number of days spent in each phase): Not assessed.
- Sperm examination (epididymal or vas sperm, concentration, motility, morphology): Not assessed.

* Parameters assessed during study F1 and F2, as appropriate: F1 parameters are listed above: pup weights and sex ratio. No F2 parameters were assessed as this was a one-generation study.

- Clinical observations performed and frequency (weight gain, growth rate, etc.): Paternal body weight was measured weekly. Pup weight was measured at birth and day 21.
- Others, for example anogenital distance, if performed: None.
- Organs examined at necropsy (macroscopic and microscopic): Not performed.

Results

>> Parental Precision/NOAEL	=		
>> Parental NOAEL dose	10	**>> Parental NUnit used**	% EtOH-derived cal.
>> Parental NOAEL effect assessed	Body weight gain		
>> Parental Precision/LOAEL	=		
>> Parental LOAEL dose	25	**>> Parental LUnit used**	% EtOH-derived cal.
>> Parental LOAEL effect assessed	Body weight gain		
>> F1 Precision/NOAEL	=		
>> F1 NOAEL dose	25	**>> F1 NUnit used**	% EtOH-derived cal.
>> F1 NOAEL effect assesse	Litter size, sex ratio, pup weight		

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity to Reproduction

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

>> F1 Precision/LOAEL >

>> F1 LOAEL dose 25 **>> F1 LUnit used** % EtOH-derived cal.

>> F1 LOAEL effect assesse LOAEL not determined

>> F2 Precision/NOAEL

>> F2 NOAEL dose 0 **>> F2 NUnit used**

>> F2 NOAEL effect assesse One-generation study only

>> F2 Precision/LOAEL

>> F2 LOAEL dose 0 **>> F2 LUnit used**

>> F2 LOAEL effect assesse One-generation study only

>> Actual dose received by dose level by sex

13.9 g/kg-d (10% EDC), 21.5 g/kg-d (25% EDC)

>> Parental/ F1 Data

No toxic responses were noted in treated males, other than decreased weight gain at 25% ethanol-derived calories in diet. Fertility over 7 weeks of treatment was not affected.

>>Offspring Data

No adverse effects on offspring were noted as a function of either level of paternal ethanol treatment or duration of treatment.

>> Statistical results

No statistically significant effects on offspring were noted. P-value for paternal body weight decrease not given.

Results Remark

* Parental data and F1 as appropriate, provide qualitative descriptions of dose-related observations where dose related observations were seen
* Body weight: Paternal body weight means are shown graphically only, and were less at 25% ethanol-derived calories than at 10 or 0%. Offspring body weights were not affected by treatment.
* Food/water consumption: High-dose males were said to consume less diet. (Note that pair-fed controls were used, however.)
* Description, severity, time of onset and duration of clinical signs: None reported.
* Fertility index (pregnancies/matings): At least 80% for each ethanol concentration at each time point. Fertility was at least as great as in pair-fed or standard controls.
* Precoital interval (w/number of days until mating and number of estrous periods until mating): Not measured.
* Duration of gestation (calculated from day 0 of pregnancy): Pregnancies were carried to term.
* Gestation index (live litters/pregnancies): Not given.
* Changes in lactation: Not studied.
* Changes in estrus cycles: Not studied.
* Effects on sperm: Not studied.
* Hematological findings incidence and severity: Not studied.

* Clinical biochemistry findings incidence and severity: Not studied.
* Mortality: None reported.
* Gross pathology incidence and severity: Not studied.
* Number of implantations: Not studied.
* Number of corpora lutea (recommended): Not studied.
* Ovarian primordial follicle counts: Not studied.
* Organ weight changes: Not studied.
- Histopathology incidence and severity: Not studied.
* Offspring toxicity F1 and F2, as appropriate, provide qualitative descriptions of dose-related observations where dose related observations were seen: No dose-related observations were made.
* Litter size and weights: Litter sizes and weights were not affected by level or duration of paternal ethanol treatment.
* Sex and sex ratios: Sex ratios were not affected by level or duration of paternal ethanol treatment.
* Viability index (pups surviving 4 days/total births): Not measured- culled at birth.
* Post natal survival until weaning: No mortality was reported.
* Effects on offspring (grossly visible abnormalities): Not studied.
* Postnatal growth, growth rate: Pup weight at day 21 was not affected by level or duration of paternal ethanol treatment.
* Vaginal opening (F) or preputial separation (M): Not studied.

* Other observations, for instance anogenital distance, if measured: Not studied.
* Organ weights: Not studied.
- Gross pathology: Not studied.

Conclusions

In this experiment, where male mice were mated every other week during 7 weeks of ethanol treatment, ethanol had no effect on fertility of males or on litter size or pup weight when present in a liquid diet at 10 or 25% of total calories. Both pair-fed controls (to maintain equal levels of nutrition) and standard controls were used.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Abel, E. (1989). Duration of paternal alcohol consumption does not influence offspring growth and development. Growth Devel. Aging 53:195-199.

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity to Reproduction

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

General

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity to Reproduction

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

Revision Date: 12/06/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed: Female fertility

>> Test Type: Female fertility

>> GLP: Unknown

>> Year study performed: 1982

>> Species: rat

>> Strain: Mammal strain: Holtzmann

>> Sex: F

>> Number of males per dose: 0

>> Number of females per dose: 10

>> Route of Administration: Oral (liquid diet)

>> Exposure period: 112

>> Frequency of treatment: Ad lib, daily

>> Doses: 5% ethanol (w/v) in liquid diet

>> Control Group: Yes

>> Premating exposure period for female.: 16 wks, or 8 wks plus 8 wks off treatment.

>> Premating exposure period for male.: None, although possible during overnight mating.

>> Statistical Method: One-way ANOVA

Remarks for Method

* Number, age, sex per dose for P, F1 and F2, if appropriate: 10 females per dose group, age 20 days, weighing 45-55 g. F1 offspring were not dosed or mated, so there was no F2 generation.
* Note whether vehicle used and concentration/volume: Ethanol was supplied in a liquid diet.
* Dosing schedules and pre and post dosing observations periods for P, F1 and F2, if appropriate: Females were given liquid diet containing ethanol ad lib for 16 weeks prior to mating, or for 8 weeks, followed by 8 weeks on standard lab chow. Dosing ended after mating. Two control groups were used, one receiving standard lab chow, and the other pair-fed to the animals receiving 5% ethanol in diet.

* Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): Mating occurred 16 wks after the start of exposures. Ratio implied is 1:1, and cohabitation was for about 14 hrs. Sperm-positive vaginal smears were considered proof of pregnancy.
- Standardization of litters (yes/no and if yes, how and when): Not applicable. Study ended with delivery of F1 pups.

* Parameters assessed during study P and F1 as appropriate
- Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Daily examination for vaginal patency and daily vaginal lavage; weekly determination of body weight.
- Estrous cycle length and pattern (number of days spent in each phase): Average duration of estrous cycle was lengthened by 16 wks' treatment with 5% ethanol, compared to pair-fed or lab chow controls. Cycle length was not increased by 8 wks of treatment followed by 8 wks of lab chow diet. The longer ethanol treatment also caused greater irregularity in cycle length.
- Sperm examination (epididymal or vas sperm, concentration, motility, morphology): Not applicable.

* Parameters assessed during study F1 and F2, as appropriate
- Clinical observations performed and frequency (weight gain, growth rate, etc.): Number and body weight of pups was recorded.
- Others, for example anogenital distance, if performed: None.
- Organs examined at necropsy (macroscopic and microscopic): Ovaries and uteri of some P females were examined, but no F1 pups were necropsied.

Results

>> Parental Precision/NOAEL	<		
>> Parental NOAEL dose	5	>> Parental NUnit used	%ethanol in diet
>> Parental NOAEL effect assessed	Estrous cycle length		
>> Parental Precision/LOAEL	<=		
>> Parental LOAEL dose	5	>> Parental LUnit used	%ethanol in diet
>> Parental LOAEL effect assessed	Estrous cycle length		
>> F1 Precision/NOAEL	<=		
>> F1 NOAEL dose	5	>> F1 NUnit used	% in maternal diet
>> F1 NOAEL effect assesse	Body weight		

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity to Reproduction

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

>> F1 Precision/LOAEL >

>> F1 LOAEL dose 5 **>> F1 LUnit used** % in maternal diet

>> F1 LOAEL effect assesse No LOAEL determined

>> F2 Precision/NOAEL

>> F2 NOAEL dose 0 **>> F2 NUnit used**

>> F2 NOAEL effect assesse F2 generation not assessed

>> F2 Precision/LOAEL

>> F2 LOAEL dose 0 **>> F2 LUnit used**

>> F2 LOAEL effect assesse F2 generation not assessed

>> Actual dose received by dose level by sex

14-21 g/kg-d

>> Parental/ F1 Data

Increased estrous cycle length and cycle irregularity after 16 weeks of ethanol treatment, but not after 8 weeks of treatment with an 8-week recovery on lab chow. No histological findings.

