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201-16678B

# I U C L I D

## Data Set

**Existing Chemical** : ID: 150-50-5  
**CAS No.** : 150-50-5  
**EINECS Name** : S,S',S'-tributyl phosphorotrithioite  
**EC No.** : 205-761-4  
**Molecular Formula** : C12H27PS3

**Producer related part**  
**Company** : Epona Associates, LLC  
**Creation date** : 11.09.2007

**Substance related part**  
**Company** : Epona Associates, LLC  
**Creation date** : 11.09.2007

**Status** :  
**Memo** :

**Printing date** : 10.01.2008  
**Revision date** :  
**Date of last update** : 10.01.2008

**Number of pages** : 103

**Chapter (profile)** : Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10  
**Reliability (profile)** : Reliability: without reliability, 1, 2, 3, 4  
**Flags (profile)** : Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE),  
Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

# 1. General Information

Id 150-50-5  
Date 10.01.2008

## 1.0.1 APPLICANT AND COMPANY INFORMATION

## 1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

## 1.0.3 IDENTITY OF RECIPIENTS

## 1.0.4 DETAILS ON CATEGORY/TEMPLATE

**Comment** : Tributyl trithiophosphite (merphos; CAS# 150-50-5)

**Remark** : Tributyl trithiophosphite (merphos; CAS# 150-50-5) is a chemical intermediate used to make the pesticide S,S,S-tributyl phosphorotrithioate (Tribufos; DEF; CAS# 78-48-8). These substances are structurally analogous. further, merphos is readily oxidized to tribufos. Data from Tribufos are used to fulfill HPV endpoints for Merphos.

07.01.2008

**Comment** : Merphos is readily oxidized to tribufos

07.01.2008

(68)

**Comment** : Merphos is readily oxidized to tribufos.

**Method** : A rapid screening GC method has been developed for the analysis of intact Folex on cotton foliage.

This procedure was used to analyze cotton foliage treated with Folex to determine the rate of conversion to DEF in the shade and in direct sun.

**Remark** : The conversion of applied Folex as it oxidized to DEF on the surface of cotton leaves in the shade and in full sun was studied. Folex was completely oxidized to DEF within two hours in full sun at 75°F. Conversion was somewhat slower in shaded plants.

**Result** : Results indicate that Folex applied in the field would certainly all be oxidized to DEF at the end of 24 hours or less under most harvest time conditions for cotton.

07.01.2008

(60)

## 1.1.0 SUBSTANCE IDENTIFICATION

**IUPAC Name** :  
**Smiles Code** :  
**Molecular formula** : C12H27PS3  
**Molecular weight** : 298.51  
**Petrol class** :

**Remark** : CAS RN 150-50-5  
10.10.2007

**IUPAC Name** :  
**Smiles Code** :  
**Molecular formula** : C12H27OPS3  
**Molecular weight** : 314.51  
**Petrol class** :

# 1. General Information

Id 150-50-5  
Date

Remark : CAS RN 78-48-8  
10.10.2007

## 1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type : typical for marketed substance  
Substance type :  
Physical status : liquid  
Purity :  $\geq 95$  % v/v  
Colour : pale amber  
Odour : mild characteristic odor

Remark : CAS RN 150-50-5  
10.10.2007

Purity type : typical for marketed substance  
Substance type :  
Physical status : liquid  
Purity : = 72 % v/v  
Colour :  
Odour :

Remark : Folex: 72% merphos and 28% inert ingredients  
05.12.2007

## 1.1.2 SPECTRA

## 1.2 SYNONYMS AND TRADENAMES

### Butyl phosphorotrithioite ((bus)3p)

11.09.2007

### Chemagro B-1776

11.09.2007

### Defef defoliant

11.09.2007

### Easy off-D

11.09.2007

### Folex

11.09.2007

### Folex 6ec

11.10.2007

### Folex/Def

11.10.2007

**Merphos**

11.09.2007

**Phosphorotrithious acid, S,S,S-tributyl ester**

11.09.2007

**Phosphorotrithious acid, tributyl ester**

11.09.2007

**S,S,S-Tributyl phosphorotrithioite**

11.09.2007

**S,S,S-Tributyl trithiophosphite**

11.09.2007

**Synonyms for S,S,-Tributyl phosphorotrithioate (CAS RN 78-48-8):**

**Remark** : Phosphorotrithioic acid, S,S,S-tributyl ester; B-1,776; Butiphos; Butyl Phosphorotrithioate ((BuS)3PO); Chemagro B-1776; De-Green; DEF; DEF Defoliant; Fos-Fall "A"; Fosfall; S<S<S-Tributyl trithiophosphate; TBTP; Butifos; Butyl phosphorotrithioate; Chemagro 1,776; E-Z-OFF D; Ortho phosphate defoliant; S,S,S-Tributyltrithiofosfat; Deleaf defoliant; Easy off-D; Folex 6EC; FOS-FALL A; Tribufos; Tribuphos; Tributylphosphorotrithioate

15.10.2007

**Tribufos**

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**Tributyl phosphorotrithioate**

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**Tributyl Phosphorotrithioite**

11.09.2007

**Tributyl phosphorotrithioite (ACN)**

11.10.2007

**Tributyl thithiophosphite**

11.09.2007

**Tributylphosphorotrithioite**

11.10.2007

**Tributylthiofosfin**

11.09.2007

**1.3 IMPURITIES**

# 1. General Information

**Id** 150-50-5  
**Date** 10.01.2008

**1.4 ADDITIVES**

**1.5 TOTAL QUANTITY**

**1.6.1 LABELLING**

**1.6.2 CLASSIFICATION**

**1.6.3 PACKAGING**

**1.7 USE PATTERN**

**1.7.1 DETAILED USE PATTERN**

**1.7.2 METHODS OF MANUFACTURE**

**1.8 REGULATORY MEASURES**

**1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES**

**1.8.2 ACCEPTABLE RESIDUES LEVELS**

**1.8.3 WATER POLLUTION**

**1.8.4 MAJOR ACCIDENT HAZARDS**

**1.8.5 AIR POLLUTION**

**1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES**

**1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS**

**1.9.2 COMPONENTS**

# 1. General Information

**Id** 150-50-5  
**Date** 10.01.2008

## 1.10 SOURCE OF EXPOSURE

## 1.11 ADDITIONAL REMARKS

## 1.12 LAST LITERATURE SEARCH

**Type of search** : Internal and External  
**Chapters covered** : 3, 4, 5  
**Date of search** : 16.08.2007

10.10.2007

## 1.13 REVIEWS

## 2. Physico-Chemical Data

Id 150-50-5

Date

### 2.1 MELTING POINT

**Value** : = 83 °C  
**Sublimation** :  
**Method** : other  
**Year** : 2007  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : (MPBPWIN v1.42):  
SMILES : CCCCSP(SCCCC)SCCCC  
CHEM : Merphos  
CAS NUM: 000150-50-5  
MOL FOR: C12 H27 P1 S3  
MOL WT : 298.50

**Result** : Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPWIN v1.42):  
Melting Pt (deg C): 82.97 (Mean or Weighted MP)  
MP (exp database): 100 deg C

**Reliability** : (2) valid with restrictions  
Modeled data

**Flag** : Critical study for SIDS endpoint  
15.10.2007 (19)

### 2.2 BOILING POINT

**Value** : = 115 - 134 °C at 10.66 hPa  
**Decomposition** :  
**Method** :  
**Year** : 1987  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (2) valid with restrictions  
Handbook data

**Flag** : Critical study for SIDS endpoint  
10.10.2007 (70)

**Value** : = 150 - 152 °C at  
**Decomposition** :  
**Method** :  
**Year** : 2002  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (2) valid with restrictions  
Handbook data  
10.10.2007 (16)

**Value** : = 270 - 276 °C at  
**Decomposition** :  
**Method** : other  
**Year** : 2001  
**GLP** : yes  
**Test substance** : other TS

**Method** : Tested in accordance with Pesticide Assessment Guidelines, Subdivision D, Product Chemistry, October 1, 1982 (testing code 63.06) and Federal

## 2. Physico-Chemical Data

Id 150-50-5

Date

Register, Vol. 44. No. 53, Friday, March 16,1979.

The boiling point of DEF technical was determined by Differential Scanning Calorimetry (DSC). The calibration of the Mettler Model 821e DSC was validated by determining the onset melting temperature and heat of fusion for an indium metal standard. An indium metal standard (Mettler standard number 29749) of known weight, 6.66 mg, was sealed in a 40-uL aluminum pan with a pierced aluminum lid. The pan was placed in the measurement position of the DSC sensor. A sealed empty 40-uL aluminum pan was placed in the reference position of the DSC sensor. The oven was heated from 120 to 180°C at a rate of 10°C/minute, using the Mettler program "Check DSC Endo In". Heat flow was measured as a function of temperature. The onset melting temperature for indium was 156.6°C and the heat of fusion was 29.0 J/g. Both values were within the experimental limits determined by Mettler 156.6 ± 0.3°C and 28.45 ± 0.6 J/g.

A 12.6 mg portion of the DEF technical was weighed into a 40-uL aluminum pan. The pan was sealed with a pierced aluminum lid, and was placed in the measurement position on the sensor. The sample was heated from 25 to 300°C at rate of 10°C/minute. Heat flow was measured as a function of temperature.

**Result** : The material boiled from approximately 270° to 276°C.  
**Test substance** : Identification: DEF Technical  
Percent Active Ingredient: S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)  
Purity: 98%

**Reliability** : (1) valid without restriction  
Guideline study

13.12.2007 (12)

**Value** : = 100 - 101 °C at .03 hPa

**Decomposition** :

**Method** :

**Year** : 1985

**GLP** : no data

**Test substance** : other TS

**Remark** : Value from the ZIC/VINITI data file provided by InfoChem

**Reliability** : (4) not assignable  
Original study not reviewed

13.12.2007 (34)

### 2.3 DENSITY

**Type** : relative density  
**Value** : = .99 - 1.01 at 20 °C  
**Method** :  
**Year** : 1987  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Result** : Specific Gravity = 0.99-1.01 @ 20 deg C/4 deg C

**Reliability** : (2) valid with restrictions  
Handbook data

13.12.2007 (70)

**Type** : relative density  
**Value** : = .987 at 20 °C  
**Method** :  
**Year** : 2002



## 2. Physico-Chemical Data

Id 150-50-5

Date

**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (2) valid with restrictions  
Handbook data

13.12.2007

(16)

**Type** : density  
**Value** : = 1.02 g/cm<sup>3</sup> at 20 °C  
**Method** :  
**Year** : 2000  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (2) valid with restrictions  
Handbook data

10.10.2007

(15) (15)

**Type** : density  
**Value** : 1.06 g/cm<sup>3</sup> at °C  
**Method** : other  
**Year** : 2001  
**GLP** : yes  
**Test substance** : other TS

**Method** : Tested in accordance with Pesticide Assessment Guidelines, Subdivision D, Product Chemistry, October 1, 1982 (testing code 63.07) and Federal Register, Vol. 44. No. 53, Friday, March 16, 1979.

The specific gravity of DEF technical was determined by test method A-5.15.

**Remark** : 8.82 lb/gal = ca. 1.06 g/cm<sup>3</sup>  
**Result** : The specific gravity at 20°C/20°C was 1.059, corresponding to a density at 20°C of 8.82 lb./gal.

**Test substance** : Identification: DEF Technical  
Percent Active Ingredient: S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)  
Purity: 98.0%

**Reliability** : (1) valid without restriction  
Guideline study

13.12.2007

### 2.3.1 GRANULOMETRY

### 2.4 VAPOUR PRESSURE

**Value** : = .00001773187 hPa at 25 °C  
**Decomposition** :  
**Method** :  
**Year** : 2007  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : (MPBPWIN v1.42):  
SMILES : CCCCSP(SCCCC)SCCCC  
CHEM : Merphos  
CAS NUM: 000150-50-5  
MOL FOR: C12 H27 P1 S3

## 2. Physico-Chemical Data

Id 150-50-5

Date

<b>Result</b>	: MOL WT : 298.50 Boiling Pt, Melting Pt, Vapor Pressure Estimations (MPBPWIN v1.42): VP(mm Hg,25 deg C): 1.33E-005 (Modified Grain method) Subcooled liquid VP: 7.13E-005 mm Hg (25 deg C, Mod-Grain method)
<b>Reliability</b>	: (2) valid with restrictions Modeled data
<b>Flag</b> 15.10.2007	: Critical study for SIDS endpoint <span style="float: right;">(19)</span>
<b>Value</b>	: = .00000079 at 25 °C
<b>Decomposition</b>	:
<b>Method</b>	: other (measured)
<b>Year</b>	: 1991
<b>GLP</b>	: yes
<b>Test substance</b>	: other TS
<b>Method</b>	: The objective of this study was to determine the vapor pressure of tribufos at three temperatures using the gas saturation method and report a value at 25°C.  The study was conducted as described below according to test methods specified in OPPTS Test Guidelines 830.7950.  Tribufos (approximately 500 uL) was spiked into a slurry of methylene chloride and 225 g glass beads (0.8 mm diameter). The methylene chloride was evaporated to dryness to coat the beads with tribufos. The coated glass beads were used to prepare three saturator columns. Each saturator column consisted of a glass impinger (-17.8 cm x 2.6 cm) fitted with a long gas inlet tube and a gas outlet tube. Approximately 75 g of the tribufos-coated glass beads containing approximately 167 mg tribufos was put into each saturator column. The columns were used to determine the vapor pressure of tribufos at three temperatures (25°C, 35°C, and 43.5°C). Each saturator column was connected to 2 cold traps containing approximately 25 mL acetone. The traps were immersed in a slurry of dry ice and methanol to retain volatilized tribufos. Glass and Teflon connectors were used to connect the saturator columns to the traps. Carrier gas (pure N2) was equilibrated to temperature through a copper coil inside the environmental chamber prior to splitting and flowing through each saturator column. The saturator columns were maintained at 25°C, 35°C, and 43.5°C ± 1°C under darkness for the duration of each experiment. The saturator columns were purged with dry N2 gas at 10, 15, and 20 cc/min for 44.5 hours at 25°C. The saturator columns equilibrated at 35°C and 43.5°C were purged with dry N2 gas at 15 cc/min for 24 hours and 18.5 hours, respectively. Vaporized test material was transported by the carrier gas and retained in the cold traps. After flow termination the acetone in each cold trap was reduced in volume by evaporation. The concentrated solution containing tribufos was analyzed by gas chromatography/mass spectrometry (GC/MSD).
<b>Result</b>	: The average vapor pressures at 25°C, 35°C, and 43.5°C were 0.079, 1.5, and 0.66 milliPascals (5.9 x 10E-7, 1.2 x 10E-5, and 4.9 x 10E-6 Torr), respectively. The value at 43.5°C is inconsistent with the data trend and previously reported values.
<b>Test substance</b>	: Identification: Technical Grade DEF Percent Active Ingredient: 99.4% S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)
<b>Reliability</b> 13.09.2007	: (1) valid without restriction Guideline study <span style="float: right;">(6)</span>

## 2. Physico-Chemical Data

Id 150-50-5  
Date 10.01.2008

### 2.5 PARTITION COEFFICIENT

**Partition coefficient** : octanol-water  
**Log pow** : ca. 7.67 at °C  
**pH value** :  
**Method** :  
**Year** : 1995  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (2) valid with restrictions  
Peer-reviewed published data  
**Flag** : Critical study for SIDS endpoint

13.12.2007 (38)

**Partition coefficient** : octanol-water  
**Log pow** : = 7.67 at °C  
**pH value** :  
**Method** :  
**Year** : 2007  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : (KOWWIN v1.67 estimate):  
SMILES : CCCCSP(SCCCC)SCCCC  
CHEM : Merphos  
CAS NUM: 000150-50-5  
MOL FOR: C12 H27 P1 S3  
MOL WT : 298.50  
**Result** : Log Kow (KOWWIN v1.67 estimate) = 7.67  
**Reliability** : (2) valid with restrictions  
Modeled data

13.12.2007 (19)

**Partition coefficient** : octanol-water  
**Log pow** : = 8.696 at °C  
**pH value** :  
**Method** : other (calculated)  
**Year** : 2002  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : Calculated using Advanced Chemistry Development (ACD) Softward  
Solaris V4.67 ((C) 1994-2002 ACD)  
**Reliability** : (2) valid with restrictions  
Modeled data

15.10.2007 (62)

**Partition coefficient** : octanol-water  
**Log pow** : = 6.02 at 25 °C  
**pH value** :  
**Method** : other (measured)  
**Year** : 2001  
**GLP** : yes  
**Test substance** : other TS

**Method** : The study was conducted as described below according to test methods specified in OPPTS Test Guidelines 830.7570 and followed principles of U. S. EPA Good Laboratory Practice Standards (FIFRA40CFRPart160).

The retention times of solutions of tribufos and a mixture of references

## 2. Physico-Chemical Data

Id 150-50-5

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standards of known octanol/water partition coefficients (log Pow) were determined based on elution from a reversephase C-18 HPLC column. The tribufos and reference standards were run in duplicate. A plot was generated by plotting the log of the octanol/water partition coefficient (log Pow) vs. the log of the capacity factor. Capacity factor (k) is defined as:  $k = (tR - t_0) / t_0$  Where tR is the retention time of the reference standard and t<sub>0</sub> is the void volume retention time. The octanol/water partition coefficient for tribufos was then calculated from this log:log plot.

