

AR 201-12978B

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

CHEMICAL AND PHYSICAL PROPERTIES:  
MELTING POINT

Chemical Name: Tris( 1,3-dichloropropyl-2) phosphate

Method/Guideline: Method Unknown

Test Type: Melting Point Determination

GLP Compliant: No

Year Test Performed: Unknown

Species: Not Applicable

Statistical Methods: Not Applicable

Remarks on Test Conduct: The melting point was determined several years ago. The data from the test is unavailable. Therefore, the method used to measure the melting point cannot be described.

Results: The melting point was determined to be 26.66°C (80.00°F).

Conclusion: The melting point was determined to be 26.66°C (80.00°F).

Data Quality: Not reliable. The underlying data that supports the melting point is unavailable. The test will be repeated to confirm the melting point.

Reference: This robust summary was prepared by an individual company from information contained on the company's MSDS. The information was obtained in a company test several years ago. Since the raw data are unavailable, the test will be repeated.

Other: Prepared March 13,200 1

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ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

CHEMICAL AND PHYSICAL PROPERTIES:  
BOILING POINT

Chemical Name: Tris(1,3-dichloropropyl-2) phosphate

Method/Guideline: Method Unknown

Test Type: Boiling Point Determination

GLP Compliant: No

Year Test Performed: Unknown

Species: Not Applicable

Statistical Methods: Not Applicable

Remarks on Test Conduct: The boiling point was determined several years ago. The data from the test are unavailable. Therefore, the method used to measure the boiling point cannot be described.

Results: The boiling point was determined to be 200.0°C (392.0°F) @ 4mmHg.

Conclusion: The boiling point was determined to be 200.0°C (392.0°F) @ 4 mm Hg.

Data Quality: Not reliable. The underlying data that supports the boiling point are unavailable. The test will be repeated to confirm the boiling point.

Reference: This robust summary was prepared by an individual company from information contained on the company's MSDS. The information was obtained in a company test several years ago. Since the raw data are unavailable, the test will be repeated.

Other: Prepared March 13, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

CHEMICAL AND PHYSICAL PROPERTIES: VAPOR  
PRESSURE

Chemical Name:	Tris(1,3-dichloropropyl-2) phosphate
Method/Guideline:	Not Applicable
Test Type:	Vapor Pressure Determination
GLP Compliant:	Not Applicable
Year Test Performed:	Not Performed
Species:	Not Applicable
Statistical Methods:	Not Applicable
Remarks on Test Conduct:	The vapor pressure of Fyrol FR-2 has not been determined experimentally.
Results:	None
Conclusion:	None
Data Quality:	No data available. A test will be conducted to determine the vapor pressure of Fyrol FR-2.
Reference:	Not Applicable.
Other:	Prepared March 13, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

CHEMICAL AND PHYSICAL PROPERTIES:  
PARTITION COEFFICIENT (log  $K_{ow}$ )

Chemical Name:	Tris( 1,3-dichloropropyl-2) phosphate
Method/Guideline:	QSAR Derived Partition Coefficient (log $K_{ow}$ ) Using CLOGP and KOWWIN Models
Test Type:	n-Octanol-Water Partition Coefficient
GLP Compliant:	Not Applicable
Year Test Performed:	2001
Species:	Not Applicable
Statistical Methods:	Not Applicable. Validated models were used to calculate the partition coefficient
Remarks on test Conduct:	Two validated models were used to estimate the n-octanol-water partition coefficient (log $K_{ow}$ ), which is the ratio of the amount of Fyrol FR-2 dissolved in the octanol phase and the water phase. The CLOGP and KOWWIN models were used estimate the Log $K_{ow}$ for Fyrol FR-2. The CLOGP model, based on the Hansch and Leo calculation procedure, sums the fragmental values and them applies correction values for branching, unsaturation, and other contributing parameters. The KOWWIN model, based on group contribution, also uses structural fragments and correction factors. Both models have been developed for the estimation of Log $K_{ow}$ values.
Results:	The CLOGP model calculated a Log $K_{ow}$ value for Fyrol FR-2 of 1.59. The KOWWIN model calculated a Log $K_{ow}$ value of 3.64. The literature contains measured Log $K_{ow}$ values of 3.65 and 3.76. However, since the citations from which these values were derived are not available, their validity could not be confirmed. The two measured values are in very close agreement with the 3.65 value calculated using the KOWWIN model. The reason for the lower Log $K_{ow}$ value obtained with the CLOGP model is unknown.

Conclusion: The Log  $K_{ow}$  value for Fyrol FR-2 is estimated to be about 3.65.

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

CHEMICAL AND PHYSICAL PROPERTIES:  
PARTITION COEFFICIENT (log  $K_{ow}$ )

Data Quality: Reliable without restrictions

Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other: Prepared March 12, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

CHEMICAL AND PHYSICAL PROPERTIES: WATER  
SOLUBILITY

Chemical Name: Tris( 1,3-dichloropropyl-2) phosphate

Method/Guideline: Method Unknown

Test Type: Water Solubility Determination

GLP Compliant: No

Year Test Performed: unknown

Species: Not Applicable

Statistical Methods: Not Applicable

Remarks on Test Conduct: The water solubility was determined several years ago. The data from the test are unavailable. Therefore, the method used to measure the water solubility of Fyrol FR-2 cannot be described.

Results: The water solubility was determined to be 0.01% at 30°C (86°F)

Conclusion: The water solubility was determined to be 0.01% at 30°C (86°F)

Data Quality: Not reliable. The underlying data that supports the water solubility of Fyrol FR-2 are unavailable. The test will be repeated.

Reference: This robust summary was prepared by an individual company from information contained on the company's MSDS. The information was obtained in a company test several years ago. Since the raw data are unavailable, the test will be repeated.

Other: Prepared March 13, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

ENVIRONMENTAL FATE AND PATHWAYS:  
PHOTODEGRADATION

Chemical Name:	Tris(1,3-dichloropropyl-2) phosphate
Method/Guideline:	Not Applicable
Test Type:	Photodegradation
GLP Compliant:	Not Applicable
Year Test Performed:	Not Performed
Species:	Not Applicable
Statistical Methods:	Not Applicable
Remarks on Test Conduct:	The photodegradation of Fyrol FR-2 has not been determined.
Results:	None
Conclusion:	None
Data Quality:	No data available
Reference:	This robust summary was prepared by an individual company. A photodegradation test will be conducted.
Other:	Prepared March 13, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

ENVIRONMENTAL FATE AND PATHWAY  
ELEMENTS: HYDROLYSIS AS A FUNCTION OF pH

Chemical Name:	Tris( 1,3-dichloropropyl-2) phosphate
Method/Guideline:	OECD Guideline 111, EPA Series 835 OPPTS Number 835.2110
Test Type:	Hydrolysis as a function of pH; Preliminary Test
GLP Compliant:	Yes
Year Test Performed:	2000
Statistical Methods:	Not Applicable
Remarks on Test Conduct:	The rate of hydrolysis (hydrolytic stability) of Fyrol FR-2 in aqueous buffered solutions was determined at pH 4, 7, and 9. The test substance was present at 10.0 mg/l, about half of the estimated water solubility. The test was performed at 50±1°C for five days. Samples were extracted and analyzed on study days 0, 2, and 4. A validated analytical method (gas chromatography with electron capture detector) was used to measure the concentration of Fyrol FR-2 in the test samples.
Results:	The percent recovery of samples in pH 4 buffer (phthalate buffer) was 93, 101, and 102% on days 0, 2, and 4, respectively, indicating no decline in concentration. Similarly, samples in pH 7 buffer (phosphate buffer) had recoveries of 114, 109, and 109% on days 0, 2, and 4, respectively, showing stability under neutral conditions. At both acid and neutral conditions the hydrolytic half-life is greater than one year. Samples in pH 9 buffer (borate buffer) yielded recoveries of 101, 94, and 84% on days 0, 2, and 4, respectively. Linear regression analysis of the pH 9 recovery data yielded a hydrolysis rate constant of 0.04727 which corresponds to a half-life of approximately 14.7 days.
Conclusion:	Fyrol FR-2 demonstrated excellent hydrolytic stability under acid and neutral conditions with some instability shown at pH 9.