>>Offspring Data

No adverse effect on # pups live at birth, litter size, or pup weight.

>> Statistical results

Increased estrous cycle length ($p<0.05$) and cycle irregularity ($p<0.01$) in the 16-week ethanol group. Increased age at vaginal patency ($p<0.01$) for both treated groups.

Results Remark

* Parental data and F1 as appropriate, provide qualitative descriptions of dose-related observations where dose related observations were seen: Effect of duration of exposure, not dose, was assessed. Effects were seen chiefly in females given ethanol in diet for 16 weeks, not in females given this diet for 8 weeks and then lab chow for 8 weeks. Estrous cycle length was increased, and cycle irregularity increased, by 16 weeks of exposure to 5% ethanol in diet. Age to vaginal patency was increased by both ethanol exposure regimens. Both lab chow and pair-fed controls were used. Histological exam was performed on the 8-week group only (and controls); no abnormalities of ovaries or uteri were found. Pregnancy rate among the 16-week animals was 80%. All pups of all litters were live-born. Ethanol treatment had no effect on litter size or pup weight.
* Body weight: Female body weights were measured, but not reported.
* Food/water consumption: Not reported, but of necessity recorded since there was a pair-fed control for the 16-week-exposure group.
* Description, severity, time of onset and duration of clinical signs: No clinical signs were reported.
* Fertility index (pregnancies/matings): Females were mated over a two-week period. Pregnancy rate was 80% (8/10) for the 16-week group, 100% in the pair-fed and 8-week groups (3/3, 7/7), and 75% in the lab chow control (3/4).

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

* Precoital interval (w/number of days until mating and number of estrous periods until mating): Not reported.
* Duration of gestation (calculated from day 0 of pregnancy): Not reported.
* Gestation index (live litters/pregnancies): All pregnant animals delivered live litters.
* Changes in lactation: Not assessed.
* Changes in estrus cycles: See above.
* Effects on sperm: Not assessed.
* Hematological findings incidence and severity: Not assessed.
* Clinical biochemistry findings incidence and severity: Not assessed.
* Mortality: None reported. All pup were born live.
* Gross pathology incidence and severity: Not assessed.
* Number of implantations: Not assessed.
* Number of corpora lutea (recommended): Not assessed.
* Ovarian primordial follicle counts: Not assessed.
* Organ weight changes: Not assessed.
- Histopathology incidence and severity: As described above, all uteri and ovaries examined were normal.
* Offspring toxicity F1 and F2, as appropriate, provide qualitative descriptions of dose-related observations where dose related observations were seen: No dose-related effects were found in F1 pups.
* Litter size and weights: Unaffected by treatment at the p=0.05 level.
* Sex and sex ratios: Not given.
* Viability index (pups surviving 4 days/total births): Not assessed.
* Post natal survival until weaning: Not assessed.
* Effects on offspring (grossly visible abnormalities): Not assessed.
* Postnatal growth, growth rate: Not assessed.
* Vaginal opening (F) or preputial separation (M): Average age of vaginal patency was 72-77 days in both groups of ethanol-treated rats, significantly older than in control groups (41-58 days).

* Other observations, for instance anogenital distance, if measured: Not assessed.
* Organ weights: Not assessed.
- Gross pathology: Not assessed.

Conclusions

Ethanol treatment (5% w/v in liquid diet) affected ovarian function in rats during a 16-week treatment period by increasing estrous cycle length and irregularity, and delayed vaginal patency during both an 8-week and a 16-week treatment. Howeve, fertility was not affected, nor litter size or pup weight. The findings support observations of menstrual dysfunction in alcoholic women.

Data Quality

Reliability

Data Reliability Remarks

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

Reference

>> Remarks

Krueger, W., Bo, W. and Rudeen, P. (1982). Female reproduction during chronic ethanol consumption in rats. Pharmacol. Biochem. Behav. 17:629-631.

General

This study was a follow-up to Bo et al. (1982), separately summarized.

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity to Reproduction

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

Revision Date: 12/06/2000

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Female reproductive toxicity

>> Test Type

Female fertility

>> GLP: Unknown

>> Year study performed: 1982

>> Species: rat

>> Strain: Mammal strain: Holtzmann

>> Sex: F

>> Number of males per dose: 0

>> Number of females per dose: 9

>> Route of Administration: Oral (liquid diet)

>> Exposure period: 55

>> Frequency of treatment: Ad lib, daily

>> Doses: 2.5% and 5% ethanol (w/v) in liquid diet

>> Control Group: Yes

>> Premating exposure period for female. 50-55 days

>> Premating exposure period for male. None: no matings attempted.

>> Statistical Method: ANOVA and Duncan's multiple range test

Remarks for Method

* Number, age, sex per dose for P, F1 and F2, if appropriate: 8-11 animals per group; age 20 days at the start. No matings were attempted, so there were no F1 or F2 animals.
* Note whether vehicle used and concentration/volume: Ethanol was supplied in a liquid diet.
* Dosing schedules and pre and post dosing observations periods for P, F1 and F2, if appropriate: Diets were supplied ad lib for 50-55 days. Pair-fed controls were used at each ethanol dose; lab chow controls were also used.

* Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): Not applicable.
- Standardization of litters (yes/no and if yes, how and when): Not applicable.

* Parameters assessed during study P and F1 as appropriate
- Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Animals were weighed weekly, and examined daily for vaginal patency. Once patent, vaginal lavages were made daily.
- Estrous cycle length and pattern (number of days spent in each phase): Patterns not determined.
- Sperm examination (epididymal or vas sperm, concentration, motility, morphology): Not applicable.

* Parameters assessed during study F1 and F2, as appropriate: Not applicable.
- Clinical observations performed and frequency (weight gain, growth rate, etc.): Not applicable.
- Others, for example anogenital distance, if performed: Not applicable.
- Organs examined at necropsy (macroscopic and microscopic): Not applicable.

Results

>> Parental Precision/NOAEL	=		
>> Parental NOAEL dose	2	>> Parental NUnit used	% ethanol in diet
>> Parental NOAEL effect assessed	Vaginal patency, uterus/ovary weights, histology		
>> Parental Precision/LOAEL	=		
>> Parental LOAEL dose	5	>> Parental LUnit used	% ethanol in diet
>> Parental LOAEL effect assessed	Vaginal patency, uterus/ovary weights, histology		
>> F1 Precision/NOAEL			
>> F1 NOAEL dose	0	>> F1 NUnit used	
>> F1 NOAEL effect assesse	No F1 generation examined		
>> F1 Precision/LOAEL			
>> F1 LOAEL dose	0	>> F1 LUnit used	
>> F1 LOAEL effect assesse	No F1 generation examined		
>> F2 Precision/NOAEL			
>> F2 NOAEL dose	0	>> F2 NUnit used	

>> F2 NOAEL effect assesse No F2 generation examined

>> F2 Precision/LOAEL

>> F2 LOAEL dose 0 **>> F2 LUnit used**

>> F2 LOAEL effect assesse No F2 generation examined

>> Actual dose received by dose level by sex

2.5% ethanol in diet: 8-12 g/kg-d. 5%:15-20 g/kg-d

>> Parental/ F1 Data

Female rats given 5% ethanol in liquid diet for 5-55 days (but not 2.5%) showed adverse effects on body weight, time to vaginal patency, and ovarian or uterine weight or histology.

>>Offspring Data

Not applicable.

>> Statistical results

All effects at the 5% ethanol concentration were significant at the 0.05 or 0.01 level.