**Result** : The octanol/water partition coefficient of tribufos (log Pow) averaged 6.02.  
**Test substance** : Identification: Tribufos (CAS Registry Number: 78-48-8); purity 99.4%  
**Reliability** : (1) valid without restriction  
Guideline study

15.10.2007 (7)

### 2.6.1 SOLUBILITY IN DIFFERENT MEDIA

**Solubility in Value** : Water  
: at °C  
**pH value concentration** :  
: at °C  
**Temperature effects** :  
**Examine different pol.** :  
**pKa** : at 25 °C  
**Description** : other: sparingly soluble in water  
**Stable** :  
**Deg. product** :  
**Method** :  
**Year** : 1987  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (2) valid with restrictions  
Handbook data  
**Flag** : Critical study for SIDS endpoint  
13.12.2007 (70)

**Solubility in Value** : Water  
: = .00352 at 25 °C  
**pH value concentration** :  
: at °C  
**Temperature effects** :  
**Examine different pol.** :  
**pKa** : at 25 °C  
**Description** :  
**Stable** :  
**Deg. product** :  
**Method** :  
**Year** : 2007  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : (WSKOW v1.41):  
SMILES : CCCCSP(SCCCC)SCCCC  
CHEM : Merphos  
CAS NUM: 000150-50-5  
MOL FOR: C12 H27 P1 S3  
MOL WT : 298.50  
  
log Kow used: 7.67 (estimated)  
no-melting pt equation used

## 2. Physico-Chemical Data

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Date

<b>Result</b>	: Water Solubility Estimate from Log Kow (WSKOW v1.41): Water Solubility at 25 deg C (mg/L): 0.003517
<b>Reliability</b>	: (2) valid with restrictions Modeled data
<b>Flag</b> 13.12.2007	: Critical study for SIDS endpoint
	(19)
<b>Solubility in Value</b>	: Water = 2.3 other: ppm at 20 °C
<b>pH value concentration</b>	: at °C
<b>Temperature effects</b>	:
<b>Examine different pol.</b>	:
<b>pKa</b>	: at 25 °C
<b>Description</b>	:
<b>Stable</b>	:
<b>Deg. product</b>	:
<b>Method</b>	: other
<b>Year</b>	: 1980
<b>GLP</b>	: no data
<b>Test substance</b>	: other TS
<b>Method</b>	: The distilled, deionized-water solubility of S,S,S-tributyl phosphorotrithioate (DEF) at 20°C and 30°C was determined by gas liquid chromatography. Twelve silanized, screw capped (teflon lined) test tubes 12 x 160 mm were used. DEF solutions of 10, 50, 250, and 500 ug/10 uL were prepared in methanol using a 100% pure standard. Ten uL of each solution was pipetted to the tubes in triplicate. All the methanol was evaporated from each test tube with a stream of nitrogen gas and mild heat applied to the tube. When 10 mL of distilled deionized water was added to the tubes, theoretical concentrations of 1, 5, 25 and 50 ppm resulted. The tubes were capped tightly, placed in a test tube rack and sonicated for 30 minutes. After sonication the tubes were placed in a shaker bath set at the appropriate temperature (either 20°C or 30°C) and shaken for four hours. After shaking, the tubes were centrifuged in an IEC-DPR 6000 temperature-controlled centrifuge at 2500 RPM (approximately 1100 x g) for 20 minutes. The tubes were carefully removed from the centrifuge and 2 mL aliquots from the upper part of the supernatant layer were carefully removed and placed in 30 mL separatory funnels. Each aliquot was then extracted three times with 6 mLs of dichloromethane (DCM). The lower layer (DCM) containing the DEF was collected each time in a 125-mL flat bottomed flask. The DCM was evaporated to a small volume on the Rotovap and then to dryness under a gentle stream of nitrogen. The remaining residue was dissolved in 2 mLs of acetone. The dissolved samples were then subjected to analysis by gas liquid chromatography (GLC). A Varian Aerograph 1400 G.C. with a 3' 10% DC-200 + 1.5% QF-1 column was used with an oven temperature of 220°C. A thermionic phosphorous detector was used. The samples were injected and peak heights compared to a known standard for quantitation.
<b>Result</b>	: The solubility of DEF at both 20°C and 30°C was 2.3 ppm. No significant difference in solubility was detected between the two temperatures. Quantitation was accomplished by comparing the size of G.C. peaks to peaks of similar magnitude produced by known standard amounts. The G.C. response was found to be linear over the working concentration range.
<b>Test substance</b>	: Identification: S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8); purity not reported
<b>Reliability</b> 15.10.2007	: (2) valid with restrictions Provides basic data
	(48)

**2.6.2 SURFACE TENSION****2.7 FLASH POINT**

**Method** :  
**Year** : 2002  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Result** : Flash point = 60-63 deg C  
**Reliability** : (2) valid with restrictions  
 Handbook data

10.10.2007 (16)

**Value** : = 295 °C  
**Type** :  
**Method** :  
**Year** : 1979  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

10.10.2007 (61)

**2.8 AUTO FLAMMABILITY****2.9 FLAMMABILITY****2.10 EXPLOSIVE PROPERTIES****2.11 OXIDIZING PROPERTIES****2.12 DISSOCIATION CONSTANT****2.13 VISCOSITY****2.14 ADDITIONAL REMARKS**

**Memo** : Henry's Law Constant

**Method** : [HENRYWIN v3.10]:  
 SMILES : CCCCSP(SCCCC)SCCCC  
 CHEM : Merphos  
 CAS NUM: 000150-50-5  
 MOL FOR: C12 H27 P1 S3  
 MOL WT : 298.50

**Result** : Henrys Law Constant (25 deg C) [HENRYWIN v3.10]:  
 Bond Method : 2.27E-005 atm-m3/mole  
 Group Method: Incomplete

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**Date** 10.01.2008

**Reliability** : (2) valid with restrictions  
Modeled data

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## 3.1.1 PHOTODEGRADATION

Type : air  
 Light source :  
 Light spectrum : nm  
 Relative intensity : based on intensity of sunlight

## INDIRECT PHOTOLYSIS

Sensitizer : OH  
 Conc. of sensitizer : 1500000 molecule/cm<sup>3</sup>  
 Rate constant : = .0000000000788399 cm<sup>3</sup>/(molecule\*sec)  
 Degradation : = 50 % after .1  
 Deg. product :  
 Method :  
 Year : 2007  
 GLP : no  
 Test substance : as prescribed by 1.1 - 1.4

Method : [AopWin v1.92]:  
 SMILES : CCCCSP(SCCCC)SCCCC  
 CHEM : Merphos  
 CAS NUM: 000150-50-5  
 MOL FOR: C12 H27 P1 S3  
 MOL WT : 298.50

Result : Atmospheric Oxidation (25 deg C) [AopWin v1.92]:  
 Hydroxyl Radicals Reaction:  
 OVERALL OH Rate Constant = 78.8399 E-12 cm<sup>3</sup>/molecule-sec  
 Half-Life = 0.136 Days (12-hr day; 1.5E6 OH/cm<sup>3</sup>)  
 Half-Life = 1.628 Hrs  
 Ozone Reaction:  
 No Ozone Reaction Estimation  
 Fraction sorbed to airborne particulates (phi): 0.0179 (Junge,Mackay)  
 Note: the sorbed fraction may be resistant to atmospheric oxidation

Reliability : (2) valid with restrictions  
 Modeled data

Flag : Critical study for SIDS endpoint  
 15.10.2007

(19)

Type : air  
 Light source : Sun light  
 Light spectrum : nm  
 Relative intensity : based on intensity of sunlight  
 Deg. product : yes  
 Method : EPA Guide-line subdivision N 161-2 "Photodegradation studies in water"  
 Year : 1990  
 GLP : yes  
 Test substance : other TS

Method : Conducted in accordance with EPA Pesticide Assessment Guidelines, Subdivision N, Series 161-2, Photodegradation in Water

The photolysis of [14C]DEF in aqueous solution were investigated under natural sunlight conditions (location latitude 38.05N; Longitude 84.30W). This study design did not include provisions for the quantitative collection of 14CO<sub>2</sub> from incubated test solutions.

Ten quartz tubes connected in a series (immersed in a bath of deionized water) were exposed to direct sunlight for 30 days in an apparatus. Air was drawn through each series of ten tubes (using a vacuum pump) into a gas dispersion tube containing ethylene glycol for the collection of volatile



### 3. Environmental Fate and Pathways

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Date

compounds. The tubes were oriented at a 30 deg C angle with respect to the horizontal such that the length of each tube was facing south, perpendicular to the sun's path. The temperature of the water bath was maintained by a circulating coolant passing through the submerged heating/cooling temperature exchange units. The temperature was continuously monitored and recorded at 20 minute intervals throughout the study. Sunlight intensity was measured continuously and recorded at 20 minute intervals throughout the study. A series of tubes were wrapped in tin foil and exposed as described above, to simulate dark conditions.

Approximately 1700 temperature measurements from the thermocouples and light intensity measurements from the photodetector probe were averaged and output every 20 minutes. Light energy (W min/cm<sup>2</sup>) was calculated as the area under the curve, accumulated, stored and output by the computer at 20 minute intervals between sunrise and sunset for each day. Ethylene glycol dispersion traps were part of the apparatus to measure volatiles.

**Result** : Following 30 days of sample irradiation mean total radiocarbon recovery throughout the study was 63 +/- 12.5%. The mean total recovery ranged from 75.5% in day 0 samples to 42.7% in day 20 samples resulting from a gradual increase in loss of radiocarbon. Radiocarbon began to appear in ethylene glycol traps at day 10 (0.4%) but never exceeded 2.4% of the total applied. It appears that the loss of radiocarbon may be due to the formation of <sup>14</sup>CO<sub>2</sub> or the formation of other volatile product(s) which were not trapped with the ethylene glycol dispersion trap employed in the study. The most likely possibilities are butyl mercaptan and dibutyl disulfide.

The half-life for dark control samples was 198 days. The half-life for irradiated samples was 44 days, indicating that photolysis probably occurred.

**Test substance** : [<sup>14</sup>C]butylthio-1-<sup>14</sup>C-DEF, S,S,S-tributyl phosphorotrithioate, 20.4 mCi/mmole; radiochemical purity 98.9%

**Reliability** : (1) valid without restriction

06.12.2007

(52)

#### 3.1.2 STABILITY IN WATER

**Type** : abiotic  
**t1/2 pH4** : at °C  
**t1/2 pH7** : at °C  
**t1/2 pH9** : at °C  
**Deg. product** :  
**Method** :  
**Year** : 2007  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : [HYDROWIN v1.67]:  
SMILES : CCCCSP(SCCCC)SCCCC  
CHEM : Merphos  
CAS NUM: 000150-50-5  
MOL FOR: C12 H27 P1 S3  
MOL WT : 298.50

**Result** : Rate constants can NOT be estimated for this structure!

**Reliability** : (2) valid with restrictions  
Modeled data

15.10.2007

(19)

**Type** : abiotic  
**t1/2 pH4** : at °C

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t1/2 pH7 : at °C  
t1/2 pH9 : at °C  
Deg. product :  
Method :  
Year : 1971  
GLP : no  
Test substance : as prescribed by 1.1 - 1.4

Remark : Water slowly hydrolyzes merphos with the formation of tetyl mercaptan, a reaction that is catalyzed by base.

Reliability : (4) not assignable  
Original study not reviewed

15.10.2007 (37)

#### 3.1.3 STABILITY IN SOIL

#### 3.2.1 MONITORING DATA

#### 3.2.2 FIELD STUDIES

#### 3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III  
Media :  
Air : % (Fugacity Model Level I)  
Water : % (Fugacity Model Level I)  
Soil : % (Fugacity Model Level I)  
Biota : % (Fugacity Model Level II/III)  
Soil : % (Fugacity Model Level II/III)  
Method : other  
Year : 2007

Result : Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.224	3.26	1000
Water	5.84	208	1000
Soil	30.2	416	1000
Sediment	63.8	1.87e+003	0

Persistence Time: 666 hr

Reliability : (2) valid with restrictions  
Modeled data

Flag : Critical study for SIDS endpoint

15.10.2007 (19)

#### 3.3.2 DISTRIBUTION

#### 3.4 MODE OF DEGRADATION IN ACTUAL USE

#### 3.5 BIODEGRADATION

### 3. Environmental Fate and Pathways

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Date

**Type** : aerobic  
**Inoculum** :  
**Deg. product** :  
**Method** : other  
**Year** : 1991  
**GLP** : yes  
**Test substance** : other TS

**Method** : The aerobic degradation of tribufos (S,S,S-tributyl phosphorotrithioate) was studied in five soils from previous dissipation study sites and from expected-use areas for this pesticide. A continuous flow-through system was used for incubation of treated soils in the dark at 20 +/- 1 deg C. The soils used were from Georgia (Tifton), Mississippi (Benoit), California (Chualar), Texas (Levelland), and Arkansas (Jackson Co.). The recommended maximum application rate for tribufos (1.9 lbs a.i./acre at 6 inches depth and 1.5 g/cc density) was used in the study.

**Result** : Degradation half-lives of tribufos in the five soils were determined to be:  
California: 9.8 days  
Texas: 30.3 days  
Georgia: 99 days  
Arkansas: 143.6 days  
Mississippi: 173.3 days

First-order degradation rate constants were calculated by using a linear regression analysis for Georgia and Mississippi soils and a nonlinear one-phase exponential decay analysis for California, Arkansas, and Texas. Significant quantities of <sup>14</sup>CO<sub>2</sub> evolved by the end of the study, ranging from 37.6% of the applied radioactivity in Mississippi to 72.3% in Texas soil. Soils with more neutral pH (>6.3) had greater CO<sub>2</sub> evolution. Arkansas, California, and Texas soils had a pH greater than 6.3 and CO<sub>2</sub> evolution accounted for greater than 65% of the applied radioactivity. For the two remaining soils (Georgia and Mississippi), the soils, the percentage of applied radioactivity recovered as <sup>14</sup>CO<sub>2</sub> was lower than the other three soils (<= 55%). Correlation analyses were done on soil characteristics with data from the end of the study (half-life and % of applied radioactivity as tribufos or CO<sub>2</sub>) as well as with biomass numbers from the beginning of the study. The pH of soil was correlated with tribufos degradation. A significant correlation (r<sup>2</sup> = 0.8) was observed between soil pH and both percentage remaining as tribufos or half-life (t<sub>1/2</sub>). The correlation coefficient for soil pH versus CO<sub>2</sub> was 0.5. The percent of clay present in soil was also correlated with degradation of tribufos, with correlation coefficients of 0.5 and 0.6 for % remaining as tribufos and T<sub>1/2</sub>, respectively. These data suggest that tribufos goes directly to CO<sub>2</sub>, without the accumulation of intermediate degradates.

**Test substance** : [<sup>14</sup>C]tribufos ([1-<sup>14</sup>C]-S,S,S-tributylphosphorotrithioate, 20.4 mCi/mmmole; radiochemical purity 98.9%

**Reliability** : (1) valid without restriction

05.12.2007

(11)

**Type** : aerobic  
**Inoculum** :  
**Contact time** :  
**Degradation** : = 50 (±) % after 745 day(s)  
**Result** :  
**Deg. product** :  
**Method** : other: EPA Guideline Ref. No.: 162-1 (e) Aerobic Soil Metabolism  
**Year** : 1991  
**GLP** : yes  
**Test substance** : other TS

**Method** : EPA Guideline Ref. No.: 162-1 (e) Aerobic Soil Metabolism

### 3. Environmental Fate and Pathways

Id 150-50-5

Date

The objective of this study is to determine the metabolism of tribufos in sandy loam (pH >6.5) under aerobic conditions in the dark at 25 +/- 1 deg C.

**Result**

Sandy loam (pH 6.9) was treated with <sup>14</sup>C-tribufos [S-S-S-butyl phosphorotrithioate] at 7 ppm and allowed to incubate aerobically in the dark at 25°C ± 1°C for 360 days. The soil was sampled at intervals of 0, 3, 7, 14, 29, 59, 91, 181, 272, and 360 days.

: The only major metabolite formed in the soil was (1-butane sulfonic acid). The 360-day sample still contained greater than 65% of the applied radioactivity as parent tribufos. A maximum of 7.6% of the applied radioactivity was evolved as <sup>14</sup>CO<sub>2</sub> during the study. The calculated half-life was 745 days.

**Test substance**

: [<sup>14</sup>C]tribufos ([1-<sup>14</sup>C]-S,S,S-tributylphosphorotrithioate, 20.4 mCi/mmole; radiochemical purity 97.9%

06.12.2007

(58)

**Type**

: anaerobic

**Inoculum**

:

**Deg. product**

:

**Method**

: other

**Year**

: 1989

**GLP**

: yes

**Test substance**

: other TS

**Method**

: Conducted in accordance with EPA Pesticide Assessment Guidelines, Subdivision N, Series 162-2, Anaerobic Soil Metabolism

The study was designed and conducted according to general protocol of the EPA Guidelines to evaluate the metabolism of [<sup>14</sup>C]DEF in sandy loam soil under anaerobic conditions.

**Result**

[<sup>14</sup>C]DEF (S,S,S-tributyl phosphorotrithioate) was prepared in acetone. Aliquots of the solution containing approximately 10.3 uCi (158 ug) of [<sup>14</sup>C]DEF were applied directly to 50 g sandy loam soil in 500 mL Erlenmeyer flasks, resulting in a final concentration of 3.2 ppm. Water was added to obtain 75% saturation and duplicate flasks for each time period (0, 30, 60 and 90 days) were sealed and placed in a dark incubator. The incubator temperatures throughout the study ranged from 18.0 - 26.5 deg C with a mean of 22.6 +/- 1.4 deg C. Incubation was under aerobic conditions for 30 days followed by a 60 day incubation period under anaerobic conditions.

: The parent compound degraded to <sup>14</sup>CO<sub>2</sub> and a product(s) which was recovered in ethylene glycol, or H<sub>2</sub>SO<sub>4</sub> gas-dispersion traps. At the end of the 90 day incubation period [<sup>14</sup>C]DEF and <sup>14</sup>CO<sub>2</sub> accounted for 26.1% and 14.1% of the applied radiocarbon, respectively (21.2%) remained in the soil following extraction with acetonitrile. Half-life of [<sup>14</sup>C]DEF under anaerobic conditions was 64.8 days.