Data Quality:

Reliable without restrictions

**ROBUST SUMMARY**

**FYROL FR-2**

**CAS# 13674-87-8**

**ENVIRONMENTAL FATE AND PATHWAY  
ELEMENTS: HYDROLYSIS AS A FUNCTION OF pH**

Reference:

This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other:

Prepared January 10, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

ENVIRONMENTAL FATE AND PATHWAY  
ELEMENTS: HYDROLYSIS AS A FUNCTION OF pH

Chemical Name:	Tris( 1,3-dichloropropyl-2) phosphate
Method/Guideline:	OECD Guideline 111, EPA Series 835 OPPTS Number 835.2110
Test Type:	Hydrolysis as a function of pH;
GLP Compliant:	Yes
Year Test Performed:	2000
Statistical Methods:	Not Applicable
Remarks on Test Conduct:	A preliminary test indicated Fyrol FR-2 was somewhat unstable at pH 9 and at the elevated temperature of 50°C, under those conditions demonstrating a half-life of about 14.7 days. Therefore this definitive hydrolytic study was performed. The hydrolytic stability of Fyrol FR-2 in a sterile borate buffer solution at pH 9 was determined at 20°C and 40°C for a 30 day period. Samples were prepared in triplicate and were analyzed at intervals to provide at least six analyses between 20 and 70% hydrolysis. A validated analytical method (gas chromatography with electron capture detector) was used to determine the concentration of Fyrol FR-2 on day 0 (at 0 and 4 hours) and on days 6, 9, 13, 17, 20, 24, 27, and 30.
Results:	For the samples maintained at 20°C, marginal hydrolytic degradation was seen. Mean percent recoveries were 113% on day 0 (0 and 4 hours), 111% on day 6, 103% on day 9, 101% on day 13, 99% on day 17, 98% on day 20, 99% on day 24, 96.5% on day 27, and 96.1% on day 30. Linear regression analysis yielded a hydrolysis rate constant of -0.005757, which corresponds to a half-life of about 120 days. Samples maintained at 40°C demonstrated significant degradation yielding mean recoveries of 113% at hour 0, 114% at hour 4, 98.8 on day 6, 88.0% on day 9, 81% on day 13, 73.2 on day 17, 68.6% on day 20, 63.2% on day 24, 58% on day 27, and 54.5% on day 30. Linear regression analysis yielded a

hydrolysis rate of -0.02461, which corresponds to a half-life of about 28 days. These data suggest that the hydrolytic stability of

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# ENVIRONMENTAL FATE AND PATHWAY ELEMENTS: HYDROLYSIS AS A FUNCTION OF pH

Fyrol FR-2 at pH 9 is highly temperature dependent. The coefficient of determination for the regression analysis at pH 9 and 20°C is 0.8810 indicating that at this temperature that the hydrolysis reaction does not follow first order kinetics. At pH 9 and 40°C the coefficient of determination was 0.9973 demonstrating excellent linearity and showing that the reaction follows first order kinetics.

Conclusion:	The hydrolysis half-life for Fyrol FR-2 at pH 9 was shown at 20°C and 40°C to be about 120 and 28 days, respectively.
Data Quality:	Reliable without restrictions
Reference:	This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.
Other:	Prepared January 11, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

ECOTOXICITY ELEMENTS: ACTIVATED SLUDGE  
RESPIRATION INHIBITION TEST

Chemical Name: Tris(1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 209 Activated Sludge – Respiration Inhibition Test

Test Type: Biodegradation

GLP Compliant: Yes

Year Test Performed: 1990

Species: Activated sludge from a sewage treatment facility

Statistical Methods: Not Applicable. Calculations of the respiration rate and inhibition of respiration are by formulas provided in Guideline 209 and presented in the final report. The EC50 and the 95% confidence limits were calculated using the computer program of Stephan.

Remarks on Test Conduct Samples of activated sludge fed with synthetic sludge were exposed to Fyrol FR-2 for 3 hours. Their rates of oxygen consumption were measured using an oxygen electrode and compared with control levels. Two tests were conducted. The first utilized nominal Fyrol FR-2 levels of 1, 10, and 100 mg/l and the second test used 1 and 10 g/l. The positive control respiration inhibitor, 3,5-dichlorophenol, was used in each test at 3.2, 10, and 32 mg/l.

Results: The nontreated sludge maintained normal respiration through the test whereas the 3,5-dichlorophenol inhibited sludge showed EC50's of 7.2 and 7.1 mg/l in the two tests. The respiration rates of the activated sludge in the presence of Fyrol FR-2 were not significantly different than that of the nontreated controls. Fyrol FR-2 did not inhibit the respiration of activated sludge and thus an EC50 could not be determined. It must be greater than 10g/l, the highest concentration used in this test.

Conclusion: Fyrol FR-2 does not inhibit active sludge respiration.

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

ENVIRONMENTAL FATE AND PATHWAY  
ELEMENTS: BIODEGRADATION

Data Quality: Reliable without restrictions

Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other: Prepared March 8, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

ENVIRONMENTAL FATE AND PATHWAY  
ELEMENTS: BIODEGRADATION

Chemical Name:	Tris( 1,3-dichloropropyl-2) phosphate
Method/Guideline:	OECD Guideline 301B (Modified Sturm Test) and 301D (Closed Bottle Test)
Test Type:	Biodegradation
GLP Compliant:	Yes
Year Test Performed:	1990
Species:	Inoculum from the effluent of a sewage treatment facility
Duration of Test:	28 days
Statistical Methods:	Not Applicable. Calculation of theoretical oxygen demand, chemical oxygen demand (COD), biochemical oxygen demand (BOD), and other values utilized the procedures and formulas provided in the guidelines cited above.
Remarks on Test Conduct:	Initially the biodegradability of Fyrol FR-2 was determined in a COD test and in a 10-day bacterial inhibition assay conducted under The Closed Bottle Test conditions. The test substance was then evaluated in the Modified Sturm Test. In these tests, the COD was determined by oxidation with an acid dichromate mixture at 1 50°C, using six replicates per test substance concentration. Fyrol FR-2 nominal concentrations added to the reaction vessels ranged from 250 to 750 mg/l. In the bacterial inhibition assay, Fyrol FR-2 concentrations of 2 and 10 mg/l were used. Groups of 6 bottles per concentration were used to provide sufficient replicates. The dissolved oxygen concentration was measured at the start of the test and after incubation at 20°C in darkness for 5 and 10 days. In the modified Sturm Test, Fyrol FR-2 concentrations of 10 and 20 mg/l were added to vessels containing the inoculum. The vessels were aerated for 28 days after which the amount of carbon dioxide

produced by each culture was measured. The amount of dissolved organic carbon (DOC), as an indication of CO<sub>2</sub> production, was the

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# ENVIRONMENTAL FATE AND PATHWAY ELEMENTS: BIODEGRADATION

endpoint measured on day 0 and on day 27.