Results Remark

* Parental data and F1 as appropriate, provide qualitative descriptions of dose-related observations where dose related observations were seen: Adverse effects were seen only in females given 5% ethanol in liquid diet for 50-55 days. These animals exhibited longer time to vaginal patency, failed to begin estrous cycles, showed decreased body weight gain, had ovaries containing only a single generation of corpora lutea, had infantile vaginal and uterine epithelium, and decreased uterine and ovarian weight. Rats given diets containing 2.5% ethanol were similar in all these respects to pair-fed and lab chow controls.
* Body weight: Body weights of 5% ethanol animals and their pair-fed controls were less than in other groups.
* Food/water consumption: These were measured, of necessity, in order to properly dose pair-fed controls, but measurements were not reported.
* Description, severity, time of onset and duration of clinical signs: No adverse signs were reported.
* Fertility index (pregnancies/matings): No matings were attempted.
* Precoital interval (w/number of days until mating and number of estrous periods until mating): Not relevant.
* Duration of gestation (calculated from day 0 of pregnancy): Not relevant.
* Gestation index (live litters/pregnancies): Not relevant.
* Changes in lactation: Not relevant.
* Changes in estrus cycles: High-dose animals did not exhibit estrous cycles, as observed by vaginal lavage.
* Effects on sperm: Not applicable.
* Hematological findings incidence and severity: Not assessed.
* Clinical biochemistry findings incidence and severity: Not assesed.
* Mortality: None.
* Gross pathology incidence and severity: Not assessed.

* Number of implantations: Not applicable.
* Number of corpora lutea (recommended): These were examined, but not reported. Animals given 2.5% ethanol showed numerous developing and prior corpora lutea, whereas animals given 5% ethanol showed only a single generation of corpora lutea.
* Ovarian primordial follicle counts: Not assessed.
* Organ weight changes: Uterine and ovarian weights were decreased in animals given 5% ethanol in liquid diet.
- Histopathology incidence and severity: As described above, ovarian, uterine, and vaginal tissues appeared immature.
* Offspring toxicity F1 and F2, as appropriate, provide qualitative descriptions of dose-related observations where dose related observations were seen: Not applicable.
* Litter size and weights: Not applicable.
* Sex and sex ratios: Not applicable.
* Viability index (pups surviving 4 days/total births): Not applicable.
* Post natal survival until weaning: Not applicable.
* Effects on offspring (grossly visible abnormalities): Not applicable.
* Postnatal growth, growth rate: Not applicable.
* Vaginal opening (F) or preputial separation (M): In two of eight rats given 5% ethanol in liquid diet, vaginal opening did not occur within the 50-day exposure period; in others, it was delayed compared to controls. Age at vaginal opening was unaffected by treatment with 2.5% ethanol.

* Other observations, for instance anogenital distance, if measured: Not applicable.
* Organ weights: Uterine weights were decreased by about 66%, and ovarian weights by about 50%, in rats treated with 5% ethanol in diet. Weights were unaffected by treatment with 2.5% ethanol.
- Gross pathology: See above.

Conclusions

Ovarian function was suppressed in rats given 5% ethanol (w/v) in liquid diet for 50 days, but not in rats given 2.5% ethanol. Both pair-fed and lab chow controls were used, so nutritional deficiency was not thought responsible for the adverse effects.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Bo, W., Krueger, W., Rudeen, P., and Symmes, S. (1982). Ethanol-induced alterations in the morphology and function of the rat ovary. Anat. Rec. 202:255-260.

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity to Reproduction

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	N

General

The findings of Bo et al. (1982) and Krueger et al. (1982) are supported by many other studies of estrous cycling and ovulatory function in rats and other species. These are briefly summarized by Gavaler, J. and Van Thiel, D. (1987). International Commission for Protection Against Environmental Mutagens and Carcinogens, ICPEMC Working Paper No. 15/7: Reproductive consequences of alcohol abuse: males and females compared and contrasted. Mutat. Res. 186:269-277.

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity in Vitro (Gene Mutations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 02/23/2001

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Protocol given by Griffiths (1979) for meiotic non-disjunction in Neurospora crassa

>> Test Type

Yeast Cytogenetic assay

>> System of Testing Non-bacterial

>> GLP Unknown

>> Year study performed 1981

>> Species

Neurospora crassa

>> Metabolic Activation

Not relevant

>> Concentration

Not stated

>> Statistical Method One-way analysis of variance

Remarks for Method

* Test Design: Paper gives summary of protocol of Griffiths (1979).
- Number of replicates: 5
- Frequency of Dosing: Once.
- Positive and negative control groups and treatment: Not described, but controls were included (see below). The spontaneous frequency of auxotrophs (see below) is very low.
- Number of metaphases analyzed for chromosomal studies: Not relevant. Two haploid strains of yeast, bearing different alleles relating to auxotrophy, are crossed. Six hours later, the crosses are flooded with solutions of the test chemical. At day 30, ascospores from the

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

highest exposure compatible with fertility is plated on minimal medium. Only ascospores that are disomic due to non-disjunction will grow.

* Solvent/vehicle, if used, and concentration: Not described.
* If follow-up study, describe how different from original: Not relevant.
* Criteria for evaluating results (e.g. cell evaluated per dose group): The number of disomics per number of colony-forming ascospores, or the number of disomics per number of treated ascospores.

Results

>> Result Negative

>> Cytotoxic Concentration

Concentration not given

>> Genotoxic Effects Unconfirmed

>> Statistical results

No significant results

Results Remark

* Note test-specific confounding factors such as pH, osmolarity, whether substance is volatile, water soluble, precipitated, etc., particularly if they effect the selection of test concentrations or interpretation of the results: None described.

* Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen: Only one dose- the maximum dose still allowing fertility- was used. No meiotic nondisjunction occurred.

* Frequency of reversions/mutations/aberrations, polyploidy as appropriate: No increase in meiotic nondisjunction occurred.
* Mitotic index: Not applicable.

Conclusions

Ethanol failed to produce meiotic nondisjunction in yeast and was judged non-genotoxic by the Gene-Tox Work Group.

Data Quality

Reliability Highly reliable

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity in Vitro (Gene Mutations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Reliability Remarks

These data were compiled from published literature by the U.S. EPA's Gene-Tox Program. Only papers meeting criteria such as acceptable experimental design, inclusion of proper controls, etc. were were evaluated.

Reference

>> Remarks

Brockman, H., de Serres, F., Ong, T., et al. (1984). Mutation tests in Neurospora crassa: A report of the U.S. Environmental Protection Agency Gene-Tox Program. Mutat. Res. 133:87-134.

The original reference for the ethanol study is Griffiths, E. (1981) in: Stich, H. and San, R., editors. "Short-Term Tests for Chemical Carcinogens." Springer: New York, NY.

General

The genotoxicity of ethanol was comprehensively reviewed in 1987 by Obe and Anderson for the International Commission for Protection Against Environmental Mutagens and Carcinogens (Mutat. Res. 186:177-200). More than 30 in vitro experiments were included. The authors concluded that ethanol per se generally does not induce genetic damage in vitro, unless the test system is capable of metaoblizing ethanol or a metabolic system is added.

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity in Vitro (Gene Mutations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 12/01/2000

Test Substance

Remarks: 91% pure ethanol

Chemical Category

Method

>> Method/Guideline followed

Bacterial mutation

>> Test Type

Ames test

>> System of Testing Bacterial

>> GLP Unknown

>> Year study performed 1992

>> Species

Salmonella typhimurium

>> Metabolic Activation

Male Sprague-Dawley rat and Syrian hamster livers; Aroclor 1254-induced; used at 10% and 30%

>> Concentration

1, 3, 10, 33, 100, 333, 1000, 3333, 10,000 micrograms/plate

>> Statistical Method None mentioned

Remarks for Method

* Test Design
- Number of replicates: Five per dose; in addition, the entire experiment was repeated.
- Frequency of Dosing: Once, including preincubation.
- Positive and negative control groups and treatment: Positive controls were included- the chemical used depended on the Salmonella strain and whether a metabolic activation system was added.
- Number of metaphases analyzed for chromosomal studies: Not applicable.

* Solvent/vehicle, if used, and concentration: Not applicable.
* If follow-up study, describe how different from original: Not applicable.
* Criteria for evaluating results (e.g. cell evaluated per dose group): Combination of magnitude of increase in number of his+ revertants and shape of dose-response curve. A chemical was judged non-mutagenic if it failed to meet criteria for a mutagenic or questionable response.