**Test substance**

: [<sup>14</sup>C]butylthio-1-<sup>14</sup>C-DEF, S,S,S-tributyl phosphorotrithioate, 20.4 mCi/mmole; radiochemical purity 98.9%

13.12.2007

(50)

**Type**

: anaerobic

**Inoculum**

:

**Contact time**

:

**Degradation**

: = 50 (±) % after 65 day(s)

**Result**

: other

**Deg. product**

: yes

**Method**

: other: U.S. EPA FIFRA N-162-3

**Year**

: 1994

**GLP**

:

**Test substance**

: other TS

**Method** : U.S. EPA Pesticide Assessment Guidelines, Subdivision N, Section 162-3, as required by 40 CFR, Sec. 158.130

The purpose for conducting anaerobic aquatic metabolism studies is to generate data to assess the nature and extent of pesticide residues in water and hydrosol, since these residues may then be taken up by irrigated crops and passed on to other parts of the aquatic food web. The objectives of this anaerobic aquatic metabolism study were to determine the nature and extent of formation of pesticide degradation products, to determine the half-life of the test material, and to describe the patterns of formation and decline of degradation products and to attempt identification of all residues occurring at greater than 0.01 ppm.

A 6-month long (181-day) anaerobic aquatic metabolism study with <sup>14</sup>C-tribufos was conducted under dark conditions on pond sediment which was flooded with pond water at 25 +/- deg C. After anaerobic conditions had been established, the samples of pond sediment were treated with sufficient <sup>14</sup>C-tribufos to achieve a nominal concentration of 1.0 ppm (1.0 ug/mL); a dose of 12.6 ppm (12.6 ug/mL was used for a metabolism identification test). The choice of 1.0 ppm as the application rate was a compromise between the demonstrated low solubility of tribufos in water (0.5 ppm) and the necessity of treating at a rate high enough so that the objectives of the study could be addressed (i.e. determination of the pattern of formation and decline of metabolites). Sediment samples and test water collected throughout the study were analyzed for residues of <sup>14</sup>C-tribufos and its degradation products by thin layer chromatography (TLC). Sediment samples were extracted prior to analysis. Quantification of radioactivity in solution was determined by liquid scintillation counting. Samples were collected at 0, 1, 3, 7, 14 days and 1, 2, 3, 4, and 6 months after dosing.

**Result** : The concentration of <sup>14</sup>C-tribufos in the test system after dosing was determined to be 0.961 ppm (mean of triplicate day 0 samples).

Extractable residues decreased from 58.5% of the applied radioactivity at day 0 to 26.2% at 6 months. Bound residues increased from 5.1% of the applied radioactivity at day 0 to 20.7% at 6 months. Volatile residues increased from <0.1% of the applied radioactivity at day 1 to 18.0% at 6 months. Measurable amounts of <sup>14</sup>C-activity were found in both the ethylene glycol and KOH traps. The mean <sup>14</sup>C-mass balance accountability for the study was 92.3%. However, the <sup>14</sup>C-mass balance accountability fell below 90% at the 3 month sample point, and continued to decline through the 6 month sample point (73.0%).

Residues of the parent compound decreased from 86.2% of the applied radioactivity at day 0 to 11.6% at 6 months. A metabolite identified as 1-butane sulfonic acid increased from 6.0% of applied radioactivity at day 0 to 19.1% at 3 months, then decreased to 14.7% at 6 months. The identity of tribufos and 1-butane sulfonic acid were confirmed by GC/MS. The half-life of tribufos under anaerobic aquatic conditions was calculated to be 65.1 days using first-order degradation kinetics.

**Test substance** : (n-butyl-1-<sup>14</sup>C) Tribufos, 3.5 mCi in benzene, 20.4 mCi/mmol; radiochemical purity 95.0%

**Reliability** : (1) valid without restriction

05.12.2007

(45)

### 3.6 BOD<sub>5</sub>, COD OR BOD<sub>5</sub>/COD RATIO

#### 3.7 BIOACCUMULATION

**BCF** : = 245.3  
**Elimination** :  
**Method** :  
**Year** : 2007  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : (BCFWIN v2.17):  
SMILES : CCCCSP(SCCCC)SCCCC  
CHEM : Merphos  
CAS NUM: 000150-50-5  
MOL FOR: C12 H27 P1 S3  
MOL WT : 298.50

**Result** : log Kow used: 7.67 (estimated)  
Bioaccumulation Estimates from Log Kow (BCFWIN v2.17):  
Log BCF from regression-based method = 2.390 (BCF = 245.3)

**Reliability** : (2) valid with restrictions  
Modeled data

15.10.2007 (19)

#### 3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type : static  
 Species : Lepomis macrochirus (Fish, fresh water)  
 Exposure period : 96 hour(s)  
 Unit : mg/l  
 LC50 : = 18.2  
 Method : other  
 Year : 1964  
 GLP : no  
 Test substance : as prescribed by 1.1 - 1.4

Method : Conducted in accordance with "Procedure for Evaluation of Acute Toxicity of Pesticides to Fish and Wildlife", USDI Fish and Wildlife Service Pesticides Review Staff, December 14, 1964.

Test vessel: 5 gallon wide-mouthed glass vessels  
 Test medium: reconstituted water which was aerated  
 Temperature: 75 deg F (+/- 2 deg F) (23.8 deg C)  
 Ratio of fish to medium did not exceed one-half gram of fish/1 liter water  
 Positive control: p,p'-DDT dissolved in acetone

Fish were held for 10 days prior to bioassay. During the last 3 days prior to bioassay they were not fed. The fish were transferred into the bioassay vessels prior to the addition of the test or control chemicals; aeration was continued during this one-day pre-exposure. The positive and negative control tests were conducted concurrently with those of Folex using fish from the same lots. The aeration apparatus was removed from the bioassay vessel immediately prior to the addition of the test chemicals. Ten fish were used in the negative control group and groups of 10 fish were exposed to concentrations of Folex ranging from 0.25 to 25.1 ppm and of reference standard p,p'-DDT from 0.316 to 31.6 ppb. The duration of exposure was 96 hours. Reactions of the fish were recorded and the dead counted and removed at the end of 24, 48, 72 and 96 hours.

Result : Survivors during study:

Conc. ppb	0	1	2	3	4
0	10	10	10	10	10
250	10	10	10	10	10
1,540	10	10	10	10	10
10,000	10	10	10	9	
20,000	10	10	9	6	
25,100	10	5	0	0	
p,p'-DDT					
0.316	10	10	10	10	
1.0	10	10	10	10	
3.16	10	2	2	1	1
10.0	10	1	0	0	0
31.6	10	0	0	0	0

LC50 for Folex to bluegill sunfish: 18,200 ppb (95% confidence limits = 14,100 - 23,500) = 18.2 ppm = 18.2 mg/l

LC50 for p,p'-DDT to bluegill sunfish; 1.90 ppb (estimated)

Test substance : Folex (72% Merphos) and 28% inert ingredients  
 Reliability : (2) valid with restrictions  
 Comparable to guideline study, but not GLP

13.12.2007

(30)

Type : static

## 4. Ecotoxicity

**Id** 150-50-5  
**Date** 10.01.2008

**Species** : Lepomis macrochirus (Fish, fresh water)  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**Method** :  
**Year** : 1986  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : Water Type: Fresh  
Temperature: Mean 22 deg C

pH: varied (see results)  
Concentrations: varied (see results)  
Species lifestage: varied (see results)  
Hardness: varied (see results)  
**Result** : Species lifestage: 0.5 g  
Hardness: Mean 40 mg/L CaCO<sub>3</sub>

pH mean: 6.5  
Concentrations: Min 1.3 mg/L; Max 4 mg/L  
96 h LC50 = 2.3 mg/L

pH mean: 7.5  
Concentrations: Min 0.88 mg/L; Max 2 mg/L  
96 h LC50 = 1.3 mg/L

pH mean: 8.5  
Concentrations: Min 1 mg/L; Max 1.8 mg/L  
96 h LC50 = 1.4 mg/L

-----  
Species lifestage: 0.8 g  
Hardness: Mean 48 mg/L CaCO<sub>3</sub>  
pH mean: 7.6  
Concentrations in 96 h study: Min 3.1 mg/L; Max 10 mg/L  
Concentrations in 24 h study: Min NA; Max 32 mg/L  
96 h LC50 = 5.6 mg/L  
24 h LC50 > 32 mg/L

-----  
Species lifestage: 0.7 g  
Hardness: Mean 44 mg/L CaCO<sub>3</sub>  
pH mean: 7.3  
Concentrations in 96 hr study: Min 4 mg/L; Max 17 mg/L  
Concentrations in 24 hr study: Min NA; Max 32 mg/L  
96 h LC50 = 8 mg/L  
24 h LC50 > 32 mg/L

**Test substance** : Phosphorotriethous acid, Tributyl ester  
CAS RN 150-50-5  
purity: 96%

**Reliability** : (2) valid with restrictions  
Data obtained from AQUIRE, a peer-reviewed database. Original data were not examined.

11.10.2007

(35)

**Type** : static  
**Species** : Oncorhynchus mykiss (Fish, fresh water)  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**LC50** : = 11.5



## 4. Ecotoxicity

Id 150-50-5  
Date 10.01.2008

**24 h LC50** : = 42.5  
**Method** :  
**Year** : 1986  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : pH mean: 6.8  
Concentrations: Min 8.4 mg/L; Max 15.8 mg/L  
Species lifestage: 0.6 g  
Water Type: Fresh  
Temperature: Mean 17 deg C  
Hardness: Mean 44 mg/L CaCO3

**Test substance** : Concentrations tested in 24 h study:  
Min 35.7 mg/L; Max 50.5 mg/L  
: Phosphorotrithious acid, Tributyl ester  
CAS RN 150-50-5  
purity: 96%

**Reliability** : (2) valid with restrictions  
Data obtained from AQUIRE, a peer-reviewed database. Original data were not examined.

11.10.2007

(35)

**Type** : static  
**Species** : Oncorhynchus mykiss (Fish, fresh water)  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**LC50** : = 5.8  
**Method** : other  
**Year** : 1964  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : Conducted in accordance with "Procedure for Evaluation of Acute Toxicity of Pesticides to Fish and Wildlife", USDI Fish and Wildlife Service Pesticides Review Staff, December 14, 1964.

Test vessel: 5 gallon wide-mouthed glass vessels  
Test medium: reconstituted water which was aerated  
Temperature: 55 deg F (+/- 2 deg F)  
Ratio of fish to medium did not exceed one-half gram of fish/1 liter water  
Positive control: p,p'-DDT dissolved in acetone

Fish were held for 10 days prior to bioassay. During the last 3 days prior to bioassay they were not fed. The fish were transferred into the bioassay vessels prior to the addition of the test or control chemicals; aeration was continued during this one-day pre-exposure. The positive and negative control tests were conducted concurrently with those of Folex using fish from the same lots. The aeration apparatus was removed from the bioassay vessel immediately prior to the addition of the test chemicals. Thirty fish were used in the negative control group and groups of 10-17 fish were exposed to concentrations of Folex ranging from 0.25 to 25.1 ppm and of reference standard p,p'-DDT from 0.25 to 25.1 ppb. The duration of exposure was 96 hours. Reactions of the fish were recorded and the dead counted and removed at the end of 24, 48, 72 and 96 hours.

**Result** : Survivors during study:

Conc. ppb	0	1	2	3	4
0	30	30	29	29	29
250	10	10	10	9	9
1540	10	10	10	10	8
10,000	17	15	15	13	10
17,500	8	4	1	1	0

## 4. Ecotoxicity

Id 150-50-5  
Date 10.01.2008

20,000	10	9	9	8	2
25,100	17	14	14	10	6

p,p'-DDT					
0.25	10	10	10	10	10
1.54	10	10	10	8	8
10.0	10	0	0	0	0
20.0	10	0	0	0	0
25.1	10	0	0	0	0

LC50 for Folex to rainbow trout: 5800 ppb (95% confidence limits = 3,200 - 10,400) = 5.8 ppm = 5.8 mg/l

LC50 for p,p'-DDT; 2.95 ppb (estimated)

**Test substance** : Folex (72% Merphos) and 28% inert ingredients

**Reliability** :

(2) valid with restrictions

This study is comparable to a guideline study. However, according to the methods the study was conducted at a water temperature of 55 +/- 2 deg F (11.66 - 13.88 deg C). The study results did not provide the actual temperatures recorded during the study. According to OECD TG 203, the temperature range for this species should be 13 - 17 deg C.

13.12.2007

(30)

**Type** : static  
**Species** : Oncorhynchus mykiss (Fish, fresh water)  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**LC50** : = 7.2  
**24 h LC50** : = 16.9  
**Method** :  
**Year** : 1986  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : pH: Mean 7.4; Min 7.2; Max 7.5  
 Concentrations: Min 7 mg/L; Max 14 mg/L  
 Species lifestage: 0.6 g  
 Water Type: Fresh  
 Temperature: Mean 12 deg C  
 Hardness: Mean 44 mg/L CaCO3 (Min 40 mg/L CaCO3; Max 50 mg/L CaCO3)  
 Alkalinity: Min 30 mg/L CaCO3; Max 35 mg/L CaCO3

**Remark** : Concentrations tested in 24 h study:  
 Min 19 mg/L; Max 28 mg/L  
 : Based on % active ingredient, the reported 96 and 24 hr EC50s of 10 and 23.5 mg/L, respectively, would be = 7.2 and 16.9 mg/L, respectively.

**Test substance** : Phosphorotrithious acid, Tributyl ester  
 CAS RN 150-50-5

**Reliability** : purity: 72%  
 : (2) valid with restrictions  
 According to the methods this study was conducted at a water temperatures of 12°C. OECD TG 203 indicates the water temperature range for this species should be 13 - 17 deg C.

13.12.2007

(33) (35)

**Type** : static  
**Species** : Oncorhynchus mykiss (Fish, fresh water)  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**LC50** : = 14.5  
**24 h LC50** : = 38  
**Method** :

## 4. Ecotoxicity

Id 150-50-5

Date 10.01.2008

<b>Year</b>	:	1986	
<b>GLP</b>	:	no data	
<b>Test substance</b>	:	as prescribed by 1.1 - 1.4	
<b>Method</b>	:	pH mean: 6.8 Concentrations: Min 11 mg/L; Max 19 mg/L Species lifestage: 0.6 g Water Type: Fresh Temperature: Mean 12 deg C Hardness: Mean 44 mg/L CaCO <sub>3</sub>	
<b>Test substance</b>	:	Concentrations tested in 24 h study: Min 29 mg/L; Max 50 mg/L Phosphorotrithious acid, Tributyl ester CAS RN 150-50-5 purity: 96%	
<b>Reliability</b>	:	(2) valid with restrictions According to the methods this study was conducted at a water temperatures of 12°C. OECD TG 203 indicates the water temperature range for this species should be 13 - 17 deg C.	
13.12.2007			(35)
<b>Type</b>	:	static	
<b>Species</b>	:	Oncorhynchus mykiss (Fish, fresh water)	
<b>Exposure period</b>	:	96 hour(s)	
<b>Unit</b>	:	mg/l	
<b>LC50</b>	:	= 23.8	
<b>Method</b>	:		
<b>Year</b>	:	1986	
<b>GLP</b>	:	no data	
<b>Test substance</b>	:	as prescribed by 1.1 - 1.4	
<b>Method</b>	:	pH: Mean 7.4; Min 7.2; Max 7.5 Concentrations: Min 20 mg/L; Max 53 mg/L Species lifestage: 0.6 g Water Type: Fresh Temperature: Mean 12 deg C Hardness: Mean 44 mg/L CaCO <sub>3</sub> ; Min 40 mg/L CaCO <sub>3</sub> ; Max 50 mg/L CaCO <sub>3</sub> Alkalinity: Min 30 mg/L CaCO <sub>3</sub> ; Max 35 mg/L CaCO <sub>3</sub>	
<b>Remark</b>	:	Based on % active ingredient, the reported 96 hr EC50 of 33 mg/L, would be = 23.2 mg/L, respectively.	
<b>Test substance</b>	:	Phosphorotrithious acid, Tributyl ester CAS RN 150-50-5 purity: 72%	
<b>Reliability</b>	:	(2) valid with restrictions According to the methods this study was conducted at a water temperatures of 12°C. OECD TG 203 indicates the water temperature range for this species should be 13 - 17 deg C.	
13.12.2007			(33) (35)
<b>Type</b>	:	flow through	
<b>Species</b>	:	Cyprinodon variegatus (Fish, estuary, marine)	
<b>Exposure period</b>	:	96 hour(s)	
<b>Unit</b>	:	mg/l	
<b>NOEC</b>	:	= .09	
<b>LC50</b>	:	= .77	
<b>Limit test</b>	:		
<b>Analytical monitoring</b>	:	yes	
<b>Method</b>	:	other: EPA OPP 72-3	
<b>Year</b>	:	1991	
<b>GLP</b>	:	yes	

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**Test substance** : other TS

**Method** : The range finding test was conducted under static conditions. The nominal concentrations selected for this test were 0.1, 1.0, and 10 mg/L. At test termination there was 100 percent mortality at 10 mg/L and sublethal effects observed at 1.0 mg/L. The nominal concentrations of DEF Technical selected for the definitive study were 0.14, 0.23, 0.39, 0.65, 1.08, 1.8, and 3.0 mg a.i./L (ppm).

A flow-through toxicity test was conducted to determine the acute toxicity of DEF Technical to the sheepshead minnow, *Cyprinodon variegatus*. The nominal test concentrations of DEF were 0.14, 0.23, 0.39, 0.65, 1.08, 1.8, and 3.0 mg/L. The solvent control chamber received an aliquot of 90 microliters of acetone per liter of water which was approximately the amount of solvent received by the highest test concentration. The definitive study was initiated after the test solutions had been flowing through the aquaria for approximately 24 hours. Sheepshead minnows were impartially distributed, by twos, to each test chamber until twenty fish were distributed to each. Test concentrations were not replicated. An overall photoperiod of 16-hours light and 8-hours dark was maintained. Survival of fish was monitored daily and dead fish removed. Observations for sublethal and behavioral effects were also made. Fish were not fed during the test and test solutions were not aerated during the study. Twenty fish from the control chamber were weighed and measured at test termination. Temperature, dissolved oxygen, salinity and pH were measured in the control, solvent control, low, middle and high concentrations containing surviving fish at 0, 48 and 96 hours of testing. Results of the test are expressed as a 96-hour median lethal concentration (LC50) which is the concentration of DEF Technical estimated to be lethal to 50 percent of the test population of fish at the specified time.