Results:

In the COD assay, the mean of six determinations was 0.85 mgO<sub>2</sub>/mg, which was 109% of the calculated theoretical oxygen demand of 0.78 mgO<sub>2</sub>/mg. This indicates that the Fyrol FR-2 present in the chambers was completely oxidized under the conditions of this test. In the bacterial inhibition assay, the reference material, sodium benzoate, when placed in the sewage effluent inoculum, was readily degraded to 57% of its theoretical oxygen demand. The presence of Fyrol FR-2 had no significant effect on the bacterial action, confirming that the product is not inhibitory to the bacterial inoculum. In the modified Sturm Test, CO<sub>2</sub> was produced in the control group in 28 days confirming the viability of the inoculum and validity of the test. No CO<sub>2</sub> was produced by day 28 in the vessels containing Fyrol FR-2, indicating the test substance was not degradable under the conditions of this test.

Conclusion:

Fyrol FR-2 is not readily biodegradable.

Data Quality:

Reliable without restrictions

Reference:

This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other:

Prepared March 8, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

ECOTOXICITY ELEMENTS: ACUTE TOXICITY TO  
FISH

Chemical Name: Tris(1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 203

Test Type: Acute toxicity to fish

GLP Compliant: Yes

Year Test Performed: 1990

Species: Rainbow trout (*Salmo gairdneri*)

Route of Administration: Added to the water in the test chamber

Duration of Test: 96 Hour exposure to Fyrol FR-2

Dose/Concentration Levels: 0 (negative control), 0.63, 1.25, 2.5, 5, and 10 mg/l

Statistical Methods: Median lethal concentration (LC50) was determined using the computer program of Stephan, incorporating the number of fish exposed and the mortality observed at each concentration.

Remarks on Test Conduct: This study was conducted to determine the acute toxicity of Fyrol FR-2 to the rainbow trout under static conditions with an exposure of 96 hours. Initially two range-finding tests were conducted to determine the appropriate doses (water concentrations) for the definitive study. In these preliminary tests, the highest concentration at which no mortality occurred and the lowest dose that caused 100% mortality were 0.1 and 10 mg/l, respectively. In the definitive test, groups consisting of ten trout were exposed to Fyrol FR-2 at nominal concentrations of 0 (negative control), 0.63, 1.25, 2.5, 5, and 10 mg/l for 96 hours. Observations were made for signs of toxicity after 2, 4, 24, 48, 72, and 96 hours of exposure.

Results: Mortality was dose-related, with a clear dose-response observed.

All mortalities occurred within the first 24 hours. One fish died in the lowest dose group (0.63 mg/l) at 24 hours. Mortality of 100%

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# ECOTOXICITY ELEMENTS: ACUTE TOXICITY TO FISH

occurred in the 5 mg/l and 10 mg/l groups. The median lethal concentration (LC50) of Fyrol FR-2 was determined to be 1.4 mg/l, with 95% confidence limits of 0.9 and 1.9 mg/l. Since one fish died in the lowest dose group, an NOEC was not observed and is therefore less than 0.63 mg/l.

Conclusion:	The 96 hour LC50 value for Fyrol FR-2 in rainbow trout was determined to be 1.4 mg/l, with confidence limits of 0.9 to 1.9 mg/l.
Data Quality:	Reliable without restrictions
Reference:	This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.
Other:	Prepared January 11, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

ECOTOXICITY ELEMENTS: ACUTE TOXICITY TO  
AQUATIC INVERTEBRATES

Chemical Name: Tris(1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 202; EPA Series 850 OPPTS Number 850.1010

Test Type: 48-Hour Flow-Through Acute Toxicity Test with Cladoceran (*Daphnia magna*)

GLP Compliant: Yes

Year Test Performed: 1999

Species: *Daphnia magna*

Strain: Not Applicable

Route of Administration: Added to the water in the test chambers containing the *Daphnia*

Duration of Test: Test organisms were continuously exposed for 48 hours

Dose/Concentration Levels: Negative Control, Solvent Control, 0.98, 1.6, 2.8, 3.8, and 5.1 mg/l (measured levels)

Statistical Methods: The EC50 value was calculated using the EPA program developed by C.E. Stephan. The program calculates the EC50 and the 95% confidence interval by probit analysis, the moving average method, and binomial probability with nonlinear interpolation.

Remarks on Test Conduct: Two replicate test chambers, each containing 10 daphnids, were utilized for each group. Daphnids were exposed in seven groups, which consisted of a negative control, solvent control (dimethylformamide), and five concentrations of Fyrol FR-2 (listed above). Test substance was added to the chamber 22 hours before the daphnids to achieve equilibrium. Observations were made at 1, 24, and 48 hours for mortality/immobility and clinical signs. Samples were taken from test chambers at the start and end of the test to quantify the concentration of the test substance, using GC with

electron capture detection.

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

ECOTOXICITY ELEMENTS: ACUTE TOXICITY TO  
AQUATIC INVERTEBRATES

Results: Environmental conditions, including dissolved oxygen, pH, and temperature were within guideline and protocol specifications. Daphnids in the negative and solvent control groups appeared healthy and normal throughout the test. Daphnids in the 0.98 and 1.6 mg/l groups also appeared normal with no mortality or signs of toxicity. After 48 hours of exposure, mortality/immobility in the 2.8, 3.8, and 5.1 mg/l groups was 0, 70, and 80%. Although no mortality occurred at 2.8 mg/l, 15% of the daphnids appeared lethargic at test termination. The 48 hr EC50 was determined to be 3.8 mg/l.

Conclusions: The 48 hour EC50 for *Daphnia magna* was 3.8 mg Fyrol FR-2/l. The 95% confidence limits were 3.5 and 4.2 mg/l. The NOEL was 1.6 mg/l.

Data Quality: Reliable without restrictions

Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other: Prepared on January 10, 2001.

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

ECOTOXICITY ELEMENTS: TOXICITY TO  
AQUATIC PLANTS

Chemical Name: Tris( 1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 201

Test Type: Alga Growth Inhibition Test (toxicity to the freshwater alga)

GLP Compliant: Yes

Year Test Performed: 1992

Species: *Selenastrum capricornutum*

Route of Administration: Added to the water in the test chamber containing the alga

Duration of Test: 96 Hour exposure to Fyrol FR-2

Dose/Concentration Levels: 0 (negative control), 2, 6, 18, 54, and 162 mg/l

Statistical Methods: The EC20, EC50, and EC80 values were determined using least square method (best fit through the points) obtained from the probit of the percent inhibition and the log of the concentration of Fyrol FR-2. Confidence limits were calculated using Fieller's theorem.