Results

>> Result Negative

>> Cytotoxic Concentration

Not reported. Initial screening studies were done to determine the appropriate dose range.

>> Genotoxic Effects With metabolic activation

>> Statistical results

Not applicable.

Results Remark

* Note test-specific confounding factors such as pH, osmolarity, whether substance is volatile, water soluble, precipitated, etc., particularly if they affect the selection of test concentrations or interpretation of the results: None.

* Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen: Ethanol did not produce even a two-fold increase in his+ revertants at any dose in any of the five Salmonella strains tested, with or without rat or hamster liver extracts.

* Frequency of reversions/mutations/aberrations, polyploidy as appropriate: Revertants did not increase by two-fold at any point.

* Mitotic index: Not applicable.

Conclusions

Ethanol failed to induce reversions in any of five Salmonella typhimurium tester strains, with or without metabolic activation, over a wide range of doses (up to 10 mg/plate).

Data Quality

Reliability Highly reliable

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity in Vitro (Gene Mutations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Reliability Remarks

Ethanol was tested within the National Toxicology Program's mutagenicity testing program, and was tested in five Salmonella strains over a wide range of concentrations, with and without two metabolic induction systems in two concentrations. Positive controls were included.

Reference

>> Remarks

Zeiger, E., Anderson, B., Haworth, S., et al. (1992). *Salmonella mutagenicity tests: V. Results from the testing of 311 chemicals.* Environ. Molec. Mutagen. 19 Suppl. 21:2-141.

General

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 01/02/2001

Test Substance

Remarks: Five types of ethanol were used: synthetic anhydrous 100%, synthetic 95%, 95% grain alcohol, 96.6% grain alcohol, and dehydrated absolute 100% grain alcohol.

Chemical Category

Method

>> Method/Guideline followed

RK mutatest

>> Test Type

Bacterial forward mutation assay

>> System of Testing Bacterial

>> GLP Unknown

>> Year study performed 1985

>> Species

E. coli RK+ (replicative killing competent; strain CHY832)

>> Metabolic Activation

None

>> Concentration

Various concentrations between 11 and 23% v/v

>> Statistical Method None described

Remarks for Method

* Test Design: This strain carries a lethal gene (RK+) that is repressed below 39 deg. C. and derepressed above this temperature. After treatment with potential mutagens at 30 deg. C., cells are plated and cultured at 42 deg. C. to detect surviving RK- mutants.
- Number of replicates: Three per concentration.
- Frequency of Dosing: Reaction mixtures were exposed to ethanol for 10 minutes before plating.
- Positive and negative control groups and treatment: Negative controls (no chemical treatments) were used.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

- Number of metaphases analyzed for chromosomal studies: Not relevant.

* Solvent/vehicle, if used, and concentration: Dilution (if any) of ethanol stocks was not discussed. Ethanol samples were tested with and without 20% dimethylsulfoxide.
* If follow-up study, describe how different from original: Not relevant.
* Criteria for evaluating results (e.g. cell evaluated per dose group): The mutation index (mutation frequency in treated cultures/mutation frequeny in controls) must be at least 2 to be considered evidence of mutagenicity.

Results

>> Result Positive

>> Cytotoxic Concentration

Cytotoxicity was measured, but results were not reported in detail.

>> Genotoxic Effects Dose-response

>> Statistical results

No statistical tests were done.

Results Remark

* Note test-specific confounding factors such as pH, osmolarity, whether substance is volatile, water soluble, precipitated, etc., particularly if they effect the selection of test concentrations or interpretation of the results: No confounding factors apparent.

* Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen: All ethanol preparations elicited RK- mutants, as indicated by mutation indices of 2 or more. Graphical results show distinct, steep dose-response curves for all preparations with thresholds of approximately 18-19% v/v.

* Frequency of reversions/mutations/aberrations, polyploidy as appropriate: All preparations increased the rate of RK- mutations, giving mutation indices of up to 50 at the highest dose tested.

* Mitotic index: Not relevant.

Conclusions

The five ethanol preparations showed similar dose-response curves for induction of RK- mutants, with thresholds of 18-19% v/v. Addition of DMSO lowered the thresholds. No metabolic activation systems were added, so mutation could be due to (a) trace contaminants in ethanol, (b) bacterial metabolite, (c) direct mutagenic effect of ethanol, (d) indirect effect of ethanol.

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity in Vitro (Gene Mutations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Hayes, S. (1985). Ethanol-induced genotoxicity. Mutat. Res. 143:23-27.

General

Revision Date: 01/02/2001

Test Substance

Remarks: Industrial 95% ethanol and analytical grade absolute 100% ethanol.

Chemical Category

Method

>> Method/Guideline followed

Sister chromatid exchange in CHO cells (as described by de Raat, 1979)

>> Test Type

Sister chromatid exchange assay

>> System of Testing Non-bacterial

>> GLP Unknown

>> Year study performed 1983

>> Species

Chinese Hamster Ovary cells

>> Metabolic Activation

Rat liver homogenate (0.02 ml/ml), induced with Aroclor 1254; and coenzyme solution

>> Concentration

0, 3.9, 7.9, 15.8, 31.6 g/l

>> Statistical Method No statistical tests of significance

Remarks for Method

* Test Design: CHO cells were incubated with ethanol for 1 hr; half of samples had a 10-minute preincubation with the metabolic activation system. After treatment, bromodeoxyuridine was added, and cells were incubated for another 24 hr before harvesting and counting of sister chromatid exchanges.
- Number of replicates: One or two per concentration.
- Frequency of Dosing: Once for 1 hr.
- Positive and negative control groups and treatment: Negative control (no ethanol) but no positive control was used.

- Number of metaphases analyzed for chromosomal studies: 20 per slide.

* Solvent/vehicle, if used, and concentration: Not discussed.
* If follow-up study, describe how different from original: Extended earlier work by testing alcoholic beverages also.
* Criteria for evaluating results (e.g. cell evaluated per dose group): No statistical tests done.

Results

>> Result Positive

>> Cytotoxic Concentration

Not tested.

>> Genotoxic Effects With metabolic activation

>> Statistical results

No statistical tests were performed.

Results Remark

* Note test-specific confounding factors such as pH, osmolarity, whether substance is volatile, water soluble, precipitated, etc., particularly if they effect the selection of test concentrations or interpretation of the results: No confounding factors apparent.

* Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen: In the presence of S9 mix, ethanol induced a two-fold increase in SCE/cell at a concentration of 3.9 g/l and a three-fold increase at 15.8 g/l. In the absence of S9, the maximum increase in SCE/cell was less than two-fold at 31.6 g/l.

* Frequency of reversions/mutations/aberrations, polyploidy as appropriate: In the presence of S9, 31.6 g/l ethanol elicited about 30 SCE/cell, compared to 9.5 in controls. In the absence of S9, 31.6 g/l ethanol elicited about 15 SCE/cell, compared to 10.5 in controls.

* Mitotic index: Not relevant.

Conclusions

In the presence of S9 metabolic activation mix, ethanol at 31.6 g/l raised SCE frequencies in CHO cells to three-fold control values. At the lowest dose tested, 3.9 g/l, frequencies were doubled. No tests of statistical significance were performed, but standard deviations were given, and are relatively small. Increases in SCE frequencies in the absence of S9 were slight, less than 100%. The effects of the two types of ethanol did not appear to differ.

Data Quality

Reliability

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Reliability Remarks

These data were considered sufficiently reliable for inclusion in a US EPA Gene-Tox report.

Reference

>> Remarks

de Raat, W., Davis, P., and Bakker, G. (1983). Induction of sister-chromatid exchanges by alcohol and alcoholic beverages after metabolic activation by rat-liver homogenate. Mutat. Res. 124:85-90.

Included in: Tucker, J., Auletta, A., Cimino, M., et al. (1993). Sister-chromatid exchange: second report of the Gene-Tox Program. Mutat. Res. 297:101-180.