**Result** : Mortality of sheepshead minnows exposed for 96 hours to DEF Technical ranged from 0 percent in the measured concentrations 0.06, 0.09, 0.14, 0.19, and 0.30 mg/L to 100 percent in the 1.37 mg/L concentration. One fish in the 0.09 mg/L test chamber appeared to have escaped through the side drain during the overnight period between 0 and 24 hours due to a drain screen that fell off. Since no mortality occurred in this test chamber during the study the loss of this fish was not included in the LC50 or NOEC analyses. There were no mortalities in the dilution water control and solvent controls. Based on the mortality data collected and the mean measured DEF concentrations the 96-hour LC50 was 0.77 mg/L with 95 percent confidence limits of 0.56 to 1.37 mg/L. The slope of the toxicity curve was 7.78 as determined by the probit method. In order to use the probit method to calculate the slope the 100 percent mortality at 1.37 mg/L was adjusted to 99.5 percent mortality to provide the two partial kills necessary for this method to be employed. This slight adjustment still allows a reasonably accurate slope to be calculated (Stephan, 1977).

Behavioral and sublethal effects observed during the exposure period included erratic behavior and loss of equilibrium. Fish in several test concentrations were observed to swim very close to the water surface. Although this was not noted in the controls this behavior was observed in the remaining fish in the test lot and, therefore, it is not thought to be due to the test compound. The no-observed-effect-concentration (NOEC) was 0.09 mg/L (measured) based upon the lack of mortality and sublethal effects at this concentration.

24 hr LC50 > 1.37 mg/l  
48 hr LC50 = 0.96 mg/l (95% confidence limits 0.56 - 1.37)  
72 hr LC50 = 0.88 mg/l (95% confidence limits 0.56 - 1.37)  
96 hr LC50 = 0.77 mg/l (95% confidence limits 0.56 - 1.37)

The test temperature during the 96-hour exposure ranged from 21.6 to 22.1

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<b>Test substance</b>	: deg C. Salinity in the test chambers ranged from 14.2 to 16.7%. Dissolved oxygen concentrations ranged from 7.3 to 8.0 mg/L representing 90 and 99 percent saturation, respectively, at 22°C. The pH values ranged from 8.2 to 8.4. Identification: DEF Technical Percent Active Ingredient: S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8) Purity: 98.6%
<b>Reliability</b>	: (1) valid without restriction Guideline study
13.12.2007	(56)
<b>Type</b>	: flow through
<b>Species</b>	: Pimephales promelas (Fish, fresh water)
<b>Exposure period</b>	: 96 hour(s)
<b>Unit</b>	: mg/l
<b>NOEC</b>	: = .27
<b>LC50</b>	: = .92
<b>LOEC</b>	: = .59
<b>Limit test</b>	:
<b>Analytical monitoring</b>	: yes
<b>Method</b>	: EPA OPP 72-1
<b>Year</b>	: 2002
<b>GLP</b>	: yes
<b>Test substance</b>	: other TS
<b>Method</b>	: A range-finding test was conducted at 0 (control and solvent control), 0.05, 0.25, 1.25 and 2.5 mg a.i./L. The exposure was conducted with a single replicate at each level. Each replicate contained 10 fish. No mortalities or sublethal effects were noted at 0.05 and 0.25 mg a.i./L in the range-find test. All individuals died at 1.25 and 2.5 mg a.i./L. Based on the results from the range-find test, concentrations in the definitive test were set at 0 (control and solvent control), 0.08, 0.16, 0.31, 0.63, and 1.25 mg a.i./L.  Definitive test: During the 48-hours immediately prior to initiation of the 96-hour exposure period, the fish were held under test conditions of 22 ± 1°C, a light cycle of 16 hours light and 8 hours dark, and an approximate light intensity of 637 lux (59 footcandles). The fish were not fed and there were no mortalities during this period.  Fathead minnows (Pimephales promelas) were exposed under flow-through conditions for 96-hours to measured concentrations of 0.07, 0.13, 0.27, 0.59, and 1.05 mg a.i./L, plus a control and a solvent control (acetone); there was one replicate of 20 fish each in the control, solvent control, and the five toxicant levels. The primary endpoint for acute toxicity was mortality. Sublethal and behavioral effects were also assessed during the course of the study.  Hardness, conductivity, alkalinity, dissolved oxygen and pH were measured in all test vessels on Day 0, 2 and/or Day 4. The 96-hour LC50 value and was calculated by a LC50 computer program developed by Stephan et al. (1984) using the binomial probability statistical method.
<b>Result</b>	: Temperature during the 96-hour exposure: 21.7 to 22.2°C (mean = 22.0°C) Dissolved oxygen concentrations ranged from 7.3 to 7.9 mg/L, representing 84 to 90 percent saturation at 22°C. pH: 7.6 to 7.8 Conductivity readings averaged 137 and ranged from 134 to 140 umhos/cm. Mean (range) hardness was 48 (44 to 52) mg/L as CaCO <sub>3</sub> Alkalinity was 37 (33 to 41) mg/L as CaCO <sub>3</sub>  The mean measured concentrations of Tribufos during the test period were

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<0.003, <0.003, 0.07, 0.13, 0.27, 0.59, and 1.05 mg a.i./L for the nominal test levels of control, solvent control, 0.08, 0.16, 0.31, 0.63, and 1.25 mg a.i./L., respectively. The mean measured concentrations ranged from 81 to 93 percent of the nominal concentrations. No undissolved test substance was observed in the test chambers. The compound was stable and soluble in the test system. All subsequent observations will refer to mean measured concentrations of the test solutions.

No behavioral/sublethal effects were observed in the dilution water control, solvent control, 0.07, 0.13, or 0.27 mg a.i./L test levels during the exposure period. Behavioral/sublethal effects (at surface, loss of equilibrium, on bottom, labored respiration) were noted in the 0.59 and 1.05 mg a.i./L test levels.

Cumulative mortality at the 1.05 mg a.i./L test concentrations was 70%. Since mortality only occurred at the 1.05 mg a.i./L test level, neither the moving average nor the probit method of analyses could produce statistically sound results. Therefore, the binomial probability test was used. Based on the mortality data, the binomial probability analysis calculated a 96-hour LC50 of 0.92 mg a.i./L using nonlinear interpolation.

Threshold Effect Concentration, TEC (geometric mean of LOEC and NOEC): 0.40 mg a.i./L.

Based on the mortality data collected and the mean measured Tribufos concentrations, the 96-hour LC50 is 0.92 mg a.i./L.

<b>Test substance</b>	:	Identification: Technical Grade Tribufos Percent Active Ingredient: 99.4% S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)
<b>Reliability</b>	:	(1) valid without restriction Guideline study
13.12.2007		(13)
<b>Type</b>	:	flow through
<b>Species</b>	:	Lepomis macrochirus (Fish, fresh water)
<b>Exposure period</b>	:	96 hour(s)
<b>Unit</b>	:	mg/l
<b>LC50</b>	:	= .63
<b>Method</b>	:	
<b>Year</b>	:	1995
<b>GLP</b>	:	no data
<b>Test substance</b>	:	other TS
<b>Method</b>	:	Type of Water: FW - fresh water Species Number : 2 Age/Life Stage: 1.9 G (grams) Control data is presented but without accompanying methodology Concentrations tested: 500 ppb - 780 ppb
<b>Test substance</b>	:	S,S,S-Tributylphosphorotrithioic acid CAS RN 78-48-8 Purity: 96.2%
<b>Reliability</b>	:	(2) valid with restrictions Data obtained from AQUIRE, a peer-reviewed database. Original data were not examined.
13.12.2007		(67)
<b>Type</b>	:	static
<b>Species</b>	:	Lepomis macrochirus (Fish, fresh water)
<b>Exposure period</b>	:	96 hour(s)
<b>Unit</b>	:	mg/l
<b>LC50</b>	:	= .245 - .78

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**Method** :  
**Year** : 1986  
**GLP** : no data  
**Test substance** : other TS

**Method** : Type of Water: FW - fresh water  
Age/Life Stage: 0.9 G (grams)  
Exposure Regimen: 96 hr  
Controls: NR - not reported  
Water Parameters:  
Temperature: 22 (mean value) deg C  
Hardness(mg/l CaCO<sub>3</sub>): 40 (mean value) mg/L CaCO<sub>3</sub>  
pH: 7.2 (mean value)  
96 hr LC50 = 0.54 mg/L

Same study parameters as above also done with 0.6 G life stage and 24 hr exposure:  
24 hr LC50 = 4.8 mg/L

Type of Water: FW - fresh water  
Age/Life Stage: 0.6 G (grams)  
Exposure Regimen: 96 hr  
Controls: NR - not reported  
Water Parameters:  
Temperature: 22 (mean value) deg C  
Hardness(mg/l CaCO<sub>3</sub>): 44 (mean value) mg/L CaCO<sub>3</sub>  
pH: 7.4 (mean value)  
96 hr LC50 = 0.57 mg/L  
24 hr LC50 = 1.35 mg/L

Same study parameters as above also done with 0.9 G life stage and 24 hr exposure:  
24 hr LC50 = 7.3 mg/L

Type of Water: FW - fresh water  
Age/Life Stage: 0.6 G (grams)  
Exposure Regimen: 24 hr  
Controls: NR - not reported  
Water Parameters:  
Temperature: 22 (mean value) deg C  
Hardness(mg/l CaCO<sub>3</sub>): 40 (mean value) mg/L CaCO<sub>3</sub>  
pH: 7.6 (mean value)  
24 hr LC50 = 2.3 mg/L

Type of Water: FW - fresh water  
Age/Life Stage: 0.6 G (grams)  
Exposure Regimen: 96 hr  
Controls: NR - not reported  
Water Parameters:  
Temperature: 22 (mean value) deg C  
Hardness(mg/l CaCO<sub>3</sub>): 40 (mean value) mg/L CaCO<sub>3</sub>  
pH: 6.5 (mean value)  
96 hr LC50 = 0.64 mg/L  
24 hr LC50 = 4.2 mg/L

Type of Water: FW - fresh water  
Age/Life Stage: 0.6 G (grams)  
Exposure Regimen: 96 hr  
Controls: NR - not reported  
Water Parameters:  
Temperature: 22 (mean value) deg C  
Hardness(mg/l CaCO<sub>3</sub>): 40 (mean value) mg/L CaCO<sub>3</sub>

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pH: 7.5 (mean value)  
96 hr LC50 = 0.64 mg/L  
24 hr LC50 = 2.8 mg/L

Type of Water: FW - fresh water  
Age/Life Stage: 0.6 G (grams)  
Exposure Regimen: 96 hr  
Controls: NR - not reported  
Water Parameters:  
Temperature: 22 (mean value) deg C  
Hardness(mg/l CaCO3): 40 (mean value) mg/L CaCO3  
pH: 8.5 (mean value)  
96 hr LC50 = 0.78 mg/L  
24 hr LC50 = 1.1 mg/L

Type of Water: FW - fresh water  
Age/Life Stage: 0.5 G (grams)  
Exposure Regimen: 96 hr  
Controls: NR - not reported  
Water Parameters:  
Temperature: 22 (mean value) deg C  
Hardness(mg/l CaCO3): 40 (mean value) mg/L CaCO3  
pH: 8.1 (mean value)  
96 hr LC50 = 0.245 mg/L  
24 hr LC50 = 1.1 mg/L

Type of Water: FW - fresh water  
Age/Life Stage: 0.5 G (grams)  
Exposure Regimen: 96 hr  
Controls: NR - not reported  
Water Parameters:  
Temperature: 22 (mean value) deg C  
Hardness(mg/l CaCO3): 320 (mean value) mg/L CaCO3  
pH: 8.1 (mean value)  
96 hr LC50 = 0.27 mg/L  
24 hr LC50 = 1.1 mg/L

**Test substance** : S,S,S-Tributylphosphorotrithioic acid  
CAS RN 78-48-8  
Purity: 95%

**Reliability** : (2) valid with restrictions  
Data obtained from AQUIRE, a peer-reviewed database. Original data were not examined.

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(35)

**Type** : flow through  
**Species** : Oncorhynchus mykiss (Fish, fresh water)  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**NOEC** : < .33  
**LC50** : = 1.52  
**Method** : EPA OPP 72-1  
**Year** : 1990  
**GLP** : yes  
**Test substance** : other TS

**Method** : The acute toxicity of technical grade DEF (96.2 % active ingredient (a.i.)) to Rainbow Trout (*Salmo gairdneri*, syn. *Oncorhynchus mykiss*) was determined in a 96-hour flow-through-test according to "OECD Guideline for Testing of Chemicals No. 203" dated 04.04.1984, "EEC DIRECTIVE 79/831, Annex V, Methods for the determination of Ecotoxicity, Method 5.1.1. Acute Toxicity for fish" (published in "Amtsblatt der Europäischen Gemeinschaften" dated 19.09.1984) and EPA Pesticide Assessment



Guideline, Subdivision E §71-1.

Groups of ten fishes, were exposed to concentrations of 0.33, 0.58, 1.02, 1.82, 3.24, and 5.77 mg a.i./l. An additional group of ten fishes, similarly exposed to 0.1 ml Acetone p.a./l, was maintained as solvent control. The control group was only exposed to untreated test water. All groups were observed for a 96 h exposure period.

During the test, fish were examined daily for mortalities and symptoms of intoxication. Dissolved oxygen and pH values were determined daily in each aquarium, water temperature was measured and recorded hourly. Water flow rate and dosing systems were controlled twice daily and water flow was re-adjusted if necessary.

Analytical determinations of the active ingredient concentrations were made in the stock solutions and test media at the beginning of the test as well at the end of the test.

The LC50 values with 95%-confidence intervals were calculated by probit analysis for each 24-hour period if possible. In cases where 0 and 100 % mortality was observed in the next lower and the next higher concentration, respectively, the geometical mean was given as LC50-value and the range between the two concentrations was given as 95%-confidence interval.

**Result**

: Hardness: 40 - 60 mg CaCO3/l  
Photo period: 16 hours light / 8 hours dark  
Water temperature: 12 ± 1°C  
Dissolved oxygen: 10.5 - 11.5 mg/l  
pH: 7.5 - 7.8

Conc. (mg/l)	Mortality (dead/dosed)			
	24 hr	48 hr	72 hr	96 hr
control	0/10	0/10	0/10	0/10
solvent	0/10	0/10	0/10	0/10
0.33	0/10	0/10	0/10	0/10
0.58	0/10	0/10	2/10	2/10
1.02	0/10	0/10	0/10	1/10
1.82	0/10	1/10	5/10	7/10
3.24	0/10	3/10	7/10	9/10
5.77	0/10	5/10	9/10	9/10

The following symptoms were observed, primarily at concentration >= 0.58 mg/l:

- Swimming behavior slightly irregular (slight symptom)
- Fish mainly at the bottom
- Fish mainly at the surface
- Tumbling during swimming
- Lying on side/back

The test revealed the following results:

LC50 (96 h) = 1.52 mg a.i./l  
95% confidence interval 1.07 - 2.16 mg a.i./l  
Lowest lethal concentration (LLC) 0.58 mg a.i./l  
No observed effect concentration (NOEC) < 0.33 mg a.i./l

There were no mortalities or symptoms of intoxication in the control and the solvent control groups, respectively.

The solubility of the substance (2.3 mg a.i./l) is in the range of the nominal concentration tested in this experiment (0.33 - 5.77 mg a.i./l). Accordingly in all test concentrations part of the test substance rose to the water surface and sedimented to the bottom of the aquaria. Thus a representative sampling for analysis of the active ingredient was not

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possible, what in turn resulted in serious variations of the analytical values). The dosing system functioned properly and the consumption of stock solutions was in accordance with the theoretical value. Therefore the reported results are related to the nominal concentration of the a.i./l.

**Test substance** : Identification: DEF Technical  
Percent Active Ingredient: S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)  
Purity: 96.2%

**Reliability** : (2) valid with restrictions  
This is a guideline study which according to the methods was conducted at a water temperature of  $12 \pm 1^\circ\text{C}$ . The study results did not provide the actual temperatures recorded during to the study. According to OECD TG 203, the temperature range for this species should be 13 - 17 deg C.

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(10)

**Type** : static  
**Species** : Lepomis macrochirus (Fish, fresh water)  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**NOEC** : = .29  
**LC50** : = .72  
**LLC** : = .51  
**Limit test** :  
**Analytical monitoring** : yes  
**Method** : EPA OPP 72-1  
**Year** : 1990  
**GLP** : yes  
**Test substance** : other TS

**Method** : The acute toxicity of technical grade DEF (96.2 % active ingredient (a.i.)) to bluegill-sunfish (*Lepomis macrochirus*) was determined in a 96-hour flow through test according to "OECD Guideline for Testing of Chemicals No. 203" dated 04.04.1984 , "EEC DIRECTIVE 79/831, Annex V, Methods for the determination of Ecotoxicity, Method 5.1.1. Acute Toxicity for fish" (published in "Amtsblatt der Europäischen Gemeinschaften" dated 19.09.1984) and EPA Pesticide Assessment Guideline, Subdivision E §72-1.

Six groups of ten fishes, were exposed to concentrations of 0.16, 0.29, 0.51, 0.91, 1.63, and 2.89 mg a.i./l (corresponding to 0.17, 0.30, 0.53, 0.95, 1.69 and 3.00 mg test substance/l). One additional group of ten fish were similarly exposed to 0.1 ml Acetone p.a./l maintained as solvent control. All groups were observed for a 96 h exposure period. During the test, fish were examined daily for mortalities and symptoms of intoxication. Dissolved oxygen and pH values were determined daily in each aquarium, water temperature was measured and recorded hourly. Analytical determinations of the active ingredient concentrations were made in the stock solutions and test media at the beginning of the test. The LC50 values with 95%-confidence intervals were calculated by the moving average method.