Remarks on Test Conduct: A dose range-finding test was initially conducted to identify the appropriate concentrations of Fyrol FR-2 for use in the definitive test. The range-finding doses were 0.1, 1, 10, and 100 mg/l. Since growth inhibition was observed in the 10 and 100 mg/l cultures, the definitive test used nominal concentrations of 2, 6, 18, 54, and 162 mg/l. Algal growth was determined by measuring the extinction at 436 nm using a spectrophotometer. The direct relationship between extinction values and cell density has been established. Cell density was also determined microscopically using a counting chamber. The extinction value for each vessel was determined at 0, 24, 48, 72, and 96 hours.

Results:

The  $E_bC50$  value, determined from the area under the curve, and the  $E_rC50$  value, determined from the specific growth rate, are 12 mg/l

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# ECOTOXICITY ELEMENTS: TOXICITY TO AQUATIC PLANTS

(95% confidence limits of 10- 15 mg/l) and 39 mg/l (95% confidence limits of 3 1-50 mg/l), respectively. The NOEL for Fyrol FR-2 was 6 mg/l.

Conclusion:

The  $E_bC50$  and  $E_rC50$  values have been determined to be 12 and 39 mg/l, respectively. The NOEL was determined as 6 mg/l.

Data Quality:

Reliable without restrictions

Reference:

This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other:

Prepared March 8, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS: ACUTE  
ORAL TOXICITY

Chemical Name: Tris(1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 401

Test Type: Acute Oral Toxicity

GLP Compliant: No

Year Test Performed: 1982

Species: Dutch-Belted Rabbits

Sex: Male

Duration of Test: 14 days

Route of Administration: Oral

Dose/Concentration levels: 0, 10,000, 7,500, and 5,000 mg/kg

Statistical Methods: The LD50 and 95% confidence intervals were calculated using the Method of Litchfield and Wilcoxon.

Remarks on Test Conduct: Groups of adult Dutch-Belted rabbits, five males per group, received a single oral dose of Fyrol FR-2 through a stomach tube (necessary to administer the large volume in a single dose). The animals were observed daily for 14 days. Clinical observations were recorded throughout the test. Survivors were sacrificed on day 14 and necropsied.

Results: Clinical signs observed shortly after dosing included ataxia, weakness, and diarrhea. All surviving animals appeared normal by day 9. Gross examination during necropsy found all animals to be normal. The high dose caused 100% mortality, beginning three days after dosing. Mortality in the mid dose was 3 of 5 rabbits. The low

dose resulted in a mortality of 1 of 5 rabbits. The acute oral LD50 for Fyrol FR-2 was calculated to be 6,800 mg/kg, with 95%

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# HUMAN HEALTH EFFECTS ELEMENTS: ACUTE ORAL TOXICITY

confidence limits of 5615 and 8234.

Conclusion: The acute oral LD50 in Dutch-Belted rabbits is 6,800 mg/kg, with 95% confidence limits of 5615 and 8234.

Data Quality: Reliable without restrictions

Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other: Prepared January 12, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS: ACUTE  
ORAL TOXICITY

Chemical Name: Tris( 1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 401

Test Type: Acute Oral Toxicity

GLP Compliant: No

Year Test Performed: 1972

Species: Sprague-Dawley Rat

Sex: Male

Duration of Test: 14 days

Route of Administration: Oral

Dose/Concentration levels: 1,000, 2,150, 4,640, and 10,000 mg/kg

Statistical Methods: The LD50 and 95% confidence intervals were calculated using the Method of Litchfield and Wilcoxon.

Remarks on Test Conduct: Groups of Sprague-Dawley rats, five males per group, received a single oral dose of Fyrol FR-2 by gavage. The animals were observed daily for 14 days. Clinical observations were recorded throughout the test. Survivors were sacrificed on day 14 and necropsied.

Results: No clinical signs were observed in the animals that received 1,000 mg/kg. Some animals that received the higher doses expressed depression, the incidence and severity increased with dose. No other clinical signs were observed. All surviving animals appeared normal by day 5. Gross examination during necropsy found all animals to be normal. Mortality was observed as 0/5, 1/5, 4/5, and

5/5 for the 1000, 2150, 4640, and 10,000 mg/kg doses, respectively.  
The acute oral LD50 for Fyrol FR-2 in rats was calculated to be

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# HUMAN HEALTH EFFECTS ELEMENTS: ACUTE ORAL TOXICITY

3,160 mg/kg, with 95% confidence limits of 2050 and 4800.

Conclusion: The acute oral LD50 in Sprague-Dawley rats is 3,160 mg/kg, with 95% confidence limits of 2050 and 4800.

Data Quality: Reliable without restrictions.

Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other: Prepared March 8, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS: ACUTE  
DERMAL TOXICITY

Chemical Name: Tris( 1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 402

Test Type: Acute Dermal Toxicity

GLP Compliant: No

Year Test Performed: 1973

Species: Rabbit

Sex: Unknown

Duration of Test: 14 days

Route of Administration: Dermal

Dose levels: 4,640 mg/kg

Statistical Methods: No Applicable. Only one dose was administered and not mortality as observed.

Remarks on Test Conduct: About 24 hours before treatment, fur was removed from an area of the trunk of each animal. Four mature New Zealand White rabbits received a single dermal application of Fyrol FR-2 to the shaved area. The treatment area was then wrapped with gauze for 24 hours. The animals were unwrapped at 24 hours, the application site washed, and the animals then observed for 14 days. The animals were then sacrificed and necropsied.

Results: No treatment-related clinical signs were observed. There was no Mortality. All four animals appeared normal throughout the test And showed no anomalies at necropsy. The dermal LD50 is therefore greater than 4,640 mg/kg.

Conclusion: The dermal LD50 is greater than 4,640 mg/kg.

**ROBUST SUMMARY**

**FYROL FR-2**

**CAS#13674-87-8**

**HUMAN HEALTH EFFECTS ELEMENTS: ACUTE  
DERMAL TOXICITY**

Data Quality: Reliable without restrictions. The data presented are reliable. However, Guideline 402 requires the use of five animals and only four animals were used in this study. Guideline 402 requires the animals to be all of one sex. The sex of the rabbits used in this study are unknown.

Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other: Prepared March 8, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS: ACUTE  
EYE IRRITATION/CORROSION

Chemical Name: Tris( 1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 405

Test Type: Acute Eye Irritation

GLP Compliant: No

Year Test Performed: 1979

Species: New Zealand White Rabbit

Sex: Male/Female

Duration of Test: 7 Days

Route of Administration: Topical application to the eye

Dose levels: 0.1 ml

Statistical Methods: Not applicable

Remarks on Test Conduct: One day before treatment, the eyes of nine rabbits were examined to assure they were normal. One tenth of an ml (0.1 ml) of Fyrol FR-2 was placed in one eye of each animals by pulling the lower lid away from the eyeball to form a cup into which the liquid was placed. The lids were held together after placement of the test substance to assure contact with the eye. The eyes of three treated rabbits were washed with water about 30 seconds after exposure and the eyes of the remaining six treated rabbits were unwashed. The untreated eye of each animal served as the untreated control. The cornea, iris, and conjunctiva were examined at 24, 48, and 72 hours and 4 and 7 days after application. The eyes were scored using the Draize method which assigns numerical scores for observed effects.