General

An earlier Gene-Tox report on SCE (Latt et al. [1981] Mutat. Res. 87:17-62) judged ethanol, in the absence of metabolic activation systems, negative in this in vitro assay based on four studies.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 01/02/2001

Test Substance

Remarks: 100% reagent-grade ethanol

Chemical Category

Method

>> Method/Guideline followed

Sister chromatid exchange in lymhocytes

>> Test Type

Sister chromatid exchange assay

>> System of Testing Non-bacterial

>> GLP Unknown

>> Year study performed 1980

>> Species

Human

>> Metabolic Activation

None

>> Concentration

0.05, 0.15, 0.5% v/v

>> Statistical Method t-test

Remarks for Method

* Test Design: Whole blood was taken from four humans (2 male, 2 female) and treated with ethanol and bromodeoxyuridine for 72 hr. After staining, sister-chromatid exchanges in lymphocytes were counted.
- Number of replicates: Three.
- Frequency of Dosing: One treatment with ethanol.
- Positive and negative control groups and treatment: Negative controls (no ethanol) but no positive controls were used.
- Number of metaphases analyzed for chromosomal studies: 40/concentration/donor.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Solvent/vehicle, if used, and concentration: None.
* If follow-up study, describe how different from original: Not relevant.
* Criteria for evaluating results (e.g. cell evaluated per dose group): Significance test.

Results

>> Result Positive

>> Cytotoxic Concentration

Not tested

>> Genotoxic Effects Without metabolic activation

>> Statistical results

All concentrations of ethanol produced statistically significanct increases in SCE frequencies ($p<0.01$).

Results Remark

* Note test-specific confounding factors such as pH, osmolarity, whether substance is volatile, water soluble, precipitated, etc., particularly if they effect the selection of test concentrations or interpretation of the results: None noted. All donors had abstained from alcohol for at least 48 hours, and none were heavy drinkers.

* Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen: The mean SCE frequencies at 0, 0.05, 0.15, and 0.50% ethanol were 3.93, 5.56, 6.57, and 6.66.

* Frequency of reversions/mutations/aberrations, polyploidy as appropriate: See above.

* Mitotic index: Not relevant.

Conclusions

Lymphocytes from whole human blood treated with ethanol in vitro showed statistically significant increases in SCE/cell. Since SCE frequency did not change between the mid and and high doses, a saturable process may be involved. No metabolic activation system was added to the blood, but blood cells themselves might be able to generate acetaldehyde.

Data Quality

Reliability

Data Reliability Remarks

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

These data were considered sufficiently reliable for inclusion in a US EPA Gene-Tox report.

Reference

>> Remarks

Alvarez, M., Cimino, L., Cory, M., and Gordon, R. (1980). Ethanol induction of sister chromatid exchanges in human cells in vitro. Cytogenet. Cell Genet. 27:66-69.

Included in: Tucker, J., Auletta, A., Cimino, M., et al. (1993). Sister-chromatid exchange: second report of the Gene-Tox Program. Mutat. Res. 297:101-180.

General

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 01/02/2001

Test Substance

Remarks: Analytical-grade ethanol

Chemical Category

Method

>> Method/Guideline followed

Sister chromatid exchange in lymphocytes

>> Test Type

Sister chromatid exchange assay

>> System of Testing Non-bacterial

>> GLP Unknown

>> Year study performed 1986

>> Species

Primary cultures - human lymphocytes

>> Metabolic Activation

The enzymes alcohol dehydrogenase (ADH) and/or acetaldehyde dehydrogenase (ALDH) were sometimes used

>> Concentration

0.5%, 1% (v/v)

>> Statistical Method None

Remarks for Method

* Test Design: The effect of incubation of human lymphocytes with ethanol and enzymes known to metabolize ethanol (ADH) or its primary metabolite, acetaldehyde (ALDH) on sister chromatid exchange frequencies was assessed in vitro.
- Number of replicates: One per donor.
- Frequency of Dosing: Cells were incubated in vitro with ethanol for 24 hours. Enzymes, if added, were present for 3 hours.
- Positive and negative control groups and treatment: No positive controls were used. Negative controls, plus controls for enzymes and cofactors, were used.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

- Number of metaphases analyzed for chromosomal studies: 17-30 metaphases per blood donor were examined.

* Solvent/vehicle, if used, and concentration: Not discussed.
* If follow-up study, describe how different from original: Not discussed.
* Criteria for evaluating results (e.g. cell evaluated per dose group): Two to four donors per dose group were used, depending on the experiment. Specific criteria denoting a positive results were not described.

Results

>> Result Positive

>> Cytotoxic Concentration

Not measured

>> Genotoxic Effects With metabolic activation

>> Statistical results

No statistical tests were performed.

Results Remark

* Note test-specific confounding factors such as pH, osmolarity, whether substance is volatile, water soluble, precipitated, etc., particularly if they effect the selection of test concentrations or interpretation of the results: None mentioned.

* Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen: The SCE frequency was higher in cultures containing 1% ethanol than 0.5%, and higher in cultures containing 1% ethanol, ADH, and NAD than 0.5% ethanol, ADH, and NAD. The highest SCE frequencies were 6-7-fold control values when enzymes were added via dialysis tubes.

* Frequency of reversions/mutations/aberrations, polyploidy as appropriate: SCE frequencies in untreated controls were about 6-7/metaphase; with 0.5% ethanol, ADH, and NAD, about 35/metaphase; with 1% ethanol, ADH, and NAD, 36-42/metaphase. For treatment with 1% ethanol alone, SCE frequency was about 7/metaphase.
* Mitotic index: Not evaluated.

Conclusions

Ethanol alone did not cause an apparent increase in the SCE frequency of human lymphocytes, but definite increases were seen with the addition of ADH or ADH plus NAD. The increases were greater when enzymes were added to cultures in dialysis tubes, rather than directly to cell cultures, probably due to a difference in washing of cells before labeling. When ethanol, ADH, NAD, and ALDH were added to cultures, the increase in SCE frequency was

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

less than without ALDH, suggesting that acetaldehyde is the mutagenic compound.

Data Quality

Reliability

Data Reliability Remarks

These data were considered sufficiently reliable to be included in a US EPA Gene-Tox report.

Reference

>> Remarks

Obe, G., Jonas, R., and Schmidt, S. (1986). Metabolism of ethanol in vitro produces a compound which induces sister-chromatid exchanges in human peripheral lymphocytes in vitro: acetaldehyde not ethanol is mutagenic. Mutat. Res. 174:47-51.

Included in: Tucker, J., Auletta, A., Cimino, M., et al. (1993). Sister-chromatid exchange: second report of the Gene-Tox Program. Mutat. Res. 297:101-180.

The Gene-Tox report references other SCE studies of ethanol not presented in this robust summary.

General

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 01/17/2001

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

TK +/- forward mutation assay, performed according to Clive et al. (1979)

>> Test Type

Mammalian cell gene mutation assay

>> System of Testing Non-bacterial

>> GLP Unknown

>> Year study performed 1988

>> Species

mouse

>> Metabolic Activation

Male Sprague-Dawley rats induced with Aroclor 1254

>> Concentration

0.092, 0.184, 0.369, 0.553, 0.738 mol/l without activation; 0.414, 0.465, and 0.517 with activation

>> Statistical Method two-tailed Student's t-test

Remarks for Method

* Test Design: mouse lymphoma cell TK +/- forward mutation assay, with and without metabolic activation.
- Number of replicates: Three per dose level, but six for negative control.
- Frequency of Dosing: One four-hour exposure.
- Positive and negative control groups and treatment: Negative control (no ethanol).
- Number of metaphases analyzed for chromosomal studies: Not relevant.

* Solvent/vehicle, if used, and concentration: Not discussed.

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* If follow-up study, describe how different from original: Not relevant.
* Criteria for evaluating results (e.g. cell evaluated per dose group): Two-fold or greater increase in mutation frequency at 10% or greater total growth (compared to control).

Results

>> Result Negative

>> Cytotoxic Concentration

Only at the maximum concentration, with metabolic activation, was total growth <10% of control.

>> Genotoxic Effects Unconfirmed

>> Statistical results

Without activation, the lowest and highest concentrations of ethanol produced statistically significant increases in mutation frequency ($p<0.05$ and <0.01, respectively). (More below.)

Results Remark

* Note test-specific confounding factors such as pH, osmolarity, whether substance is volatile, water soluble, precipitated, etc., particularly if they effect the selection of test concentrations or interpretation of the results: None.

* Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen: No clear dose-related effects on mutation were seen in the absence of metabolic activation. With activation, the highest concentration of ethanol produced a statistically significant increase in mutation frequency.