**Result** : Mortality Data

Nominal Conc. (mg a.i./l)	Duration of Study				
	4 hr	24 hr	48 hr	72 hr	96 hr
control	0/0	0/0	0/0	0/0	0/0
Solvent control	0/0	0/0	0/0	0/0	0/0
0.16	0/0	0/0	0/0	0/0	0/0
0.29	0/0	0/0	0/0	0/0	0/0
0.51	0/0	0/0	0/0	0/10 SN	3/10 OB/TS/SN
0.91	0/0	0/0	0/0	2/10 SN	6/10 OB/SN
1.63	0/0	0/0	0/0	6/10 TS/OB	10/10

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OB = fish mainly at the surface  
TS = tumbling during swimming  
SN = swimming behavior slightly irregular (slight symptom)

There were no mortalities or symptoms of intoxication in the control and the solvent control groups, respectively.

96 hr LC50: 0.72 mg a.i./l; 95% confidence interval: 0.56 - 0.93 mg a.i./l  
72 hr LC50: 1.36 mg a.i./l; 95% confidence interval: 1.07 - 1.73  
Lowest lethal concentration (LLC): 0.51 mg a.i./l  
No observed effect concentration (NOEC): 0.29 mg a.i./l

The solubility of the substance (2.3 mg a.i./l) is in the range of the nominal concentration tested in this experiment (0.16 - 2.89 mg a.i./l). Accordingly in the higher test concentrations part of the test substance rose to the water surface and sedimented to the bottom of the aquaria. Thus a representative sampling for analysis of the active ingredient in these tanks was not possible.

The dosing system functioned properly and the consumption of stock solutions was in accordance with the theoretical value. Therefore the reported results are related to the nominal concentration of the a.i.

Hardness: 40 - 60 mg CaCO<sub>3</sub>/l  
Photo period: 16 hours light / 8 hours dark  
Water temperature: 21 +/- 1°C  
Dissolved oxygen: 9.2 -10.1 mg/l  
pH: 7.2 - 7.6

**Test substance** : Identification: Technical Grade DEF  
Percent Active Ingredient: 96.2 S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)

**Reliability** : (2) valid with restrictions  
This is a guideline study which according to the methods was conducted at a water temperature of 21 ± 1°C. The study results did not provide the actual temperatures recorded during to the study. According to OECD TG 203, the temperature range for this species should be 21 -25 deg C.

13.12.2007 (9)

**Type** : static  
**Species** : Cyprinodon variegatus (Fish, estuary, marine)  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**LC50** : > 100  
**NOEL** : = 100  
**Method** :  
**Year** : 1981  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : Static, unaerated, 21-22 deg C, 96 hr  
Sheepshead minnows: less than 7 days old  
Seawater: Natural, filtered from Big Lagoon (a Gulf of Mexico estuary), 17-18 parts per thousand salinity  
Test vessel: conducted in 3.8 l uncovered glass jars  
Solvent/carrier: none  
Range-finding test concentrations: 0, 0.1, 1.0, 10, 30, and 100 mg/l  
Nominal test conc. range: Based on a range-finding test, fish were tested at nominal concentrations of 0, 13, 22, 36, 60 and 100 mg/l; ten fish per jar  
Effect criterion: Mortality

**Result** : Mortality in range-finding test:  
20% mortality in 30 mg/l  
40% mortality in 100 mg/l

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Definitive test: After 96 hours of exposure to test material in the definitive test, fish were not affected in any test concentration. Mortality was 0% in all test concentrations. There is no known explanation for the difference between the range-finding and definitive tests.

Initial/Final pH: 8.1/7.5-7.8

Initial/final dissolved oxygen concentration: >= 97% / >=76%

96 hr LC50: > 100 ppm (mg/l)

95% confidence limits: not determined

NOEL: 100 mg/l

**Test substance** : Folex (72% Merphos) and 28% inert ingredients

**Reliability** : (3) invalid

The results of the definitive study are suspect due to the inconsistency when compared to the preliminary range-finding results.

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(18)

**Type** : flow through

**Species** : Lepomis macrochirus (Fish, fresh water)

**Exposure period** : 96 hour(s)

**Unit** : mg/l

**LC50** : = .61

**Method** :

**Year** : 1995

**GLP** : no data

**Test substance** : other TS

**Method** : Type of Water: FW - fresh water

Species Number: 2

Age/Life Stage: 2.3 G (grams)

Control data is presented but without accompanying methodology

Concentrations tested: not reported

**Test substance** : S,S,S-Tributylphosphorotrithioic acid

CAS RN 78-48-8

Purity: 72.3%

**Reliability** : (4) not assignable

Concentrations and number of animals exposed not reported. Original study not located; additional details not available.

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(67)

**Type** : static

**Species** : Carassius auratus (Fish, fresh water)

**Exposure period** : 96 hour(s)

**Unit** : mg/l

**LC50** : = 21

**Method** : other

**Year** : 1964

**GLP** : no

**Test substance** : as prescribed by 1.1 - 1.4

**Method** : Conducted in accordance with "Procedure for Evaluation of Acute Toxicity of Pesticides to Fish and Wildlife", USDI Fish and Wildlife Service Pesticides Review Staff, December 14, 1964.

Test vessel: 5 gallon wide-mouthed glass vessels

Test medium: reconstituted water which was aerated

Temperature: 75 deg F (+/- 2 deg F) (23.8 deg C)

Ratio of fish to medium did not exceed one-half gram of fish/1 liter water

Positive control: p,p'-DDT dissolved in acetone

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Fish were held for 10 days prior to bioassay. During the last 3 days prior to bioassay they were not fed. The fish were transferred into the bioassay vessels prior to the addition of the test or control chemicals; aeration was continued during this one-day pre-exposure. The positive and negative control tests were conducted concurrently with those of Folex using fish from the same lots. The aeration apparatus was removed from the bioassay vessel immediately prior to the addition of the test chemicals. Fifteen fish were used in the negative control group and groups of 10 fish were exposed to concentrations of Folex ranging from 1.54 to 25.1 ppm and of reference standard p,p'-DDT from 0.25 to 10.0 ppb. The duration of exposure was 96 hours. Reactions of the fish were recorded and the dead counted and removed at the end of 24, 48, 72 and 96 hours.

**Result**

: Survivors during study:

Conc. ppb	0	1	2	3	4
0	15	15	15	14	14
1,540	10	10	10	10	10
10,000	10	10	10	10	10
20,000	10	10	10	9	5
25,100	10	9	9	7	3

p,p'-DDT

0.25	10	10	10	10	10
1.59	10	10	10	10	10
3.98	10	10	10	10	9
6.31	10	10	10	9	7
10.0	10	10	10	10	5

LC50 for Folex to goldfish: 21,000 ppb (95% confidence limits = 13,600 - 32,300) = 21.0 ppm = 21.0 mg/l

LC50 for p,p'-DDT to bluegill sunfish; 10.0 ppb (estimated)

**Test substance**

: Folex (72% Merphos) and 28% inert ingredients

**Reliability**

: (3) invalid

13.12.2007

Not a fish species recommended for testing according to OECD TG 203.

(30)

**Type**

: static

**Species**

: *Ictalurus punctatus* (Fish, fresh water)

**Exposure period**

: 96 hour(s)

**Unit**

: mg/l

**LC50**

: = 3.2

**24 h LC50**

: > 10

**Method**

:

**Year**

: 1986

**GLP**

: no data

**Test substance**

: as prescribed by 1.1 - 1.4

**Method**

: pH mean: 7.5

Concentrations: Min 2.7 mg/L; Max 3.7 mg/L

Species lifestage: 0.22 g

Water Type: Fresh

Temperature: Mean 22 deg C

Hardness: Mean 38 mg/L CaCO<sub>3</sub>

**Test substance**

: Phosphorotrithious acid, Tributyl ester

CAS RN 150-50-5

purity: 96%

**Reliability**

: (3) invalid

Not a fish species recommended for testing according to OECD TG 203.

11.10.2007

(35)

**Type**

: static

**Species**

: *Ictalurus punctatus* (Fish, fresh water)

**Exposure period**

: 96 hour(s)

## 4. Ecotoxicity

Id 150-50-5

Date 10.01.2008

**Unit** : mg/l  
**LC50** : = 6.5  
**24 h LC50** : > 32  
**Method** :  
**Year** : 1986  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : pH mean: 7.1  
Concentrations: Min 5.9 mg/L; Max 7.1 mg/L  
Species lifestage: 1.1 g  
Water Type: Fresh  
Temperature: Mean 22 deg C  
Hardness: Mean 43 mg/L CaCO3

**Test substance** : Phosphorotrithious acid, Tributyl ester  
CAS RN 150-50-5  
purity: 96%

**Reliability** : (3) invalid  
Not a fish species recommended for testing according to OECD TG 203.  
11.10.2007 (35)

**Type** : static  
**Species** : Lepomis macrochirus (Fish, fresh water)  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**Method** :  
**Year** : 1986  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : Species lifestage: 0.7 g  
Water Type: Fresh  
Hardness: Mean 44 mg/L CaCO3  
pH mean: 7.3  
Temperature: varied (see results)

**Result** : Temperature: Mean 17 deg C  
Concentrations in 96 h study: Min 7 mg/L; Max 34 mg/L  
Concentrations in 24 h study: Min NA; Max 32 mg/L  
96 h LC50 = 15 mg/L  
24 h LC50 > 32 mg/L

Temperature: Mean 12 deg C  
Concentrations in 96 h study: Min NA; Max 32 mg/L  
Concentrations in 24 h study: Min NA; Max 32 mg/L  
96 h LC50 > 32 mg/L  
24 h LC50 > 32 mg/L

**Test substance** : Phosphorotrithious acid, Tributyl ester  
CAS RN 150-50-5  
purity: 96%

**Reliability** : (3) invalid  
According to the methods these studies were conducted at water temperatures of 12 or 17°C. OECD TG 203 indicates the water temperature range for this species should be 21 - 25 deg C.

06.12.2007 (35)

**Type** : static  
**Species** : Oncorhynchus mykiss (Fish, fresh water)  
**Exposure period** : 24 hour(s)  
**Unit** : mg/l  
**LC50** : = 1.74  
**Method** :  
**Year** : 1986

## 4. Ecotoxicity

Id 150-50-5

Date 10.01.2008

<b>GLP</b>	:	no data
<b>Test substance</b>	:	other TS
<b>Method</b>	:	Type of Water: FW - fresh water Species Number : 4 Age/Life Stage: 0.6 G (grams) Exposure Regimen: 24 hr Controls: NR - not reported Water Parameters: Temperature: 22 (mean value) deg C Hardness(mg/l CaCO3): 44 (mean value) mg/L CaCO3 pH: 7.2 (mean value)
<b>Test substance</b>	:	S,S,S-Tributylphosphorotrithioic acid CAS RN 78-48-8 Purity: 95%
<b>Reliability</b>	:	(3) invalid According to the methods these studies were conducted at water temperatures of 22°C. OECD TG 203 indicates the water temperature range for this species should be 13 - 17 deg C.
11.10.2007		(35)
<b>Type</b>	:	static
<b>Species</b>	:	Oncorhynchus mykiss (Fish, fresh water)
<b>Exposure period</b>	:	96 hour(s)
<b>Unit</b>	:	mg/l
<b>LC50</b>	:	= .66 - .83
<b>Method</b>	:	
<b>Year</b>	:	1986
<b>GLP</b>	:	no data
<b>Test substance</b>	:	other TS
<b>Method</b>	:	Type of Water: FW - fresh water Age/Life Stage: 0.6 G (grams) Exposure Regimen: 96 hr Controls: NR - not reported Water Parameters: Temperature: 13 (mean value) deg C Hardness(mg/l CaCO3): 44 (mean value) mg/L CaCO3 pH: 7.1 (mean value) 96 hr LC50 = 0.66 mg/L 24 hr LC50 = 2.7 mg/L
		Type of Water: FW - fresh water Age/Life Stage: 0.55 G (grams) Exposure Regimen: 96 hr Controls: NR - not reported Water Parameters: Temperature: 17 (mean value) deg C Hardness(mg/l CaCO3): 44 (mean value) mg/L CaCO3 pH: 6.8 (mean value) 96 hr LC50 = 0.83 mg/L 24 hr LC50 = 3.5 mg/L
<b>Test substance</b>	:	S,S,S-Tributylphosphorotrithioic acid CAS RN 78-48-8 Purity: 95%
<b>Reliability</b>	:	(4) not assignable Concentrations and number of animals exposed not reported. Original study not located; additional details not available.
13.12.2007		(35)
<b>Type</b>	:	static
<b>Species</b>	:	Oncorhynchus mykiss (Fish, fresh water)

## 4. Ecotoxicity

Id 150-50-5

Date

**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**LC50** : = 10  
**24 h LC50** : = 42.5  
**Method** :  
**Year** : 1986  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : pH mean: 6.8  
Concentrations: Min 7 mg/L; Max 14 mg/L  
Species lifestage: 0.6 g  
Water Type: Fresh  
Temperature: Mean 7 deg C  
Hardness: Mean 44 mg/L CaCO3

**Test substance** : Concentrations tested in 24 h study:  
Min 33.3 mg/L; Max 54.3 mg/L  
Phosphorotrithious acid, Tributyl ester  
CAS RN 150-50-5  
purity: 96%

**Reliability** : (3) invalid  
According to the methods this study was conducted at a water temperatures of 7°C. OECD TG 203 indicates the water temperature range for this species should be 13 - 17 deg C.

13.12.2007

(35)

**Type** : static  
**Species** : Salmo gairdneri (Fish, estuary, fresh water)  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**LC50** : = 33  
**Method** :  
**Year** : 1980  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : weight 0.6 g  
12 deg C  
Static bioassay without aeration  
pH 7.2-7.5  
water hardness 40-50 mg/l as calcium carbonate  
alkalinity of 30-35 mg/l  
**Result** : 96 hr LC50 = 33 mg/l (95% confidence limit 20-53 mg/l)

**Reliability** : (4) not assignable  
According to the methods this study was conducted at a water temperature of 12°C. OECD TG 203 indicates the water temperature range for this species should be 13 - 17 deg C.  
Concentrations tested and number of animals exposed not reported.  
Additional information not available.

13.12.2007

(66)

### 4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

**Type** : static  
**Species** : Daphnia magna (Crustacea)  
**Exposure period** : 48 hour(s)  
**Unit** : mg/l  
**NOEC** : = .01  
**EC50** : = .12



## 4. Ecotoxicity

Id 150-50-5  
Date 10.01.2008

**LOEC** : = .032  
**Analytical monitoring** : yes  
**Method** : OECD Guide-line 202  
**Year** : 1989  
**GLP** : yes  
**Test substance** : other TS

**Method** : Daphnia magna (first instars) were exposed to different concentrations of the test substance (0.01, 0.032, 0.056, 0.10, 0.32, 0.56 and 1.00), a test medium control, and a solvent control (0.1 ml acetone/l) under static conditions. These concentrations were chosen on the basis of preliminary range-finding studies (data not reported). All concentrations were tested in triplicate. 100 ml beakers were used as the test vessels. The study was conducted at 20 +/- 1 deg C and with a 16:8 light:dark cycle. The water fleas were not fed. After 24 and 48 hours, the inability to swim and/or immobility of the animals was determined. The nominal test concentrations in the test were between 0.01 and 1 mg a.i./l. Temperature, O2 content and pH values of the test water were determined.

At the beginning of the test, all concentrations tested were analysed after preparing the test solutions. The a.i. content was analysed with the test concentration of 0.1 mg a.i./litre after the exposure period of 48 hours.

The EC50 determination was by Probit-Analysis after the "Maximum-Likelihood" method using a calculator.

**Result** : Immobilisation Data

Conc. (mg a.i./l)	%Immobilised Daphnia after 24 hr	%Immobilised Daphnia after 48 hr
control	0	0
Acetone control	0	0
1.00	47	100
0.56	10	100
0.32	17	80
0.10	3	50
0.056	0	17
0.032	0	3
0.01	0	0

The measured concentrations during this test were 101.8 to 130.0% of the nominal concentrations (for an average 110.5%). A determination of a.i. content after the exposure period of 48 hours showed a modest degradation of 20.9% of the a.i.

Initial/Final pH: 7.98/7.97 - 7.99  
Initial/Final oxygen saturation: 92%/95 - 96%

The EC50 for Daphnia magna after 24 hours was about 1 mg a.i./l, and 0.12 mg a.i./l after 48 hours (95% confidence limits 0.10 - 0.15 mg a.i./l, nominal concentrations). The no-observed-effect-concentration (NOEC) (48 hours) was 0.010 mg a.i./l. The lowest-observed-effect-concentration (LOEC) was 0.032 mg a.i./l.

**Test substance** : Identification: Technical Grade DEF  
Percent Active Ingredient: 98.7 S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)

**Reliability** : (1) valid without restriction  
Guideline study

13.12.2007

(8)

**Type** : static  
**Species** : Daphnia magna (Crustacea)  
**Exposure period** : 48 hour(s)  
**Unit** : mg/l

## 4. Ecotoxicity

Id 150-50-5

Date

**EC50** : = .061  
**Method** :  
**Year** : 1995  
**GLP** : no data  
**Test substance** : other TS

**Method** : Type of Water: FW - fresh water  
Species Number : 5  
Age/Life Stage: <24 H (hours)  
Controls: K - control data is presented but without accompanying Methodology  
Concentrations tested: 50 ppb (minimum); 73 ppb(maximum)

**Test substance** : S,S,S-Tributylphosphorotrithioic acid  
CAS RN 78-48-8  
Purity: 72.3%

**Reliability** : (2) valid with restrictions  
Data obtained from AQUIRE, a peer-reviewed database. Original data were not examined.