Results:

The eyes of all nine animals were observed at each of the specified time points through day 7. No sign of eye irritation was seen in any

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# HUMAN HEALTH EFFECTS ELEMENTS: ACUTE EYE IRRITATION/CORROSION

of the animals at any of the time points. Therefore the average total score was zero. Fyrol FR-2 did not cause eye irritation in this test.

Conclusion:

Fyrol FR-2 is not an eye irritant.

Data Quality:

Reliable without restrictions.

Reference:

This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other:

Prepared March 2, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS: ACUTE  
DERMAL IRRITATION/CORROSION

Chemical Name: Tris( 1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 404

Test Type: Acute Dermal Irritation

GLP Compliant: No

Year Test Performed: 1979

Species: New Zealand White Rabbit

Sex: Male/Female

Duration of Test: 72 Hours

Route of Administration: Dermal

Dose levels: 0.5 ml per application site

Statistical Methods: Not applicable

Remarks on Test Conduct: One day before treatment, the backs of the six rabbits were shaved. Each shaved area was divided into four areas and then two of the areas were abraded. The Fyrol FR-2 (0.5 ml) was applied to one abraded and one non-abraded site. The two other sites acted as controls. All four sites were covered with a patch for a 24 hour exposure period. The patches were then removed and the application sites were examined for irritation. Irritation was scored using the Draize method for edema, erythema, and eschar. Observations were to be made at 24 and 72 hours post-exposure, and for up to 14 days if irritation persists.

Results: At 24 hours post-application, intact treated sites on five of the six rabbits showed a grade 1 erythema. One showed a grade 2. Four

abraded sites showed a grade 1 erythema while two abraded sites showed grade 2 erythema. No edema was reported in any animals.

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# HUMAN HEALTH EFFECTS ELEMENTS: ACUTE DERMAL IRRITATION/CORROSION

All signs of skin irritation disappeared by the 72 hour observation. The primary irritant score was 0.63, indicating Fyrol FR-2 was a mild skin irritant.

- Conclusion: Fyrol FR-2 was shown to be a mild skin irritant.
- Data Quality: Reliable without restrictions. The data presented are reliable. However, Guideline 404 requires the use of intact skin whereas this test utilized both intact and abraded skin. Guideline 404 requires a 4 hour exposure whereas a 24 hour exposure was used in this test.
- Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.
- Other: Prepared March 2, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS: GENERAL  
TOXICITY (REPEATED DOSE)

Chemical Name: Tris(1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 453

Test Type: Combined Chronic Toxicity/Carcinogenicity Study

GLP Compliant: No

Years Test Performed: 1978-1981

Species: Sprague-Dawley Rats

Sex: Male and Female

Duration of Test: 24 Months

Route of Administration: Dietary (blended in the diet)

Dose/Concentration Levels: 0, 5, 20, and 80 mg/kg/day

Statistical Methods: Body weight, food consumption, and organ weights of treated groups were compared to control by the Dunnett's test. Hematology and clinical chemistry parameters were analyzed using the F-test and Student's t-test. Mortality incidence was analyzed by the chi-square method. Tumor incidence was examined by the Fisher Exact test (one tailed).

Remarks on Test Conduct: This study was conducted to determine the chronic toxicity and carcinogenic potential of Fyrol FR-2 when administered to rats for 24 months. Each of the four groups consisted of 60 male and 60 female rats. Dietary doses administered were 0, 5, 20, or 80 mg/kg/day. Diets were adjusted weekly for 13 weeks and then biweekly from week 14 through 104. Ten animals per sex per group were used for an interim sacrifice after 12 months. The animals were observed daily for clinical signs, morbidity and

mortality. Body weights, food consumption, hematological and clinical chemistry parameters, ophthalmoscopic examinations, and

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# HUMAN HEALTH EFFECTS ELEMENTS: GENERAL TOXICITY (REPEATED DOSE)

urinalysis were performed periodically on a defined schedule. Surviving animals were sacrificed at the end of the 24<sup>th</sup> month and were subjected to gross examination during necropsy. Microscopic examinations were performed on all tissues from the control and high dose animals and on gross lesions, tissue masses, liver, kidneys, adrenal glands, and testes from the low and mid dose animals. Organ weights were recorded at the interim and terminal necropsies.

### Results:

Mortality in the high dose males was significantly higher than that of the control males, beginning early in the study's second year. The mortality observed for the other groups was comparable to the control group. Body weights of the high dose males and females were significantly lower than the weights of the control animals through most of the study. The increased mortality and decreased body weights in the high dose animals confirms that the high dose was the maximum tolerated dose (MTD). Most of the mid and low dose animals had body weights that were comparable to the control animals. Food consumption appeared unaffected by treatment in all groups. Certain hematological values were lower in the high dose animals, as was serum alkaline phosphatase levels at most intervals. Clinical observations and urinalysis revealed no treatment-related differences between groups.

A higher incidence of gross postmortem anomalies of the liver, kidneys, testes, and seminal vesicles were observed in treated animals. Microscopic examination of the tissues revealed a higher incidence of morphologic alterations in the liver, renal cortex, testes, and adrenal cortex in the treated animals, primarily in the high dose group. A significant increase in benign adrenal cortical tumors were seen in high dose females and hepatocellular adenomas were observed in both male and female high dose animals. A significant increase in renal cortical adenomas were seen in both sexes and testicular interstitial cell tumors were observed in male animals from the high and mid dose groups. Hepatocellular

adenomas, benign interstitial cell tumors, and benign adrenal cortical tumors commonly occur in aging rats. Chronic

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# HUMAN HEALTH EFFECTS ELEMENTS: GENERAL TOXICITY (REPEATED DOSE)

administration of Fyrol FR-2 apparently exacerbates the formation of these spontaneously occurring tumors. The body weight difference between the high dose and control animals of more than 20% at the end of the study suggests the high dose exceeded the MTD and may have made the animals more susceptible to the chronic toxicity of the test substance. An NOEL for toxicity and benign neoplasms was the dietary dose of 5 mg/kg/day.