* Frequency of reversions/mutations/aberrations, polyploidy as appropriate: Without metabolic activation, the mutation index values (relative mutation frequency) in treated groups, from lowest to highest dose, were 1.3, 1.1, 1.2, 1.1, and 1.6. With metabolic activation, the mutation index values were 1.1, 1.3, and 1.8.
* Mitotic index: Not strictly applicable. Total growth, compared to control cultures, were 88, 84, 53, 34, and 17%, from lowest to highest concentrations of ethanol, in the absence of metabolic activation. With activation, total growth measurements were 43, 24, and 6%, from lowest to highest ethanol concentration.

Conclusions

Ethanol was tested at five concentrations in the absence of metabolic activation, and at three concentrations with activation, for its ability to cause forward mutations in cultured mouse lymphoma cells. Regardless of activation, no concentration increased the mutation index to 2, the minimum criterion for a positive result in this assay. Ethanol was thus judged not to have significant mutagenic activity by the investigators.

Data Quality

Reliability

EPA High Production Volume (HPV) Track

Toxicity End point:
Toxicity in Vitro (Gene Mutations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Reliability Remarks

Reference

>> Remarks

Wangenheim, J. and Bolcsfoldi, G. (1988). Mouse lymphoma L5178Y thymidine kinase locus assay of 50 compounds. Mutagen. 3(3):193-205.

The results are supported by the work of Amacher, D., Paillet, S., Turner, G., et al. (1980). Point mutations at the thymidine kinase locus in L5178Y mouse lymphoma cells. II. Test validation and interpretation. Mutat. Res. 72:447-474. Ethanol was tested, without metabolic activation, up to 0.779 mol/l and was non-mutagenic.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 02/23/2001

Test Substance

Remarks: Distilled ethanol

Chemical Category

Method

>> Method/Guideline followed

Bone marrow micronucleus assay

>> Test Type

Micronucleus assay

>> GLP Unknown

>> Year study performed 1977

>> Species

mouse

>> Strain Mammal strain Swiss

>> Sex M

>> Number of males per dose 5

>> Number of females per dose 0

>> Route of Administration

Oral (drinking water)

>> Doses Time-weighted average: 23% and 33% ethanol

>> Exposure period 27 days

>> Statistical Method Student's t-test

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age at study initiation: 72-75 days.
* No. of animals per dose: 3 in negative control, 5 in ethanol groups, and 6 in positive control
* Vehicle: Ethanol given in water.
* Duration of test: 27 days.
* Frequency of treatment: Ethanol given ad lib. For positive control, ethyl methanesulfonate (EMS) was injected twice before sacrifice.
* Sampling times and number of samples: Animals were sacrificed on the 27th day. Four slides of stained bone marrow were prepared for each animal.
* Control groups and treatment: Negative controls received water without ethanol. Positive controls received I.p. injections of ethyl methanesulfonate 30 and 6 h before sacrifice.
* Clinical observations performed (clinical pathology, functional observations, etc.): Weight.
* Organs examined at necropsy (macroscopic and microscopic): Bone marrow tissue only.
* Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): An average of 4000 polychromatic erythrocytes (PCE; and corresponding normochromatic erythrocytes) were counted for each animal. The % of cells with mincronuclei and group means were calculated.
* Criteria for selection of maximum tolerated dose: Not discussed. Two animals receiving the highest concentration (40% over the last two weeks) died.

Results

>> Effects on Mitosi

The P/N ratio was not affected by ethanol, but was significantly increased by EMS.

>> Genotoxic Effects

Negative

>> Statistical results

Incidence of micronuclei was significantly increased ($p<0.05$) by EMS but not by ethanol. The P/N ratio was significantly decreased ($p<0.05$) by EMS but not by ethanol.

Results Remark

* Mortality at each dose level by sex: Two animals in the high-dose group, receiving 40% ethanol over the last two weeks of treatment, died, perhaps of dehydration. Two mice receiving EMS also died. No low-dose ethanol or negative control animals died.
* Mutant/aberration/mPCE/polyploidy frequency, as appropriate: The percentages of PCEs with micronuclei in the negative control, low-dose, high-dose, and positive control groups were 0.37, 0.26, 0.24, and 0.88, respectively. The P/N ratios for these same groups were 1.04, 1.07, 1.00, and 0.64, respectively. Standard errors are given.
* Description, severity, time of onset and duration of clinical signs at each dose level and sex: Not discussed.
* Body weight changes by dose and sex: Body weights at day 0 and day 26 were not affected by treatment.
* Food/water consumption changes by dose and sex: Not discussed.

Conclusions

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	1
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Male mice were exposed to increasing concentrations of ethanol in drinking water over 27 days, reaching a maximum of 30% and 40% in the low- and high-dose groups. Time-weighted average concentrations of ethanol were 23% and 33%. Actual intakes were not determined. Ethanol did not induce any statistically significant increase in micronucleus frequency in bone marrow cells, compared to negative controls, whereas the positive control (EMS) did induce a significant increase. Cell turnover was not affected by ethanol treatment.

Data Quality

Reliability

Data Reliability Remarks

These data were considered sufficiently reliable by US EPA for inclusion in a Gene-Tox Program report.

Reference

>> Remarks

Chaubey, R., Kavi, B., Chauhan, P., and Sundaram, K. (1977). Evaluation of the effect of ethanol on the frequency of micronuclei in the bone marrow of Swiss mice. Mutat. Res. 43:441-444.

These data were included in: Heddle, J., Hite, M., Kirkhar, B., et al. (1983). The induction of micronuclei as a measure of genotoxicity: A report of the U.S. Environmental Protection Agency Gene-Tox Program. Mutat. Res. 123:61-118.

General

The genotoxicity of ethanol was comprehensively reviewed in 1987 by Obe and Anderson for the International Commission for Protection Against Environmental Mutagens and Carcinogens (Mutat. Res. 186:177-200). More than 30 tests of ethanol in animals in vivo were included. The authors concluded that, in mammalian cells, ethanol is mostly non-genotoxic, but can induce SCE if a metabolic activation system is present.

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 01/02/2001

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Dominant lethal mutation assay

>> Test Type

Dominant lethal assay

>> GLP Unknown

>> Year study performed 1975

>> Species

mouse

>> Strain Mammal strain CBA

>> Sex M

>> Number of males per dose 6

>> Number of females per dose 0

>> Route of Administration

Gavage

>> Doses 1.24, 1.88 g/kg

>> Exposure period 3 d

>> Statistical Method Not specified

Remarks for Method

* Age at study initiation: About 10 weeks.
* No. of animals per dose: Thirteen at the lower dose, six at the higher dose.
* Vehicle: Distilled water.
* Duration of test: After treatment, mated to untreated females about every 4 days for 7 weeks.
* Frequency of treatment: Gavaged with ethanol once daily for 3 consecutive days.
* Sampling times and number of samples: Pregnant females were sacrificed 13-15 days after conception.
* Control groups and treatment: Untreated controls were used.
* Clinical observations performed (clinical pathology, functional observations, etc.): None.
* Organs examined at necropsy (macroscopic and microscopic): No male tissues were examined. In females, corpora lutea and live and dead implants were counted.
* Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): Dominant lethal mutation index was calculated as 100%x(1- live implants in experimental group/live implants in control group).
* Criteria for selection of maximum tolerated dose: Not discussed.

Results

>> Effects on Mitosi

Not relevant

>> Genotoxic Effects

Positive

>> Statistical results

Dead implants increased, and live implants decreased, significantly ($p<0.01$) compared to controls, in litters of matings 4-13 days after treatment of males.

Results Remark

* Mortality at each dose level by sex: None.
* Mutant/aberration/mPCE/polyploidy frequency, as appropriate: Not relevant.
* Description, severity, time of onset and duration of clinical signs at each dose level and sex: None described.
* Body weight changes by dose and sex: Not discussed.
* Food/water consumption changes by dose and sex: Not discussed.

Conclusions

The dominant lethal mutation index increased to a maximum of 46% in the low-dose litters and 67% in the high-dose litters produced by matings 4-13 days after exposure of male mice to ethanol. Given the lack of effect on the dominant lethal index for matings at other times, it was concluded that late spermatids were most affected by ethanol treatment.