13.12.2007

(67)

**Type** : static  
**Species** : Daphnia magna (Crustacea)  
**Exposure period** : 48 hour(s)  
**Unit** : mg/l  
**EC50** : = .0068  
**Method** :  
**Year** : 1986  
**GLP** : no data  
**Test substance** : other TS

**Method** : Type of Water: FW - fresh water  
Latin Name: Daphnia magna  
Common Name: Water flea  
Taxonomic Group: animal kingdom  
Species Number: 5  
Age/Life Stage: 1ST INSTAR  
Exposure Regimen: 48 h  
Water Parameters:  
Temperature: 15 (mean value) deg C  
Hardness(mg/l CaCO3): 272 (mean value) mg/L CaCO3  
pH: 7.4 (mean value)

**Test substance** : S,S,S-Tributylphosphorotrithioic acid  
CAS RN 78-48-8  
Purity: 95%

**Reliability** : (4) not assignable  
Concentrations and number of animals exposed not reported. Original study not located; additional details not available.

13.12.2007

(35)

### 4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

**Species** : other aquatic plant: Duckweed (Lemna gibba G3)  
**Endpoint** : other: standing crop, growth rate and cumulative biomass  
**Exposure period** : 14 day(s)  
**Unit** : µg/l  
**NOEC** : < 17.2  
**LOEC** : = 17.2  
**EC50** : = 866  
**EC25** : = 342  
**Limit test** :

## 4. Ecotoxicity

Id 150-50-5

Date 10.01.2008

**Analytical monitoring** : yes  
**Method** : EPA OPP 122-2  
**Year** : 2002  
**GLP** : yes  
**Test substance** : other TS

**Method** : A static renewal 14-day duckweed growth test was conducted to determine the growth effects of Tribufos technical to Lemna gibba G3. The primary objective of this growth study was to estimate the fifty percent effective concentration (EC50) for Tribufos technical. An effect is one that is a statistically significant ( $p < 0.05$ ) reduction from the control for the parameter being measured. The parameters measured in this study were standing crop, growth rate and cumulative biomass (as area under the growth curve). The variable used to calculate these response parameters was frond number as determined by direct frond counts. Frond dry weight was also measured at test termination.

All test solutions, including the negative and solvent controls, were prepared as uniform batches. Each replicate was inoculated with three Lemna plants for a total of 12 or 13 fronds at study initiation. Three replicate vessels were prepared for each concentration. The number of fronds in each test vessel were manually counted on Days 0, 2, 5, 7, 9, 12 and 14. At the same time phytotoxicity observations were performed to determine the health of the plants in each test vessel. On Day 14, after the frond count was completed, the plants from each replicate were transferred to a labeled, tared weigh pan. The plants from each replicate were dried at approximately 60 °C for at least 24 hours, transferred to a dessicator to cool to ambient temperature, and then weighed to determine the dry weight ( $\pm 0.1$  mg).

Duckweed Lemna gibba G3 was exposed for 14 days under static renewal conditions. Test solutions were renewed on Day 7. Nominal concentrations (mean measured of Day 0 and Day 7 new solutions) were control (<4.94), solvent control (<4.94), 20.5 (17.2), 51.2 (49.5), 128 (119), 320 (228), 800 (611), 2000 (1555) ug a.i./L. Growth was determined by count of fronds on days 0, 2, 5, 7, 9, 12 and 14.

**Result** : 14-day EC50 - standing crop: 866 ug a.i./L  
14-day EC50 - growth rate: >1555 ug a.i./L  
14-day EC50 - cumulative biomass: 1176 ug a.i./L  
14-day EC50 - frond dry weight: 1249 ug a.i./L  
Lowest Concentration With an Effect (LOEC): 17.2 ug a.i./L  
Highest Concentration Without Toxic Effect (NOEC): <17.2 ug a.i./L

Observations noted in all test concentrations included a few fronds with brown and yellow coloration as well as their having a darkened root system. The low number of these observations were similar to that of the number noted in the solvent control vessels. Observations at the highest test concentration (1555 ug a.i./L) included several plants with thin curled roots systems.

The EC25 and EC50 in the 14-day exposure of Lemna gibba G3 to Tribufos technical were 342 and 866 ug a.i./L, respectively.

**Test substance** : Tribufos technical, purity: 99.4% a.L  
**Reliability** : (1) valid without restriction  
Guideline study

15.10.2007

(14)

**Species** : Skeletonema costatum (Algae)  
**Endpoint** : other: growth  
**Exposure period** : 96 hour(s)  
**Unit** : mg/l  
**EC50** : = .366

## 4. Ecotoxicity

Id 150-50-5

Date 10.01.2008

**Method** :  
**Year** : 1980  
**GLP** : no data  
**Test substance** : other TS

**Method** : Route/Method: S - static  
Type of Water: SW - salt water  
Species Identification:  
Latin Name: Skeletonema costatum  
Common Name: Diatom  
Taxonomic Group: plant kingdom  
Age/Life Stage: EXPONENTIAL GROWTH PHASE  
Exposure Regimen: 96 h  
Controls: S - satisfactory control  
Water Parameters:

**Test substance** : S,S,S-Tributylphosphorotrithioic acid (Technical grade)  
CAS RN 78-48-8  
Purity: not reported

**Reliability** : (4) not assignable  
Data obtained from AQUIRE, a peer-reviewed database. Original data were not examined. Concentrations not reported

13.12.2007

(69)

**Species** : Selenastrum capricornutum (Algae)  
**Endpoint** : other: standing crop values  
**Exposure period** : 7 day(s)  
**Unit** : mg/l  
**NOEC** : = .0585  
**EC50** : = .179  
**EC25** : = .144  
**Method** : EPA OPP 123-3  
**Year** : 1990  
**GLP** : yes  
**Test substance** : other TS

**Method** : Also conducted in accordance with U.S.-EPA-FIFRA, 40 CFR, Section 158.145

The objectives of this test were to determine the 7-day EC25, EC50 and NOEC values of DBF Technical for the freshwater green alga, Selenastrum capricornutum. The algal assay bottle test is the most commonly used tool for assessing the effect of a test material on the growth of a selected species of algae. Algal growth is expressed in terms of the standing crop attained after a specified period of exposure to the test material. Standing crop values are used to calculate the percent inhibition or stimulation, relative to the control (or solvent control), for each test concentration. The effective concentrations (EC) causing 25 and 50 percent inhibition of growth are designated the EC25 and EC50, respectively. The highest concentration tested in which standing crop is not significantly different from that in the control (or solvent control) is designated the no observed effect concentration (NOEC).

Selenastrum capricornutum was exposed over a 7-day period to six concentrations (nominal: 0.0312, 0.0625, 0.125, 0.25, 0.5 and 1.0 mg/L) of DBF Technical, 99.9% active ingredient (a.i.). The material was tested using N,N-dimethylformamide as a solvent (0.5 mL/L DMF). Biomass was determined by cell counts on days 2, 3, 4, and 7.

Test temperature: 24 +/- 2 deg C  
Test medium: Synthetic AAP medium  
Photoperiod: Continuous light

## 4. Ecotoxicity

Id 150-50-5

Date 10.01.2008

**Result** : Test concentrations were measured and determined to be 0.0280, 0.0585, 0.118, 0.254, 0.504, and 1.043 mg/L for nominal concentrations of 0.0312, 0.0625, 0.125, 0.25, 0.5, and 1.0 mg/L, respectively. Results are based upon measured concentrations, which ranged from 0.0280 to 1.043 mg/L.

Initial pH values: 7.23 - 7.39

Final pH values: 7..43 - 7.89

Percent inhibition, relative to solvent control, based upon mean standing crop, cells/ml, on day 7

Measured Conc. (mg/l)	Percent Inhibition
Solvent	--
Control	11.6
0.0280	6.2
0.0585	11.7
0.118	9.7
0.254	87.3*
0.504	99.9*
1.043	99.9*

\*Significantly different from control

Percent inhibition, relative to the solvent control, was calculated for each concentration based upon the mean standing crop in cells/mL at seven days. Effects ranged from 6.2% to 99.9% inhibition. The EC25 and EC50 values were determined by weighted least squares nonlinear regression of the log of concentration against cell counts. The 7-day EC25 is 0.144 mg/L (95% confidence limits 0.008 - 2.680 mg/L) and the 7-day EC50 is 0.179 mg/L (95% confidence limits 0.025 - 1.303 mg/L). The no observed effect concentration (NOEC), based upon the mean standing crop values on day 7, was determined by an analysis of variance and Dunnett's test to be 0.0585 mg/L.

**Test substance** : Identification: Technical Grade DEF  
Percent Active Ingredient: 99.9% S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)

**Reliability** : (1) valid without restriction  
Guideline study

13.09.2007

(53)

### 4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

#### 4.5.1 CHRONIC TOXICITY TO FISH

#### 4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

#### 4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

#### 4.6.2 TOXICITY TO TERRESTRIAL PLANTS

#### 4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

## 4. Ecotoxicity

**Id** 150-50-5  
**Date** 10.01.2008

### 4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

### 4.7 BIOLOGICAL EFFECTS MONITORING

### 4.8 BIOTRANSFORMATION AND KINETICS

### 4.9 ADDITIONAL REMARKS

## 5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

## 5.1.1 ACUTE ORAL TOXICITY

**Type** : LD50  
**Value** : = 910 - 1475 mg/kg bw  
**Species** : rat  
**Strain** : Sherman  
**Sex** : male/female  
**Number of animals** : 100  
**Vehicle** : peanut oil  
**Doses** :  
**Method** : other  
**Year** : 1969  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : Exact dosage levels were not provided. The test article was formulated so that the different dosage levels could be given by stomach tube by giving the formulation at a constant rate of 0.005 ml/g of body weight. The rats were adults and they were individually caged.

**Result** : The LD50 values were calculated by the method of Litchfield and Wilcoxon, 1949, with 19/20 confidence limits. Survival times were recorded. LD1 values were also calculated because it is probably a more realistic measure of the toxic hazard of a compound than is the LD50 value, and with the LD50 value, it indicates the slope of the dose-response line.

**Result** : Survival time (males):  
 Minimum = 44 hr  
 Maximum = 8 days

Survival time (females):  
 Minimum = 43 hr  
 Maximum = 6 days

**Test substance** : LD50 (males) = 1475 mg/kg; 19/20 confidence limits = 1229 - 1770 mg/kg  
 LD50 (females) = 910 mg/kg; 19/20 confidence limits = 664 - 1247 mg/kg  
 LD1 (males) = 610 mg/kg  
 LD1 (females) = 215 mg/kg  
 Lowest dose to kill a rat (males) = 800 mg/kg  
 Lowest dose to kill a rat (females) = 400 mg/kg  
**Reliability** : Technical grade  
 (2) valid with restrictions  
 Comparable to guideline study, but not GLP

06.12.2007

(20) (22)

**Type** : LD50  
**Value** : = 2480 mg/kg bw  
**Species** : rat  
**Strain** : other: Charles River  
**Sex** : male/female  
**Number of animals** : 16  
**Vehicle** : other: none  
**Doses** : 900, 1350, 2025, 3038 mg/kg  
**Method** :  
**Year** : 1973  
**GLP** : no

## 5. Toxicity

Id 150-50-5

Date

**Test substance** : as prescribed by 1.1 - 1.4

**Method** : The test article was administered undiluted by gavage to groups of fasted rats (2 sex/dose level) at dose levels of 900, 1350, 2025 and 3038 mg/kg. Animals were observed for mortality and signs of toxicity over 14 days. Body weights were determined at study initiation and termination. A necropsy was conducted on any animal which died during the study and on all animals at study termination. The oral LD50 was calculated using the techniques of Weil, Thompson and Thompson and Weill.

**Result** : Mortality and Body Weight Data

Dose (mg/kg)	Sex	Initial Body Weight (grams)	Final Body Weight (grams)	Dead/Dosed	% Dead
900	M	159	268	0/4	0
	M	153	266		
	F	188	230		
	F	193	236		
1350	M	200	299	0/4	0
	M	203	301		
	F	187	232		
	F	188	236		
2025	M	209	297	0/4	0
	M	214	306		
	F	184	230		
	F	190	234		
3038	M	150	(2 days)	4/4	100
	M	158	(4 days)		
	F	189	(2 days)		
	F	183	(4 days)		

Acute oral LD50 = 2480 mg/kg  
Standard deviation of LD50 = +/- 134.5 mg/kg

Signs of toxicity included hypoactivity and ruffled fur at all dose levels; muscular weakness and tremors at the 3 highest doses; convulsions and vocalization at 3038 mg/kg. Necropsy examination of the animals that died revealed enteritis. No gross pathologic alterations were noted among the animals that survived until study termination.

**Test substance** : Test article 651 identified as:  
Merphos technical: 98.5% a.i. %w/%w  
(tributyl phosphorotrithioite - 96)  
(tributyl phosphorotrithioate - 2.5)  
Acetic anhydride: 0.5%

**Reliability** : (2) valid with restrictions

06.12.2007 (31)

**Type** : LD50  
**Value** : = 234 - 435 mg/kg bw  
**Species** : rat  
**Strain** : Sprague-Dawley  
**Sex** : male/female  
**Number of animals** : 30  
**Vehicle** : other: corn oil  
**Doses** : nominal 200, 245, 300, 450 and 552 mg/kg; analytically determined: 294, 429 and 552 mg/kg for males; 192, 235 and 294 mg/kg for females  
**Method** : OECD Guide-line 401 "Acute Oral Toxicity"  
**Year** : 1991  
**GLP** : yes  
**Test substance** : other TS



**Method** : This study was conducted in accordance with:

- 1) US-EPA-FIFRA, Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, Guideline 81-1, November 1984.
- 2) US-EPA-TSCA, Health Effects Testing Guidelines, 40 CFR Section 798.1175, July 1988.
- 3) OECD Guidelines for Testing of Chemicals, Section 4, Guideline 401, February 1987.
- 4) Japan, Ministry of Agriculture, Forestry and Fisheries, Guidance on Toxicology Study Data for Application of Agricultural Chemical Registration, 59 NohSan No. 4200, January 1985.

The acute oral toxicity of technical grade tribufos was tested in young adult fasted male and female (five/sex/dose) Sprague-Dawley rats. The test substance was administered by gavage in corn oil (5 ml/kg) at analytically-confirmed doses of 294, 429 and 552 mg/kg for males and 192, 235 and 294 mg/kg for females. Animals were observed for 14 days after dosing for mortality and clinical signs. Body weights were recorded just prior to treatment (day 0) and on days 7 and 14. At the end of the study the surviving animals were sacrificed and a gross necropsy was performed. Dosing solutions were analyzed for tribufos by gas chromatographic analysis. LD50 values, 95% confidence intervals and the slope of the dose mortality curves were calculated using a modified probit analysis computer program from Stephen.

**Result** : Mortality Data

Dose (mg/kg)	Sex	Dead/Dosed	Days to Death
294	M	0/5	--
429	M	3/5	1-2
552	M	4/5	1-5
192	F	0/5	NA
235	F	4/5	1-2
294	F	4/5	1-2

The incidence of mortality increased with dose for both males and females, with all deaths occurring within days 1 through 5. A variety of signs of toxicity (decreased activity, lacrimation (clear and red), lacrimal stain (clear and red), clear nasal discharge and stain, red nasal stain, salivation, oral stain, diarrhea, perianal stain, urine stain, decreased reactivity, tremor and convulsions) were evident within the first two days following exposure with recovery in surviving animals by day 6. Body weight gain was decreased only in the one male that survived the high dose. Evidence of salivation, lacrimation and ventral staining, as well as fluid and dark discolored zones in the stomach and duodenum, nasal stain and pale liver were considered treatment-related gross lesions in animals found dead. There were no gross lesions observed in animals that survived to day 14.

The acute oral LD50 for males, with 95% confidence intervals, was 435 mg/kg (302-581 mg/kg), with a slope in the dose-mortality curve of 10.6. For females the acute oral LD50, with 95% confidence intervals, was 234 mg/kg (183-296 mg/kg), with a slope of 13.4. The no-observed effect level for tribufos was <294 mg/kg for males and <192 mg/kg for females.

**Test substance** : Identification: Technical Grade DEF  
Percent Active Ingredient: 98.1 S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)

**Reliability** : (1) valid without restriction  
Guideline study

05.12.2007

(55)

**Type** : LD50

## 5. Toxicity

Id 150-50-5

Date 10.01.2008

**Value** : = 1710 - 2050 mg/kg bw  
**Species** : rat  
**Strain** : Sprague-Dawley  
**Sex** : male/female  
**Number of animals** : 90  
**Vehicle** : water  
**Doses** : 1000, 1500, 2000, 2500, 3000, and 3300 mg/kg  
**Method** :  
**Year** : 1980  
**GLP** : yes  
**Test substance** : other TS

**Method** : The study was conducted in two phases. The first phase involved five dose groups for both males and females (six rats/dose). The second phase was necessary to obtain more refined acute toxicity data to define the LD50 and involved three dose groups for the females and two dose groups for the males (six rats/dose). The test article was administered diluted in distilled water by gavage in the first phase at dose levels of 1000, 1500, 2000, 2500, and 3000 mg/kg to fasted rats, and in phase two at dose levels of 2500, 3000, and 3300 mg/kg to fasted females and dose levels of 1000 and 2000 mg/kg to fasted male rats. Animals were observed for mortality and signs of toxicity continuously for the first hour after dosing, hourly for the next 48 hours, and twice daily thereafter for 14 days. Body weights were determined at study initiation and termination. A necropsy was conducted on any animal which died during the study and on all animals at study termination. The oral LD50 was calculated using probit analyses.