- Conclusion: Chronic dietary administration of Fyrol FR-2 to rats resulted in the induction of benign neoplasms in the liver, kidney, testes, and adrenal cortex. The NOEL for chronic toxicity and the induction of benign tumors is 5 mg/kg/day.
- Data Quality: Reliable with restrictions. A high dose satellite group was not included. The high dose caused a body weight loss in excess of 10% at the end of the study. Mortality in the high dose males at the end of the study was in excess of 50%. Although over 40 tissues were taken for microscopic examination, tissues listed in the OECD guideline that were not examined include rectum, esophagus, thoracic and lumbar regions of the spinal cord, and sternum.
- Reference: This robust summary was prepared by an individual company. The full study has been published in the International Journal of Toxicology, 19: 119- 125, 2000, as a peer-reviewed article.
- Other: Prepared January 16, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS: GENETIC  
TOXICITY

Chemical Name: Tris( 1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 471

Test Type: Bacterial Reverse Mutation Test (Ames Test)

GLP Compliant: No

Year Test Performed: 1977

Genus/Species/Strains: Salmonella typhimurium TA-1535, TA-1537, TA-1538, TA-98, TA- 100, and Saccharomyces cerevisiae D4

Dose/Concentration Levels: 5.0, 1.0, 0.1, 0.01, an 0.001 µl/plate

Remarks on Test Conduct: Fyrol FR-2 was evaluated for its potential to induce mutations in five strains of Salmonella typhimurium and in one strain of Saccharomyces cerevisiae, in the absence and presence of a metabolic activating system. The high dose level was chosen from a preliminary cytotoxicity test in which it was shown to cause cytotoxicity. Appropriate positive control chemicals were included in the test to confirm the viability and sensitivity of the assay.

Results: Fyrol FR-2 did not demonstrate mutagenic activity in any of the strains with which it was evaluated, either in the absence or presence of a metabolic activating system. All of the positive control chemicals demonstrated mutagenic activity, confirming the validity of the test.

Conclusion: Fyrol FR-2 did not demonstrate mutagenic activity in this test.

Data Quality: Reliable without restrictions

Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other:

Prepared January 12, 2001

**ROBUST SUMMARY**

**FYROL FR-2**

**CAS#13674-87-8**

**HUMAN HEALTH EFFECTS ELEMENTS: GENETIC  
TOXICITY**

Chemical Name: Tris( 1,3-dichloropropyl-2) phosphate

Method/Guideline: A Specially Designed Bacterial Mutagenicity Test

Test Type: Bacterial Reverse Mutation Test (Ames Test)

GLP Compliant: No

Year Test Performed: 1978

Genus/Species/Strains: Salmonella typhimurium Strains TA-1535, TA-1537, TA-98, and TA-100, and male CD-1 mice

Dose/Concentration Levels: 0.1, 0.2, or 0.3 ml of urine from treated animals

Remarks on Test Conduct: This test was conducted to evaluate urine from animals treated with Fyrol FR-2 to determine whether mutagenic metabolites are formed. Fyrol FR-2 was administered orally for five days to groups of male CD-1 mice. Each group contained at least 7 mice. The urine from each group was collected for 16 hours after the last dose and combined. The urine samples were divided such that one aliquot was tested as collected while the second aliquot was first treated with  $\beta$ -glucuronidase to free conjugated metabolites that may be present and then assayed for the presence of mutagenic metabolites. Doses of either 0, 0.1, 0.2, or 0.3 ml of urine were added to the test system.

Results: None of the urine samples assayed showed mutagenic activity, indicating that the urinary excretory products (metabolites) were not mutagenic.

Conclusion: Urine from mice that received five oral doses of Fyrol FR-2 did not express mutagenic activity, indicating that the metabolites of Fyrol FR2 excreted into the urine were not mutagenic.

Data Quality: Reliable without restrictions

Reference:

This robust summary was prepared by an individual company from  
**ROBUST SUMMARY**  
**FYROL FR-2**  
**CAS#13674-87-8**

**HUMAN HEALTH EFFECTS ELEMENTS: GENETIC  
TOXICITY**

an unpublished study. The underlying study contains confidential  
business information.

Other:

Prepared January 15, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS: GENETIC  
TOXICITY

Chemical Name:	Tris( 1,3-dichloropropyl-2) phosphate
Method/Guideline:	A Specially Designed Bacterial Mutagenicity Test
Test Type:	Bacterial Reverse Mutation Test (Ames Test)
GLP Compliant:	Yes
Year Test Performed:	1982
Genus/Species/Strains:	Salmonella typhimurium Strain TA-100
Dose/Concentration Levels:	10,000, 8,000, 6,000, 4,000, 2,500, 1,500, 1,250, 1,200, 1,000, 800, 625, 600, 500, 400, 3 13,200, 156, 100, and 50 µl/ml.
Remarks on Test Conduct:	Previously conducted standard Ames Tests have shown Fyrol FR-2 to be without mutagenic activity. This test was conducted to determine if mutagenic activity occurs under conditions of severe cytotoxicity with loss of most of the test colony. Therefore, Fyrol FR-2 was evaluated for its potential to induce mutations, with and without a metabolic activating system, in one Salmonella typhimurium strain , TA-100, at noncytotoxic and cytotoxic doses. Appropriate positive control chemicals were included in the assays to confirm viability and sensitivity. Both a standard plate assay and a suspension assay were conducted.
Results:	In the standard plate assay, Fyrol FR-2 was not mutagenic at any dose in the absence of metabolic activation. In the presence of an activating system, the standard dose of 50 µl was without activity. Significant mutagenic activity was observed at doses of 500 µl and higher. At these doses significant cytotoxicity and cytolethality was observed. In the special suspension assay, there was no mutagenic activity at any dose in the absence of a metabolic activating system. In the presence of an activating system, significant mutation frequencies were observed at doses of 1000 µg/ml and higher. However, at these very high doses cell survival was reduced to 5

percent and less. Therefore in this special assay, Fyrol FR-2 demonstrated mutagenic activity only at doses that expressed

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# HUMAN HEALTH EFFECTS ELEMENTS: GENETIC TOXICITY

extreme cytotoxicity and cell lethality. Since these results were obtained under abnormal, exceptionally severe assay conditions, they are most probably not biologically significant. Fyrol FR-2 was not mutagenic under standard assay conditions.

- Conclusion: Fyrol FR-2 was not mutagenic under standard assay conditions. When tested in the presence of a metabolic activating system and at doses that cause severe cytotoxicity and cell lethality (cell survival less than 5%), Fyrol FR-2 demonstrated mutagenic activity. The biological significance of results obtained under extreme testing conditions is unknown.
- Data Quality: Reliable without restrictions
- Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.
- Other: Prepared January 15, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS: GENETIC  
TOXICITY

Chemical Name: Tris( 1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 476

Test Type: In Vitro Mammalian Cell Gene Mutation Test

GLP Compliant: No

Year Test Performed: 1977

Cell Type: L5 178Y Mouse Lymphoma Cell Line

Dose/Concentration Levels: 0, 0.125, 0.098, 0.085, 0.072, 0.064, 0.032, 0.016, and 0.008  $\mu\text{l/ml}$

Remarks on Test Conduct: Fyrol FR-2 was evaluated in the mouse lymphoma multiple endpoint assay. In this assay, in addition to assessing for gene mutation, the assay determines, using separate groups of cells, the potential for causing chromosomal aberrations and sister chromatid exchange. The assays were conducted in the presence and absence of a metabolic activating system. Ethyl methanesulfonate was used as the positive control in nonactivated cultures whereas dimethylnitrosamine, which requires activation to express mutagenic activity, was used in the activated assays. Doses chosen for this set of assays were based on the results of a preliminary cytotoxicity test. Gene (point) mutation was measured by scoring the number of cells that have undergone forward mutation. Cells were examined for treatment related induction of chromosomal aberration and sister chromatid exchange by harvesting, staining and microscopically evaluating the cells. The results obtained from the cells treated with Fyrol FR-2 were compared to the negative and positive control data.