Data Quality

Reliability

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	2
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Reliability Remarks

Reference

>> Remarks

Badr, F. and Badr, R. (1975). Induction of dominant lethal mutation in male mice by ethyl alcohol. Nature 253:134-136.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 01/02/2001

Test Substance

Remarks: USP alcohol, 200-proof

Chemical Category

Method

>> Method/Guideline followed

Dominant lethal mutation assay

>> Test Type

Dominant lethal assay

>> GLP Unknown

>> Year study performed 1982

>> Species

rat

>> Strain Mammal strain Long-Evans

>> Sex M

>> Number of males per dose 10

>> Number of females per dose 0

>> Route of Administration

Oral (drinking water)

>> Doses 20% v/v in drinking water

>> Exposure period 60 d

>> Statistical Method Pearson and Yates chi-square and t tests.

Remarks for Method

* Age at study initiation: Not stated. Animals weighed 200-300 g and were acclimated for 2 weeks before mating in rooms with controlled temperature, humidity, and a 12-hr light,12-hr dark cycle. Food was given ad lib.
* No. of animals per dose: 10
* Vehicle: Distilled water.
* Duration of test: Males were treated for 60 days, then mated to three females over three weeks.
* Frequency of treatment: Ad lib for 60 days.
* Sampling times and number of samples: Male testicular tissues were examined after the third mating. Females were sacrificed on gestation day 20 for examination of uterine contents.
* Control groups and treatment: Untreated males were included.
* Clinical observations performed (clinical pathology, functional observations, etc.): Male body weights were measured before and after the 60-day exposure, and at sacrifice.
* Organs examined at necropsy (macroscopic and microscopic): Testicular tissue, microscopically.
* Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): The dominant lethal index was calculated as: 100% x (1- litter size in treated group/litter size in control group).
* Criteria for selection of maximum tolerated dose: Not discussed.

Results

>> Effects on Mitosi

Not relevant

>> Genotoxic Effects Positive

>> Statistical results

Resorptions, as % of implants, was statistically significantly increased at all times by ethanol treatment ($p<0.05$).

Results Remark

* Mortality at each dose level by sex: None.
* Mutant/aberration/mPCE/polyploidy frequency, as appropriate: Not relevant.
* Description, severity, time of onset and duration of clinical signs at each dose level and sex: No adverse signs were observed.
* Body weight changes by dose and sex: Male body weights were not significantly altered by ethanol treatment.
* Food/water consumption changes by dose and sex: Not presented.

Conclusions

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	3
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Exposure of male rats to 20% ethanol in water for 60 days caused statistically significant decreases in absolute and relative testicular weights and mean diameter of seminiferous tubules, and an increase in tubules containing cellular debris. Litter size and weight were decreased by paternal ethanol treatment, and the incidence of resorptions was increased. The dominant lethal index averaged 11.9 over the three weeks of matings, decreasing from 16.4 in the first mating to 7.8 in the third.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Mankes, R., LeFevre, R., Benitz, K-F., et al. (1982). Paternal effects of ethanol in the Long-Evans rat. J. Toxicol. Environ. Health 10:871-878.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 01/02/2001

Test Substance

Remarks: Absolute ethanol, extra pure

Chemical Category

Method

>> Method/Guideline followed

Chromosomal aberrations in lymphocytes

>> Test Type

Cytogenetic assay

>> GLP Unknown

>> Year study performed 1981

>> Species

Chinese hamster

>> Strain Mammal strain Inbred colony

>> Sex Both

>> Number of males per dose 2

>> Number of females per dose 7

>> Route of Administration

Oral (drinking water)

>> Doses 10% v/v (180 g/kg-d)

>> Exposure period 322 d

>> Statistical Method Chi-square test

Remarks for Method

* Age at study initiation: 15 months. Animals were housed individually and received food ad lib.
* No. of animals per dose: Controls, 3 males, 2 females. Ethanol, 2 males, 5 females.
* Vehicle: Water
* Duration of test: 46 weeks.
* Frequency of treatment: Drinking water (with or without ethanol) provided ad lib.
* Sampling times and number of samples: Blood samples were taken in the 47th week. Two samples per animal were analyzed.
* Control groups and treatment: Controls received plain drinking water.
* Clinical observations performed (clinical pathology, functional observations, etc.): None reported.
* Organs examined at necropsy (macroscopic and microscopic): None.
* Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): Chromosomal aberrations included chromatid breaks, isochromatid breaks, and chromatid translocations. An aberrant metaphase cell contained at least one aberration.
* Criteria for selection of maximum tolerated dose: Not discussed.

Results

>> Effects on Mitosi

Not relevant.

>> Genotoxic Effects

Negative

>> Statistical results

Percentages of aberrant metaphases or specific aberrations were not significantly altered by ethanol exposure.

Results Remark

* Mortality at each dose level by sex: None.
* Mutant/aberration/mPCE/polyploidy frequency, as appropriate: Percentage of aberrant metaphases: control, 7.7%; ethanol, 10.8%.
* Description, severity, time of onset and duration of clinical signs at each dose level and sex: None described.
* Body weight changes by dose and sex: Body weights were followed throughout the exposure, and did not differ significantly.
* Food/water consumption changes by dose and sex: Animals consuming ethanol in water ate about 30% less food than did controls.

Conclusions

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	4
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Chinese hamsters consumed large amounts of ethanol in water (180 g/kg-d) for 46 weeks. Whole-blood lymphocyte cultures from these animals did not show increased rates of chromosomal aberrations.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Korte, A. and Obe, G. (1981). Influence of chronic ethanol uptake and acute acetaldehyde treatment on the chromosomes of bone-marrow cells and peripheral lymphocytes of Chinese hamsters. Mutat. Res. 88:389-395.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 01/02/2001

Test Substance

Remarks: Absolute ethanol, extra pure

Chemical Category

Method

>> Method/Guideline followed

Sister chromatid exchange assay in bone marrow cells

>> Test Type

Sister chromatid exchange assay

>> GLP Unknown

>> Year study performed 1981

>> Species

Chinese hamster

>> Strain Mammal strain inbred colony

>> Sex Both

>> Number of males per dose 1

>> Number of females per dose 4

>> Route of Administration

Oral (drinking water)

>> Doses 10% v/v (180 g/kg-d)

>> Exposure period 322 days

>> Statistical Method ANOVA

Remarks for Method

* Age at study initiation: 15 months. Animals were housed individually and received food ad lib.
* No. of animals per dose: Controls, 2 males, 1 female; ethanol, 1 male, 4 females.
* Vehicle: Water.
* Duration of test: 46 weeks.
* Frequency of treatment: Drinking water (with or without ethanol) given ad lib.
* Sampling times and number of samples: Bone marrow preparations were made in the 47th week.
* Control groups and treatment: Controls received plain drinking water.
* Clinical observations performed (clinical pathology, functional observations, etc.): None described.
* Organs examined at necropsy (macroscopic and microscopic): None.
* Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): 30-60 bone marrow metaphases per animal were examined.
* Criteria for selection of maximum tolerated dose: Not discussed.

Results

>> Effects on Mitosi

Not relevant.

>> Genotoxic Effects

Negative

>> Statistical results

Frequencies of SCE in metaphase cells of control and ethanol-treated groups did not differ with statistical signficance.

Results Remark

* Mortality at each dose level by sex: None.
* Mutant/aberration/mPCE/polyploidy frequency, as appropriate: Mean SCE per metaphase in control and ethanol-treated animals: 4.0 and 3.68, respectively.
* Description, severity, time of onset and duration of clinical signs at each dose level and sex: None.
* Body weight changes by dose and sex: Body weights were measured throughout exposure and were not significantly affected by ethanol exposure.
* Food/water consumption changes by dose and sex: Animals given ethanol in drinking water consumed 30% less food than did controls.

Conclusions

Chinese hamsters were given 10% v/v ethanol in drinking water for 46 weeks. The frequency of sister chromatid exchanges in bone-marrow cells was not significantly altered by treatment.

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	5
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Quality

Reliability

Data Reliability Remarks

These data were considered sufficiently reliable for inclusion in a US EPA Gene-Tox report.

Reference

>> Remarks

Korte, A. and Obe, G. (1981). Influence of chronic ethanol uptake and acute acetaldehyde treatment on the chromosomes of bone-marrow cells and peripheral lymphocytes of Chinese hamsters. Mutat. Res. 88:389-395.