**Result** : Mortality Data

Dose	Dead/Dosed	Days to Death
FEMALES		
1000 mg/kg	0/6	> 14
1500 mg/kg	1/6	> 14
2000 mg/kg	3/6	> 14
2500 mg/kg	9/12	4
3000 mg/kg	10/12	3
3300 mg/kg	6/6	35 hours
MALES		
1000 mg/kg	0/6	> 14
1500 mg/kg	3/6	> 14
2000 mg/kg	7/12	6
2500 mg/kg	5/6	6
3000 mg/kg	6/6	35 hours
3300 mg/kg	6/6	39 hours

Acute oral LD50 (females) = 2052 mg/kg (95% CL 1630 - 2360)  
Acute oral LD50 (males) = 1710 mg/kg (95% CL 1350 - 1970)  
Acute oral LD50 (combined) = 1870 mg/kg (95% CL 1610 - 2070)

Typical signs of toxicity included hunched posture, prostration, ruffled fur, sedation, muscle relaxation and depressed respiration. The pain threshold was alternately depressed and increased, sometimes in the same animal at different times during the study. Also noted were relative hypothermia, lacrimation, occasional blood from the eyes or nose, watery excessive salivation, diarrhea, and urine present on the coat.

Necropsy revealed a variety of abnormalities in the test animals, including blood tears in the eyes and /or blood or exudate from the nose; atrophy of several organs, including liver, thymus, and spleen; enlargement of the adrenals; hemorrhaging or hyperemia of the brain; thin yellow fluid present in the duodenum, jejunum and colon; and greenish-yellow fluid in the stomach.

## 5. Toxicity

Id 150-50-5

Date 10.01.2008

**Test substance** : Folex (72% Merphos) and 28% inert ingredients  
**Reliability** : (1) valid without restriction  
Comparable to a guideline study; conducted according to GLP  
06.12.2007 (36)

**Type** : LD50  
**Value** : = 150 - 233 mg/kg bw  
**Species** : rat  
**Strain** : Sherman  
**Sex** : male/female  
**Number of animals** : 100  
**Vehicle** : peanut oil  
**Doses** :  
**Method** : other  
**Year** : 1969  
**GLP** : no  
**Test substance** : other TS

**Method** : Exact dosage levels were not provided. The test article was formulated so that the different dosage levels could be given by stomach tube by giving the formulation at a constant rate of 0.005 ml/g of body weight. The rats were adults and they were individually caged.

The LD50 values were calculated by the method of Litchfield and Wilcoxon, 1949, with 19/20 confidence limits. Survival times were recorded. LD1 values were also calculated because it is probably a more realistic measure of the toxic hazard of a compound than is the LD50 value, and with the LD50 value, it indicates the slope of the dose-response line.

**Result** : Survival time (males):  
Minimum = 9 hr  
Maximum = days

Survival time (females):  
Minimum = 24 hr  
Maximum = 3 days

LD50 (males) = 233 mg/kg; 19/20 confidence limits = 206 - 263 mg/kg  
LD50 (females) = 150 mg/kg; 19/20 confidence limits = 125 - 180 mg/kg  
LD1 (males) = 117 mg/kg  
LD1 (females) = 66 mg/kg  
Lowest dose to kill a rat (males) = 175 mg/kg  
Lowest dose to kill a rat (females) = 100 mg/kg

**Test substance** : DEF Technical grade  
**Reliability** : (2) valid with restrictions  
Comparable to guideline study, but not GLP  
05.12.2007 (20)

**Type** : LD50  
**Value** : = 1300 mg/kg bw  
**Species** : rat  
**Strain** : no data  
**Sex** : no data  
**Number of animals** :  
**Vehicle** :  
**Doses** :  
**Method** :  
**Year** : 1984  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (4) not assignable  
Original study not reviewed

## 5. Toxicity

Id 150-50-5

Date

05.12.2007

(21)

**Type** : LD50  
**Value** : = 130  
**Species** : rat  
**Strain** : no data  
**Sex** : no data  
**Number of animals** :  
**Vehicle** :  
**Doses** :  
**Method** :  
**Year** : 1969  
**GLP** : no data  
**Test substance** : other TS

**Reliability** : (4) not assignable  
Original study not reviewed

05.12.2007

(1)

### 5.1.2 ACUTE INHALATION TOXICITY

**Type** : LC50  
**Value** : = 2460 - 4650 mg/m<sup>3</sup>  
**Species** : rat  
**Strain** : Sprague-Dawley  
**Sex** : male/female  
**Number of animals** : 54  
**Vehicle** :  
**Doses** : Average analytical concentrations of 1590, 2920, 3190, 5690, and 6030 mg/m<sup>3</sup>  
**Exposure time** : 4 hour(s)  
**Method** : OECD Guide-line 403 "Acute Inhalation Toxicity"  
**Year** : 1990  
**GLP** : yes  
**Test substance** : other TS

**Method** : The study was conducted in accordance with the following test guidelines:  
1) US-EPA-FTFRA, Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, Guideline 81-3, November 1984.  
2) US-EPA-TSCA, Health Effects Testing Guidelines, 40 CFR Section 798.1150, July 1988.  
3) OECD Guidelines for Testing of Chemicals, Section 4, Guideline 403, May 1981.  
4) Japan, Ministry of Agriculture, Forestry and Fisheries, Guidance on Toxicology Study Data for Application of Agricultural Chemical Registration, 59 NohSan No. 4200, January 1985.

The acute toxicity of technical grade DEF, tested as a liquid aerosol, was evaluated in Sprague-Dawley rats. Groups of six male and six female rats were exposed for four hours under nose-only exposure conditions to analytically-confirmed concentrations ranging from 1590 to 6030 mg/m<sup>3</sup>. Comparable groups of rats were sham-exposed to conditioned room air and served as controls. Animals were observed twice daily for signs of toxicity, including mortality, for 14 days. Body weights were recorded just prior to exposure and on days 3, 7, and 14 post-exposure. At study termination all animals were subject to complete gross necropsy.

Nominal concentrations were determined by dividing the weight loss of the

Result

test substance (determined by measuring the volume of solution nebulized and correcting for the concentration of test substance in this solution) by the volume of the air flowing through the chamber for the period during which the test substance was generated. Analytical concentrations of generated atmospheres were assessed by taking samples near the rats' breathing zone within the chamber. Samples were collected hourly (at a minimum) during exposure. The distribution of particle size within the exposure chamber was also determined.

: Mortality Data

Dose (mg/m3)	Sex	Dead/Dosed	Days to Death
0	M	0/6	NA
2920	M	1/6	2
5690	M	4/6	2
6030	M	5/6	2,3
0 (1)	F	0/6	NA
0 (2)	F	0/6	NA
1590	F	1/6	2
2920	F	3/6	2,3,4
3190	F	6/6	1,2,3

Exposure-related signs included: abnormal body position, adipsia, anorexia, apparent paralysis, ataxia, bloody urine, dyspnea, excitability, hypoactivity, increased vocalization, lacrimation, muscle fasciculations, nasal discharge, rales, red and yellow eye discharge, red nasal discharge, red oral discharge, red vaginal discharge, tremors, and urine staining. These signs were first observed shortly after exposure (day 0) and a complete recovery by day 6 was observed.

A substantial reduction in weight gain, as compared to controls, was observed from all exposed groups through day 14.

Exposure-related gross lesions from animals that died during the 14-day observation period included: evidence of salivation and lacrimation, ventral staining, nasal stain, reddened lungs, mottled thymus and reddened nasal turbinates.

Mortalities were apparently concentration dependent for each sex. LC50 values were estimated to be (95% confidence limits):  
Males: 4650 (1410 - 6180)  
Females: 2460

Test substance

: A no-observed-effect level (NOEL) was not determined in this study.  
Identification: Technical Grade DEF  
Percent Active Ingredient: 98.8 S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)

Reliability

: (1) valid without restriction  
Guideline study

06.12.2007

(51)

5.1.3 ACUTE DERMAL TOXICITY

- Type : LD50
- Value : = 450 mg/kg bw
- Species : rabbit
- Strain : New Zealand white
- Sex : male/female

## 5. Toxicity

Id 150-50-5

Date

**Number of animals** : 16  
**Vehicle** : other: none  
**Doses** : 400, 500, 600, 900 and 1350 mg/kg  
**Method** :  
**Year** : 1973  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : The test article was administered undiluted to the clipped, intact skin of five groups of rabbits (2 sex/dose level) at dose levels of 400, 500, 600, 900 and 1350 mg/kg under an occlusive cover. After a contact period of 24 hours the occlusive cover was removed and the residual test material was removed. The test site was examined for local skin reactions. Animals were observed for mortality and signs of toxicity over 14 days. Body weights were determined at study initiation and termination. A necropsy was conducted on any animal which died during the study and on all animals at study termination. The dermal LD50 was calculated using the techniques of Weil, Thompson and Thompson and Weill.

**Result** : Mortality and Body Weight Data

Dose (mg/kg)	Sex	Body Weight (kg)		Dead/Dosed	% Dead
		Initial	Final		
400	M	3.12	2.66	0/4	0
	M	2.50	2.32		
	F	2.86	2.30		
	F	2.40	2.34		
500	M	2.20	(5 d)	4/4	100
	M	2.34	(4 d)		
	F	2.38	(6-22hr)		
	F	2.64	(8 d)		
600	M	3.30	(3 d)	4/4	100
	M	2.78	(3 d)		
	F	3.14	(2 d)		
	F	2.66	(4 d)		
900	M	3.12	(3 d)	4/4	100
	M	2.74	(2 d)		
	F	2.30	(4 d)		
	F	2.50	(3 d)		
1350	M	2.64	(3 d)	4/4	100
	M	2.52	(6-22hr)		
	F	2.42	(6-22hr)		
	F	2.70	(7 d)		

Acute dermal LD50 = 450 mg/kg

The following skin reactions were noted at each dose level:

400 mg/kg:

24 hr: Red, well-defined erythema; Moderate edema (area well-defined and raised approximately 1 mm); Chemical burns

7 days: Chemical burns; Desquamation

14 days: Desquamation

500 mg/kg:

24 hr: Red, well-defined erythema; Moderate edema (area well-defined and raised approximately 1 mm); Chemical burns

7 days: Chemical burns; Desquamation

14 days: --

## 5. Toxicity

Id 150-50-5

Date 10.01.2008

600 mg/kg:

24 hr: Red, well-defined erythema; Moderate edema (area well-defined and raised approximately 1 mm); Chemical burns

7 days: --

14 days: --

900 mg/kg:

24 hr: Red, well-defined erythema; Moderate edema (area well-defined and raised approximately 1 mm); Chemical burns

7 days: --

14 days: --

1350 mg/kg:

24 hr: Red, well-defined erythema; Moderate edema (area well-defined and raised approximately 1 mm); Chemical burns

7 days: Chemical burns; Desquamation

14 days: --

No untoward behavioral reactions were noted among the rabbits dosed at 400 mg/kg. Hypoactivity, muscular weakness, and salivation were exhibited by animals exposed at dose levels of 500, 600, 900 and 1350 mg/kg. Onset of the reactions was noted 24 hours after dosing. The reactions persisted until the animals died.

Necropsy examination of the animals that died revealed pale brown discoloration of the lungs. No gross pathologic alterations were noted among the animals that survived to study termination.

**Test substance**

: Test article 651 identified as:  
Merphos technical: 98.5% a.i. %w/%w  
(tributyl phosphorotrithioite - 96)  
(tributyl phosphorotrithioate - 2.5)  
Acetic anhydride: 0.5%

**Reliability**

: (2) valid with restrictions  
Similar to current guidelines.

06.12.2007

(31)

**Type**

: LD50

**Value**

: = 740 - 1030 mg/kg bw

**Species**

: rabbit

**Strain**

: New Zealand white

**Sex**

: male/female

**Number of animals**

: 217

**Vehicle**

: other: none

**Doses**

: 750, 1000, 1500, 1640, 2000, 2020, 2500, 3200, 4000 mg/kg

**Method**

:

**Year**

: 1980

**GLP**

: yes

**Test substance**

: as prescribed by 1.1 - 1.4

**Method**

: The study was conducted in two phases. The first phase involved four dose groups for the females (750, 1640, 2020 and 2500 mg/kg), with six female control animals, and four dose groups for the males (2000, 2500, 3200, and 4000 mg/kg) with seven male control animals. The second phase was necessary to obtain more refined acute toxicity data to define the LD50 and included four dose groups (750, 1000, 1500, and 2500 mg/kg) for both males and females (12/sex/dose; 6 intact/dose and 6 abraded/dose) and control groups of six rabbits for both sexes. The test article was applied undiluted to the clipped, intact and abraded sites on the back/trunk of each rabbit under an occlusive cover for 24 hours. After 24 hours, the cover was removed and any residual material was removed by wiping the area with water. Animals were observed for mortality and signs of toxicity hourly for 48 hours and twice daily thereafter for 14 days. Body

**Result**

weights were determined at study initiation and termination. A necropsy was conducted on any animal which died during the study and on all animals at study termination. In addition, a skin sample was taken from the animals in the second phase and evaluated histopathologically. The dermal LD50 was calculated using probit analyses.

## : Phase 1: Mortality Data

Dose	Dead/Dosed	Days to Death
FEMALES		
0 mg/kg	0/6	--
750 mg/kg	0/12	--
1640 mg/kg	11/12	4
2020 mg/kg	12/12	3
2500 mg/kg	12/12	3

## MALES

0 mg/kg	0/7	--
2000 mg/kg	11/12	4
2500 mg/kg	11/12	39 hours
3200 mg/kg	12/12	44 hours
4000 mg/kg	12/12	35 hours

## Phase 2: Mortality Data

Dose	Dead/Dosed	Days to Death
FEMALES		
0 mg/kg	0/6	--
750 mg/kg	4/12	> 14 days*
1000 mg/kg	2/12	> 14 days*
1500 mg/kg	10/12	3
2500 mg/kg	12/12	3

## MALES

0 mg/kg	0/6	--
750 mg/kg	4/12	> 14 days*
1000 mg/kg	6/12	> 14 days*
1500 mg/kg	11/12	3 days
2500 mg/kg	12/12	2 days

## Intact Skin:

Acute dermal LD50 (females) = 1030 mg/kg (95% CL 850 - 1240)  
 Acute dermal LD50 (males) = 740 mg/kg (95% CL 200 - 1050)  
 Acute dermal LD50 (combined) = 950 mg/kg (95% CL 770 - 1100)

## Abraded Skin:

Acute dermal LD50 (females) = 1180 mg/kg (95% CL 990 - 1400)  
 Acute dermal LD50 (males) = 1110 mg/kg (95% CL 790 - 1390)  
 Acute dermal LD50 (combined) = 1160 mg/kg (95% CL 1000 - 1320)

Typical signs of toxicity included salivation and erythema. At higher doses typical signs included hunched posture, prostration, excitability, malaise, sedation, muscle tremors, loss of or slow righting reflex, respiratory problems (stimulated or depressed, rales) skin irritation, (erythema, edema and eschar), analgesia, changes in relative body temperature (hypothermia and hyperthermia), nasal exudate, watery salivation and diarrhea.

Necropsy revealed a variety of abnormalities in the test animals, including excess saliva in the oral cavity, erythema (sometimes edema and eschar), perianal staining, vascularization of the brain and full bladders. Noted less often were several instances of fulminating pneumonia, icteric livers, enlarged gall bladders, and nasal exudate.



Skin samples taken from animals in phase 2 showed some degree of histopathologic change in all male and female rabbits. A pattern of increasing amounts of histopathology with increasing dose levels except for the highest dose (2500 mg/kg). At this level, both males and females had total histopathologic score averages slightly less than the next highest dose (1500 mg/kg). The explanation for this finding may be that the reduced survival times in the rabbits treated with the 2500 mg/kg dose did not allow time for the maximal histopathologic changes to take place. There appears to be a possible sexual dimorphism at the 750 mg/kg and 1000 mg/kg doses. Lower total skin histopathologic score averages were seen in the females compared to males. This may indicate a resistance in the females at these doses in comparison to males. At the 1500 and 2500 mg/kg levels this difference in pathologic changes disappears since the total histopathologic score averages for both sexes are very similar. Out of the 10 histopathologic changes evaluated in the experimental animals three changes were most prevalent, and in descending order these were:

1. Surface debris
2. Changes from normal in the dermal collagen
3. Dermal inflammation

**Test substance** : Folex (72% Merphos) and 28% inert ingredients  
**Reliability** : (2) valid with restrictions  
 Comparable to a guideline study; conducted according to GLP  
 13.12.2007 (36)

**Type** : LD50  
**Value** : = 1093 mg/kg bw  
**Species** : rabbit  
**Strain** : New Zealand white  
**Sex** : male/female  
**Number of animals** : 30  
**Vehicle** :  
**Doses** : 500, 1000 and 2000 mg/kg  
**Method** : OECD Guide-line 402 "Acute dermal Toxicity"  
**Year** : 1991  
**GLP** : yes  
**Test substance** : other TS

**Method** : This study was conducted in accordance with:  
 1) US-EPA-FIFRA, Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, Guideline 81-2, November 1984.  
 2) US-EPA-TSCA, Health Effects Testing Guidelines, 40 CFR Section 798.1100, July 1988.  
 3) OECD Guidelines for Testing of Chemicals, Section 4, Guideline 402, February 1987.  
 4) Japan, Ministry of Agriculture, Forestry and Fisheries, Guidance on Toxicology Study Data for Application of Agricultural Chemical Registration, 59 NohSan No. 4200, January 1985.

The acute dermal toxicity of technical grade tribufos (DBF) was tested in young adult male and female (5/sex/dose) New Zealand White rabbits. The undiluted test substance was applied at doses of 500 to 2000 mg/kg to an approximate 240 cm<sup>2</sup> clipped area of the back and the dose site was covered with an occlusive patch. After 24 hours the patch was removed and the dose site was wiped to remove the test substance. The animals were observed for 14 days after dosing for mortality and clinical signs. Body weights were recorded on the day of treatment (day 0) and on days 7 and 14. At the end of the study the animals were sacrificed and a gross necropsy was performed. LD50 values, 95% confidence intervals and the slope of the dose-mortality curves were calculated using a modified probit analysis computer program. If the LD50 could not be estimated by probit analysis it was estimated by nonlinear interpolation.