Results: In the gene mutation test, Fyrol FR-2 did not increase the incidence of colonies of mutated cells, either in the presence or absence of a metabolic activating system, indicating that the product does not cause gene (point) mutation in mammalian cells. In the sister

chromatid exchange assay, the results were somewhat variable. A careful evaluation showed no trend indicative of a dose-related

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# HUMAN HEALTH EFFECTS ELEMENTS: GENETIC TOXICITY

inducting of sister chromatid response. The data were analyzed in three configurations and considered negative. In the chromosomal aberration assay, Fyrol FR-2 showed a dose-related trend in the induction of aberrations, especially in the presence of a metabolic activating system. Only at the maximum tolerated dose (MTD) of 0.072  $\mu\text{l/ml}$  and in the presence of a metabolic activating system was the percent aberration significantly increased over the negative control group. Fyrol FR-2 demonstrated a weak ability to induce the formation of chromosomal aberrations in mammalian cells at the MTD dose.

- Conclusion: Treatment of L5 178Y mouse lymphoma cells with Fyrol FR-2 did not result in a significant level of gene mutation or the occurrence of an increased incidence of sister chromatid exchanges. However, in the presence of a metabolic activating system, and at the MTD, the product did cause a significant increase in chromosomal aberrations.
- Data Quality: Reliable with restrictions. While statistical methods were used in the evaluation of the assay data, the specific types of statistical tests used were not identified. The number of cells scored (analyzed) per slide and per treatment group was not identified.
- Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.
- Other: Prepared January 15, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS: GENETIC  
TOXICITY

Chemical Name: Tris(1,3-dichloropropyl-2) phosphate

Method/Guideline: Transformation of Mammalian Cells in Culture

Test Type: In Vitro Malignant Transformation of BALB/3T3 Cells

GLP Compliant: No

Year Test Performed: 1978

Cell Type: BALB/3T3 Cells

Dose/Concentration Levels: 0.3 12, 0. 156, 0.078, 0.039, and 0.020 µl/ml

Remarks on Test Conduct: Fyrol FR-2 was evaluated for its potential to transform BALB/3T3 cells in an in vitro assay. BALB/3T3 cells cease cell division upon forming a confluent monolayer. Transformed cells lose this contact inhibition and continue to proliferate, forming dense colonies and foci. The abnormally proliferating cells show a characteristic appearance that correlates with their ability to form tumors when injected into immunologically tolerant hosts. A positive control chemical, 3-methylcholanthrene, was included in the test to assure the viability and sensitivity of the assay. A negative control group was also included. The dose levels used in this test were based on the results of a preliminary cytotoxicity test. BALB/3T3 cells were exposed to Fyrol FR-2 or 3-methylcholanthrene for 48 hours, and then washed free of the chemicals and incubated for an additional four weeks. This test is used as a predictive assay for carcinogenic potential.

Results: 3-Methylcholanthrene induced cell transformation. Fyrol FR-2 did not transform the BALB/3T3 cells. The results suggest that Fyrol FR-2 is not carcinogenic to mammalian cells.

Conclusion: Fyrol FR-2 did not transform the BALB/3T3 cells. This suggests the chemical does not have carcinogenic activity.

Data Quality: Reliable without restrictions

**ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8**

**HUMAN HEALTH EFFECTS ELEMENTS: GENETIC  
TOXICITY**

Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other: Prepared January 15, 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS:  
REPRODUCTIVE TOXICITY

Chemical Name: Tris(1,3-dichloropropyl-2) phosphate

Method/Guideline: Special study, no applicable guideline

Test Type: Reproductive Toxicity Determination in Male Animals

GLP Compliant: Yes

Year Test Performed: 1982

Species: Dutch-belted Rabbits

Sex: Males treated, females used to assess male fertility

Duration of Test: Animals were dosed for 12 weeks and then mated

Route of Administration: Oral Gavage

Dose/Concentration Levels: 0, 2, 20, or 200 mg/kg/day;

Statistical Methods: Incidence data, including mating, pregnancy and fertility indices were analyzed by the Fischer exact probability test. Enumeration data from each litter and sperm parameters were analyzed by the Mann-Whitney U two sample rank test. Other data, i.e. body and organ weights, were analyzed by one-way analysis of variance and the Dunnett's t-test.

Remarks on Test Conduct: This study was conducted to determine the effect of Fyrol FR-2 on spermatogenesis and on male fertility. Ten male rabbits were assigned to each of 4 dose groups and received daily oral doses of Fyrol FR-2 for 12 weeks. Animals were weighed weekly and were observed daily for clinical signs. During the last treatment week, fertility was assessed by mating each treated male with two untreated female rabbits. Females were sacrificed mid-gestation to evaluate their uteri. The male rabbits were sacrificed after the

mating period at which time sperm samples were collected from the cauda epididymides and evaluated for motility, morphology, and

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# HUMAN HEALTH EFFECTS ELEMENTS: REPRODUCTIVE TOXICITY

concentration. Blood samples were collected to measure hematologic and clinical chemistry parameters. At necropsy, the pituitary, testes plus epididymides, liver, and kidneys were collected, weighed, and examined microscopically.

Results:

There were no treatment-related changes in mating behavior, male fertility, sperm quality, or sperm quantity. Further, there was no effect on body weight gain, clinical signs, hematology, or clinical chemistry parameters. There were significant increases in absolute kidney weights in the high dose group. Relative liver weights were also increased at 200 mg/kg/day. Diagnostic pathology revealed no tissue alterations that had an incidence or severity suggestive of a treatment-related effect. Therefore repeated oral treatment with up to 200 mg/kg/day of Fyrol FR-2 did not affect male rabbit fertility or spermatogenesis.

Conclusion:

Daily treatment with Fyrol FR-2 for 12 weeks did not adversely effect male fertility or spermatogenesis.

Data Quality:

Reliable without restrictions

Reference:

This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other:

Prepared January 30 , 2001

## ROBUST SUMMARY

FYROL FR-2

CAS# 13674-87-8

### HUMAN HEALTH EFFECTS ELEMENTS: DEVELOPMENTAL TOXICITY

Chemical Name: Tris( 1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 414

Test Type: Developmental Toxicity (Teratology)

GLP Compliant: No

Year Test Performed: 1978

Species: Sprague-Dawley Rats

Sex: Pregnant females dosed gestation days 6 through 15

Duration of Test: 20 days

Route of Administration: Oral Gavage

Dose/Concentration Levels: 0, 25, 100, and 400 mg/kg/day

Statistical Methods: Body weight, food consumption, ovarian and uterine weights, and fetal weights were evaluated by the Student's t -test and Cochran's approximation of  $t(t')$ . Reproduction indices were analyzed by the chi-square method using a probability level of 0.05.

Remarks on Test Conduct: This study was conducted to determine the teratogenic potential of Fyrol FR-2 in pregnant rats. The test substance was administered daily by oral gavage from gestation day 6 through gestation day 15 to groups of rats (20 pregnant rats per group) at doses of 0, 25, 100, or 400 mg/kg/day. Data collected and evaluated include animal appearance, behavior, survival, body weight changes, food consumption, pregnancy rates, litter size, fetal viability, number of corpora lutea per uterus, number of implants and resorptions, fetal pathology (visceral and skeletal), and other information specified in the guideline.