Included in: Tucker, J., Auletta, A., Cimino, M., et al. (1993). Sister-chromatid exchange: second report of the Gene-Tox Program. Mutat. Res. 297:101-180.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 01/02/2001

Test Substance

Remarks: 100% ethanol

Chemical Category

Method

>> Method/Guideline followed

Embryonic sister chromatid exchange assay

>> Test Type

Sister chromatid exchange assay

>> GLP Unknown

>> Year study performed 1980

>> Species

mouse

>> Strain Mammal strain ICR

>> Sex F

>> Number of males per dose 0

>> Number of females per dose 4

>> Route of Administration

intraperitoneal

>> Doses 2, 4 g/kg

>> Exposure period One injection

>> Statistical Method Student's t-test

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age at study initiation: Not specified
* No. of animals per dose: Four pregnant animals were used per dose group.
* Vehicle: Water, by implication.
* Duration of test: Dams were sacrificed 7 hours after ethanol injection.
* Frequency of treatment: One treatment or 10% ethanol.
* Sampling times and number of samples: On the 10th gestation day, one hour before ethanol injection, dams received injections of BrdU and thymidine. From each dam, all embryos were removed and homogenized.
* Control groups and treatment: Untreated controls.
* Clinical observations performed (clinical pathology, functional observations, etc.): None.
* Organs examined at necropsy (macroscopic and microscopic): None.
* Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): Twelve or 13 metaphase spreads of embryonic cells were examined per dam. Statistical significances between mean values in treatment groups were the indicator of effect.
* Criteria for selection of maximum tolerated dose: Not discussed. The high dose, however, produced a blood alcohol level of 225 mg/dl, an intoxicating level.

Results

>> Effects on Mitosi

Not examined

>> Genotoxic Effects

Positive

>> Statistical results

Compared to the control group, a statistically significant ($p<0.001$) increase was observed in the SCE frequency in embryonic cells from high-dose dams.

Results Remark

* Mortality at each dose level by sex: None.
* Mutant/aberration/mPCE/polyploidy frequency, as appropriate: SCE frequencies in control, low-, and high-dose groups: 2.44/cell, 2.92/cell, and 3.96/cell. Standard errors are given.
* Description, severity, time of onset and duration of clinical signs at each dose level and sex: None described.
* Body weight changes by dose and sex: Not measured.
* Food/water consumption changes by dose and sex: Not measured.

Conclusions

A single injection of 4 g/kg ethanol, but not 2 g/kg, into pregnant mice induced a statistically significant increase in the SCE frequency in embryonic cells.

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	6
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Quality

Reliability

Data Reliability Remarks

These data were considered sufficiently reliable for inclusion in a US EPA Gene-Tox report.

Reference

>> Remarks

Czajka, M., Tucci, S., and Kaye, G., (1980). Sister chromatid exchange frequency in mouse embryo chromosomes after in utero ethanol exposure. Toxicol. Lett. 6:257-261.

Included in: Tucker, J., Auletta, A., Cimino, M., et al. (1993). Sister-chromatid exchange: second report of the Gene-Tox Program. Mutat. Res. 297:101-180.

The Gene-Tox report includes other data not reviewed in this robust summary.

General

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 01/11/2001

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Sister chromatid exchange assay in bone marrow cells

>> Test Type

Sister chromatid exchange assay

>> GLP: Unknown

>> Year study performed: 1993

>> Species

mouse

>> Strain: Mammal strain: NIH

>> Sex: M

>> Number of males per dose: 5

>> Number of females per dose: 0

>> Route of Administration

intraperitoneal

>> Doses: 0.3, 0.6, 1.2, 2.4 g/kg

>> Exposure period: Single injection

>> Statistical Method: Student's t-test

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age at study initiation: Not stated. Animals weighed approximately 26 g and were housed at 24 deg. C with food and water ad lib.
* No. of animals per dose: 5
* Vehicle: Distilled water.
* Duration of test: Single injection of 50% ethanol; BrdU was given one hour before ethanol injection, and colchicine 21 hours later. Animals were sacrificed 24 hours after ethanol injection.
* Frequency of treatment: Once.
* Sampling times and number of samples: 30 second-division bone marrow cells were examined per mouse.
* Control groups and treatment: Negative controls were used (no ethanol).
* Clinical observations performed (clinical pathology, functional observations, etc.): None.
* Organs examined at necropsy (macroscopic and microscopic): None.
* Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): 30 cells/mouse were examined. Student's t-test was used to judge the significance of differences between group means.
* Criteria for selection of maximum tolerated dose.: The highest dose was 1/4 to 1/2 the previously determined LD50.

Results

>> Effects on Mitosi

Average generation time of bone marrow cells was not affected by ethanol treatment.

>> Genotoxic Effects

Positive

>> Statistical results

Ethanol doses of 0.6 g/kg or more induced statistically significant increases (at p=0.01) in SCE frequencies.

Results Remark

* Mortality at each dose level by sex: None.
* Mutant/aberration/mPCE/polyploidy frequency, as appropriate: SCE frequencies in control and ethanol treatment groups (low to high dose) were, respectively: 3.20, 3.60, 3.73, 3.90, 4.42.
* Description, severity, time of onset and duration of clinical signs at each dose level and sex: Not described.
* Body weight changes by dose and sex: Not described.
* Food/water consumption changes by dose and sex: Not described.

Conclusions

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	7
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Ethanol, given intraperitoneally once at doses of 0.6 g/kg or more, increased the frequency of sister chromatid exchanges in bone marrow cells of male NIH mice.

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Pina Calva, A. and Madrigal-Bujaidar, E. (1993). SCE frequencies induced by ethanol, tequila and brandy in mouse bone marrow cells in vivo. Toxicol. Lett. 66:1-5.

General

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	8
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Revision Date: 01/11/2001

Test Substance

Remarks: Ethanol, not described

Chemical Category

Method

>> Method/Guideline followed

Sister chromatid exchange assay in spermatogonial cells

>> Test Type

Sister chromatid exchange assay

>> GLP Unknown

>> Year study performed 1988

>> Species

mouse

>> Strain Mammal strain C57BL

>> Sex M

>> Number of males per dose 10

>> Number of females per dose 0

>> Route of Administration

oral (drinking water)

>> Doses 20% in drinking water

>> Exposure period 10 weeks

>> Statistical Method Mann-Whitney rank test

Remarks for Method

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	8
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

* Age at study initiation: 8 weeks.
* No. of animals per dose: 10.
* Vehicle: By implication, water.
* Duration of test: 10 weeks.
* Frequency of treatment: Water provided ad lib.
* Sampling times and number of samples: After 10 weeks, mice were administered BrdU and colcemid, and sacrificed after 66 hours of BrdU treatment. Preparations were made from testicular tissue.
* Control groups and treatment: Negative controls were used (no ethanol).
* Clinical observations performed (clinical pathology, functional observations, etc.): None mentioned.
* Organs examined at necropsy (macroscopic and microscopic): None.
* Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): Thirty cells per animal were examined. Statistical significance was used to evaluate the effect of treatment.
* Criteria for selection of maximum tolerated dose: Not discussed.

Results

>> Effects on Mitosi

Not measured

>> Genotoxic Effects

Positive

>> Statistical results

Increase in SCE frequency in spermatogonial cells of treated animals was significant ($p<0.01$).

Results Remark

* Mortality at each dose level by sex: No mortality mentioned.
* Mutant/aberration/mPCE/polyploidy frequency, as appropriate: Mean SCE/cell in control and ethanol groups: 1.38 and 1.94, respectively.
* Description, severity, time of onset and duration of clinical signs at each dose level and sex: Not discussed.
* Body weight changes by dose and sex: Not discussed.
* Food/water consumption changes by dose and sex: Not discussed.

Conclusions

In male mice given 20% ethanol in water as their only fluid for 10 weeks, SCE occurred at slightly higher frequency in spermatogonial cells than in control animals. Mouse testis contains alcohol and aldehdye dehdrogenases.

EPA High Production Volume (HPV) Track

Toxicity End Point:
Toxicity in Vivo (Chromosomal Aberrations)

Sponsor ID	9999999	Sponsor Named in Consortium		Create Date	10/16/2000
CAS Number	64175	Ethyl alcohol		Study Number	8
Consortia ID	1101157	Ethanol HPV Challenge Consortium		Completed:	Y

Data Quality

Reliability

Data Reliability Remarks

Reference

>> Remarks

Hirai, M. (1988). Effects of alcohol-drinking on mouse chromosones. II. Sister-chromatid exchange and chromosome dissociation in male germ cells of mice administered ethanol. Jpn. J. Alcohol Drug Dependence 23(3):243-251.

General