Results: Three animals in the high dose group died (one from improper

## ROBUST SUMMARY

FYROL FR-2

CAS#13674-87-8

# HUMAN HEALTH EFFECTS ELEMENTS: DEVELOPMENTAL TOXICITY

Results, continued: handling). No deaths occurred in the other groups. Beginning on day 7, some high dose animals expressed clinical signs including urine stains, hunched appearance, and alopecia, The urine stains and alopecia persisted to day 19. Sporadic signs were seen in a few mid dose animals, primarily urine stains and hunched appearance. There were no clinical signs in the low dose group. There was a significant decrease in body weight gain followed by a mean body weight loss in the high dose group. Low food consumption was noted in the high dose group throughout the study. No treatment related effects were seen on the mean number of corpora lutea or implantation efficiency. Embryo and fetotoxicity were observed at the high dose, including a significant increase in resorptions and a corresponding decrease in fetal viability, lower mean fetal weight and length. Delayed skeletal development observed in a few high dose fetuses seen as incomplete ossification. There was no indication of teratogenicity. Only one malformation was found in this study, an umbilical hernia in one low dose fetus, which was not treatment related. All other changes were reported as representative of developmental variations. Since there were no treatment-related effects in the low dose animals, the NOEL is 25 mg/kg/day for general toxicity. The NOEL for developmental toxicity is 400 mg/kg/day (highest dose tested).

Conclusion: Fyrol FR-2 does not demonstrate teratogenic activity. The high dose caused maternal, embryo and feto-toxicity without inducing developmental defects. The NOEL for general toxicity is 25 mg/kg/day and for developmental toxicity is 400 mg/kg/day.

Data Quality: Reliable without restrictions

Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other: Prepared January 12 , 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS:  
NEUROTOXICITY

Chemical Name: Tris(1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 4 18

Test Type: Delayed Neurotoxicity of Organophosphorus Substances, Acute Exposure, NTE Assay

GLP Compliant: No

Year Test Performed: 1977

Species: White Leghorn hens

Sex: Female

Duration of Test: 24 Hours

Route of Administration: Oral Gavage

Dose/Concentration Levels: Fyrol FR-2: 10,000 mg/kg; Positive Control (TOCP): 500 mg/kg;

Statistical Methods: Statistical analysis was not required in the study.

Remarks on Test Conduct: This study was conducted to determine whether a single very high dose of Fyrol FR-2 (10,000 mg/kg) will significantly inhibit neurotoxic esterase (NTE) activity in atropine and PAM protected adult White Leghorn hens. The positive and negative control groups contained three hens each whereas the Fyrol FR-2 group consisted of four hens. All animals were pretreated (protected from acute cholinergic effects) with 2-PAM and atropine. The animals were observed for 24 hours for clinical signs and then sacrificed to measure brain NTE activity.

Results: There was no mortality in any of the control or treatment groups. Treatment with Fyrol FR-2 caused a mean NTE inhibition of 7%. The mean NTE inhibition in the hens treated with TOCP was 85%.

It has been determined by several laboratories that an NTE inhibition of greater than 70% is necessary to indicate a test

## ROBUST SUMMARY

FYROL FR-2

CAS# 13674-87-8

# HUMAN HEALTH EFFECTS ELEMENTS: NEUROTOXICITY

substance has neurotoxic potential. The 7% inhibition in this test indicates Fyrol FR-2 cannot induce delayed peripheral neuropathy.

- Conclusion: A single high dose (10,000 mg/kg) of Fyrol FR-2 did not significantly inhibit brain NTE activity. Therefore, Fyrol FR-2 does not have the potential for causing delayed peripheral neuropathy.
- Data Quality: Reliable with restrictions. Guideline 418 requires the use of six hens per group while only three or four hens per group were used in this test. Guideline 418 also requires histopathology after another group of treated hens are held for 21 days post-dosing. This group was not included in the test. However, another Robust Summary describes a repeated dose subchronic test with Fyrol FR-2 in which histopathology was conducted.
- Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.
- Other: Prepared February 27 , 2001

ROBUST SUMMARY  
FYROL FR-2  
CAS#13674-87-8

HUMAN HEALTH EFFECTS ELEMENTS:  
NEUROTOXICITY (REPEATED DOSE STUDY)

Chemical Name: Tris(1,3-dichloropropyl-2) phosphate

Method/Guideline: OECD Guideline 419

Test Type: Delayed Neurotoxicity of Organophosphorus Substances

GLP Compliant: No

Year Test Performed: 1979

Species: White Leghorn hens

Sex: Female

Duration of Test: 90 days

Route of Administration: Oral Gavage

Dose/Concentration Levels: 0, 4, 20, and 100 mg/kg/day; Positive Control (TOCP): 30 mg/kg

Statistical Methods: Statistical analysis was not required in the study.

Remarks on Test Conduct: This study was conducted to determine the neurotoxic potential of Fyrol FR-2 in adult White Leghorn hens after repeated exposure. There were 3 treatment groups, a negative control group, and a positive control group, with each group consisting of 10 hens. The animals were observed daily for behavioral changes and were evaluated for evidence of locomotor impairment three times weekly. At study termination, the following tissues were removed from each hen for diagnostic pathology: brain, spinal cord, and sciatic nerves. Transverse and longitudinal sections were taken from the cervical, thoracic, and lumbar regions of the spinal cord. Multiple sections of the brain were taken. Sections of neurological tissues were stained with hematoxylin and eosin and additional slides with Luxol fast blue.

Results: There was no mortality in the Fyrol FR-2 groups whereas significant

**ROBUST SUMMARY**  
**FYROL FR-2**  
**CAS#13674-87-8**

## HUMAN HEALTH EFFECTS ELEMENTS: NEUROTOXICITY (REPEATED DOSE STUDY)

mortality was observed in the TOCP group. The mean body weight for the high dose hens decreased during the latter part of the study. Mean body weight for the TOCP hens decreased consistently over the course of the study. Hens treated with Fyrol FR-2 exhibited no clinical signs of neurotoxicity whereas the TOCP treated hens exhibited locomotor impairment and ataxia, which increased in severity with time. Fyrol FR-2 did not cause delayed peripheral neurotoxicity.

Conclusion: Daily treatment with Fyrol FR-2 for 90 days did not result in behavioral or histopathologic changes indicative of neurotoxicity. Therefore, Fyrol FR-2 did not demonstrate neurotoxic activity.

Data Quality: Reliable without restrictions. Guideline 419 requires dosing for 28 days whereas hens were dosed for 90 days in this study. The guideline requires 6 animals per dose group for histopathology and this study utilized 10 hens per group. Guideline 419 indicates a subgroup of hens should be used for the measurement of NTE activity. NTE was not measured in this study. The effects of Fyrol FR-2 on NTE activity was determined in a separate study and the results are reported in another Robust Summary. Fyrol FR-2 did not significantly inhibit NTE activity.

Reference: This robust summary was prepared by an individual company from an unpublished study. The underlying study contains confidential business information.

Other: Prepared March 8 , 2001