## 5. Toxicity

Id 150-50-5

Date 10.01.2008

**Result** : The incidence of mortality increased with dose for both males and females, with deaths occurring within 0-5 days following treatment. Treatment-related signs of toxicity (tremors, muscle fasciculations, decreased motor activity, erythema and/or dry flaking skin at the dose site, increased reactivity, ataxia, diarrhea, perianal stain and various secretions and stains about the head) were apparent on day 0 and resolved in surviving animals by day 13. Alopecia observed in one female on days 13 and 14 was not thought to be treatment-related. Body weight gain decreased from days 0-7 in a dose-related manner in surviving males and females, with recovery evident by day 14. Reddened thymus, erythema of the treated skin, salivation/oral stain, dark perianal stain and nasal stain in both males and females and pale zones in small intestines and red fluid in abdominal cavity in females only, were considered treatment-related gross lesions. In animals found dead. The only treatment-related gross lesions observed in animals that survived to day 14 were crusty zones on the treated skin of two males and one female at the 1000 mg/kg dose level. Alopecia found in one female sacrificed on day 14 was not thought to be treatment-related.

The dermal LD50 for both males and females (estimated by nonlinear interpolation) was 1093 mg/kg. This method was used since only one dose resulted in an intermediate level of mortality, precluding the use of probit or moving average methods to estimate the LD50. The no-observed effect level was <500 mg/kg for both sexes.

**Test substance** : Identification: Technical Grade DEF  
Percent Active Ingredient: 98.1% S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)

**Reliability** : (1) valid without restriction  
Guideline study

06.12.2007

(54)

**Type** : LD50  
**Value** : = 5000 - 10000 mg/kg bw  
**Species** : rabbit  
**Strain** : no data  
**Sex** : no data  
**Number of animals** :  
**Vehicle** :  
**Doses** :  
**Method** :  
**Year** : 1984  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (4) not assignable  
Original study not reviewed

05.12.2007

(21)

**Type** : LD50  
**Value** : = 4600 mg/kg bw  
**Species** : rabbit  
**Strain** : no data  
**Sex** : no data  
**Number of animals** :  
**Vehicle** :  
**Doses** :  
**Method** :  
**Year** : 1982  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Reliability** : (4) not assignable  
Original study not reviewed

## 5. Toxicity

Id 150-50-5  
Date 10.01.2008

05.12.2007 (22)

**Type** : LD50  
**Value** : = 168 mg/kg bw  
**Species** : rat  
**Strain** : no data  
**Sex** : no data  
**Number of animals** :  
**Vehicle** :  
**Doses** :  
**Method** :  
**Year** : 1970  
**GLP** : no  
**Test substance** : other TS

**Reliability** : (4) not assignable  
Original study not reviewed

05.12.2007 (2)

**Type** : LD50  
**Value** : = 97 mg/kg bw  
**Species** : rabbit  
**Strain** : no data  
**Sex** : no data  
**Number of animals** :  
**Vehicle** :  
**Doses** :  
**Method** :  
**Year** : 1982  
**GLP** : no data  
**Test substance** : other TS

**Reliability** : (4) not assignable  
Original study not reviewed

05.12.2007 (32)

**Type** : LD50  
**Value** : = 615 - 690 mg/kg bw  
**Species** : rat  
**Strain** : no data  
**Sex** : no data  
**Number of animals** : 100  
**Vehicle** : other: xylene  
**Doses** :  
**Method** :  
**Year** : 1969  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : Exact dosage levels were not provided. The test article was formulated so that the different dosage levels could be given by the dermal route at a constant rate of 0.0016 ml/g of body weight. The rats were adults and they were individually caged. None of the rats were restrained following treatment by the dermal route and no attempt was made to remove any of the test article following treatment by dermal application.

The LD50 values were calculated by the method of Litchfield and Wilcoxon, 1949, with 19/20 confidence limits. Survival times were recorded. LD1 values were also calculated because it is probably a more realistic measure of the toxic hazard of a compound than is the LD50 value, and with the LD50 value, it indicates the slope of the dose-response line.

**Result** : Merphos:

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	Survival time (males): Minimum = 90 hr Maximum = 9 days	
	Survival time (females): Minimum = 64 hr Maximum = 8 days	
	LD50 (males) = 690 mg/kg; 19/20 confidence limits = 519 - 818 mg/kg LD50 (females) = 615 mg/kg; 19/20 confidence limits = 160 - 226 LD1 (males) = 355 mg/kg LD1 (females) = 460 mg/kg Lowest dose to kill a rat (males) = 600 mg/kg Lowest dose to kill a rat (females) = 500 mg/kg	
<b>Reliability</b>	: (3) invalid Does not meet criteria of current guidelines.	
13.12.2007		(20) (22)
<b>Type</b>	: LD50	
<b>Value</b>	: = 168 - 360 mg/kg bw	
<b>Species</b>	: rat	
<b>Strain</b>	: Sherman	
<b>Sex</b>	: male/female	
<b>Number of animals</b>	: 90	
<b>Vehicle</b>	: other: xylene	
<b>Doses</b>	:	
<b>Method</b>	:	
<b>Year</b>	: 1969	
<b>GLP</b>	: no	
<b>Test substance</b>	: other TS	
<b>Method</b>	: Exact dosage levels were not provided. The test article was formulated so that the different dosage levels could be given by the dermal route at a constant rate of 0.0016 ml/g of body weight. The rats were adults and they were individually caged. None of the rats were restrained following treatment by the dermal route and no attempt was made to remove any of the test article following treatment by dermal application.	
	The LD50 values were calculated by the method of Litchfield and Wilcoxon, 1949, with 19/20 confidence limits. Survival times were recorded. LD1 values were also calculated because it is probably a more realistic measure of the toxic hazard of a compound than is the LD50 value, and with the LD50 value, it indicates the slope of the dose-response line.	
<b>Result</b>	: Survival time (males): Minimum = 39 hr Maximum = 10 days	
	Survival time (females): Minimum = 40 hr Maximum = 4 days	
	LD50 (males) = 360 mg/kg; 19/20 confidence limits = 288 - 450 mg/kg LD50 (females) = 168 mg/kg; 19/20 confidence limits = 127 - 222 mg/kg LD1 (males) = 154 mg/kg LD1 (females) = 58 mg/kg Lowest dose to kill a rat (males) = 200 mg/kg Lowest dose to kill a rat (females) = 100 mg/kg	
<b>Test substance</b>	: DEF; technical grade	
<b>Reliability</b>	: (3) invalid Does not meet criteria of current guidelines.	
13.12.2007		(20)

## 5.1.4 ACUTE TOXICITY, OTHER ROUTES

## 5.2.1 SKIN IRRITATION

**Species** : rabbit  
**Concentration** : undiluted  
**Exposure** : Occlusive  
**Exposure time** : 24 hour(s)  
**Number of animals** : 6  
**Vehicle** :  
**PDII** : 3.3  
**Result** : moderately irritating  
**Classification** :  
**Method** : Draize Test  
**Year** : 1973  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : 0.5 ml of the test article was applied to the clipped intact and clipped abraded skin on the back and flanks of each of six rabbits (two application sites) under an occlusive cover for 24 hours. At the end of 24 hours the occlusive covers were removed and the intact and abraded test sites were examined and scored separately for erythema and edema on a graded scale of 0 to 4. At 72 hours, the sites were examined and scored again. In evaluating the average irritation present, the mean scores for erythema and edema of the intact test sites after 24 and 72 hours were added. Similarly the mean scores for erythema and edema of the abraded test sites after 24 and 72 hours were added. These two values were totaled and divided by four to obtain the mean primary irritation score. A grading system was used to determine the descriptive primary skin irritation rating.

**Result** : Irritation Scores for Abraded Skin Sites:

Animal No.	24 Hours		72 Hours	
	Er.	Ed.	Er.	Ed.
1	2	1	2	1
2	2	1	2	1
3	2	1	2	1
4	2	1	2	1
5	2	3	2	2
6	2	2	2	1
Mean	2.0	1.5	2.0	1.2
Subtotal = 6.7				

Irritation Scores for Intact Skin Sites:

Animal No.	24 Hours		72 Hours	
	Er.	Ed.	Er.	Ed.
1	2	1	2	1
2	2	1	2	1
3	2	1	2	1
4	2	1	2	1
5	2	2	2	2
6	2	2	2	1
Mean	2.0	1.3	2.0	1.2
Subtotal = 6.5				

Primary Irritation Score = 3.3

Based on the results of this study, the test article was determined to be moderately irritating (3.3/8.0).

**Test substance** : Test article 651 identified as:  
 Merphos technical: 98.5% a.i. %w/%w

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<b>Reliability</b>	:	(tributyl phosphorotrithioite - 96) (tributyl phosphorotrithioate - 2.5) Acetic anhydride: 0.5% (2) valid with restrictions Comparable to guideline study, but no data on GLP	(31)
10.10.2007			
<b>Species</b>	:	rabbit	
<b>Concentration</b>	:	undiluted	
<b>Exposure</b>	:	Occlusive	
<b>Exposure time</b>	:	4 hour(s)	
<b>Number of animals</b>	:	6	
<b>Vehicle</b>	:		
<b>PDII</b>	:	3.71	
<b>Result</b>	:	moderately irritating	
<b>Classification</b>	:	irritating	
<b>Method</b>	:	EPA OPP 81-5	
<b>Year</b>	:	1991	
<b>GLP</b>	:	yes	
<b>Test substance</b>	:	other TS	
<b>Method</b>	:	This study was conducted in accordance with: 1) US-EPA-FIFRA, Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, Guideline 81-5, November 1984. 2) US-EPA-TSCA, Health Effects Testing Guidelines, 40 CFR Section 798.4470, July 1988. 3) OECD Guidelines for Testing of Chemicals, Section 4, Guideline 404, May 1981. 4) Japan, Ministry of Agriculture, Forestry and Fisheries, Guidance on Toxicology Study Data for Application of Agricultural Chemical Registration, 59 NohSan No. 4200, January 1985.	
<b>Result</b>	:	Six New Zealand White rabbits (three females and three males) were used to test technical grade tribufos for its potential to cause primary dermal irritation. 0.5 ml of the test substance was held in contact with shaved skin under an occlusive patch for four hours. Scoring for erythema and edema at the dose site was performed at 30 to 60 minutes and at 24, 48 and 72 hours after removal of the patch and again at 7 and 14 days after exposure. Erythema (score = 2) was present in all animals 30-60 minutes following exposure and resolved in all rabbits by 72 hours. Dry, cracked skin was observed at the dose site of two animals at the 48-hour exam and on all animals at 72 hours. This condition was still present on day 14. Very slight (score = 1) edema was seen in five animals 30-60 minutes following exposure. Twenty-four hours following exposure all animals exhibited signs of edema; five had moderate edema (score = 3) and one animal had severe edema (score = 4, based on elevation of raised area). Edema was resolving by 72 hours, such that four animals had moderate edema (score = 3) and two animals had very slight edema (score = 1). Edema had cleared in all animals by day 7. Other lesions and toxic signs were not observed. The primary irritation index was 3.7. Based on these results/ tribufos is a moderate primary dermal irritant.	
<b>Test substance</b>	:	Identification: Technical Grade Tribufos Percent Active Ingredient: 99.7% S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)	
<b>Reliability</b>	:	(1) valid without restriction Guideline study	
14.09.2007			(57)

## 5. Toxicity

Id 150-50-5

Date 10.01.2008

### 5.2.2 EYE IRRITATION

**Species** : rabbit  
**Concentration** : undiluted  
**Dose** : .1 ml  
**Exposure time** :  
**Comment** : not rinsed  
**Number of animals** : 6  
**Vehicle** :  
**Result** :  
**Classification** :  
**Method** : Draize Test  
**Year** : 1973  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : 0.1 ml of the test article was instilled into the conjunctival sac of the right eye of each of 6 rabbits. The left eye served as a control. At 1 minute, 1 hour, 48 and 72 hours and 7 days the cornea, iris and conjunctiva were examined and graded for irritation according to the Draize scale. A maximum score of 110 points is possible. The classification of eye irritation potential was determined by selecting the maximum mean irritation score at 1, 24 or 72 hours after instillation.

**Result** : Maximum mean irritation scores at:

1 minute = 8.0  
1 hr = 8.0  
24 hr = 8.0  
72 hr = 5.3  
72 hr = 0  
7 days = 0

Based on these results, the test article was determined to be minimally irritating (8.0/110).

**Test substance** : Test article 651 identified as:  
Merphos technical: 98.5% a.i. %w/%w  
(tributyl phosphorotrithioite - 96)  
(tributyl phosphorotrithioate - 2.5)  
Acetic anhydride: 0.5%

**Reliability** : (2) valid with restrictions  
Comparable to guideline study, but no data on GLP

10.10.2007

(31)

**Species** : rabbit  
**Concentration** : undiluted  
**Dose** : .1 ml  
**Exposure time** :  
**Comment** : not rinsed  
**Number of animals** : 6  
**Vehicle** :  
**Result** :  
**Classification** : not irritating  
**Method** : EPA OPP 81-4  
**Year** : 1992  
**GLP** : yes  
**Test substance** : other TS

**Method** : This study was conducted in accordance with:  
1) US-EPA-FIFRA, Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, Guideline 81-4, November 1984.

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- 2) US-EPA-TSCA, Health Effects Testing Guidelines, 40 CFR Section 798.4500, July 1990.
- 3) OECD Guidelines for Testing of Chemicals, Section 4, Guideline 405, February 1987.
- 4) Japan, Ministry of Agriculture, Forestry and Fisheries, Guidance on Toxicology Study Data for Application of Agricultural Chemical Registration, 59 NohSan No. 4200, January 1985.

Six young adult male New Zealand White rabbits were used to determine the potential for technical grade tribufos to cause primary eye irritation. The test substance (0.1 ml) was placed into the conjunctival sac of one eye of each rabbit, and the eyes were examined at 1, 24, 48, and 72 hours following treatment. The eyes were also examined at 7 days post-dosing, or as long as irritation persisted, in order to characterize the time course and reversibility of lesions.

**Result** : The test substance did not produce corneal or iridal lesions. Conjunctival redness (grade 1), chemosis (grade 1) and discharge (grade 3) were observed in all six animals one hour after dosing. On day 7 there were no signs of irritation in any animal. Using the FIFRA criteria for evaluation of ocular lesions, technical grade tribufos is a minimal eye irritant, with no positive effects.

**Test substance** : Identification: Technical Grade Tribufos  
Percent Active Ingredient: 99.2% S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)

**Reliability** : (1) valid without restriction  
Guideline study

14.09.2007

(44)

### 5.3 SENSITIZATION

**Type** : Buehler Test  
**Species** : guinea pig  
**Concentration** : 1<sup>st</sup>: Induction 10 % occlusive epicutaneous  
2<sup>nd</sup>: Challenge 1 % occlusive epicutaneous  
3<sup>rd</sup>:

**Number of animals** : 35  
**Vehicle** : other: PEG 400  
**Result** : not sensitizing  
**Classification** : not sensitizing  
**Method** : EPA OPP 81-6  
**Year** : 1990  
**GLP** : yes  
**Test substance** : other TS

**Method** : This study was conducted in accordance with:  
1) US-EPA-FIFRA, Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, Guideline 81-6, November 1984.  
2) US-EPA-TSCA, Health Effects Testing Guidelines, 40 CFR Section 798.4100, July 1988.  
3) OECD Guidelines for Testing of Chemicals, Section 4, Guideline 406, May 1981.  
4) Japan, Ministry of Agriculture, Forestry and Fisheries, Guidance on Toxicology Study Data for Application of Agricultural Chemical Registration, 59 NohSan No. 4200, January 1985.

The potential for tribufos to produce a dermal sensitization response was tested in guinea pigs using the Buehler Topical Closed-Patch Technique. A total of 35 adult male Hartley albino guinea pigs were assigned to one of five groups: tribufos test group (15 animals), tribufos noninduced control



group (five animals, for challenge), tribufos noninduced control group (five animals, for rechallenge), 1-chloro-2-4-dinitrobenzene (DNCB - positive control) test group (five animals) and DNCB noninduced control group (five animals). The tribufos was administered as a 10% solution in PEG 400 for the three induction doses and the challenge dose and as a 1% solution in PEG 400 for the rechallenge dose. Animals in the test groups received three topical induction applications of the appropriate formulation on study days 0, 7 and 14, followed by a 13-day "rest" period and a challenge application on day 27. Animals in the two noninduced control groups (tribufos challenge and DNCB) received only the challenge dose on day 27. A rechallenge dose of tribufos was applied on day 34 (test and noninduced control groups) in order to verify that the erythema present in the test group after the challenge dose was due to local irritation rather than to a sensitization reaction. All induction and challenge sites were scored for erythema at approximately 24 and 48 hours after removal of the test substance except after the first induction dose only a 24-hour scoring was done. Two calculations were used to estimate the response. The first, incidence, was defined as the number of animals showing a response score of 1.0 or greater at either 24 or 48 hours divided by the number of animals tested. The second, severity, was defined as the mean of the response scores at 24 and 48 hours for all animals.

**Result** : The DNCB test animals had an incidence score of 1.0 and a severity score of 1.3 following the challenge dose. No erythema was observed at the dose site of any of the DNCB noninduced control group animals after the challenge dose. Following the challenge dose, the tribufos test animals had an incidence score of 0.7 and a severity score of 0.5 and the tribufos noninduced control animals had an incidence score of 0.6 and a severity score of 0.3. The occurrence of erythema in the naive animals indicates the response observed in the test group represented primary dermal irritation, not a sensitization reaction. In order to verify that this response was due to irritation, a lower concentration (1%) of tribufos was applied to test and noninduced (naive) animals one week following the primary challenge. The concentration was reduced to approximately the highest concentration that would not produce primary irritation. No erythema was observed at the dose site of any of the tribufos test and noninduced control group animals after the rechallenge dose. The absence of erythema at the dose site following rechallenge is additional evidence that the mild response to the challenge exposure (test and naive animals) was only due to primary irritation.

**Test substance** : Thus, the results of this study indicate that tribufos does not cause a dermal sensitization reaction in guinea pigs using the Buehler Topical Closed-Patch Technique.  
 : Identification: DEF Technical  
 Percent Active Ingredient: S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)  
 Purity: 99.7%

**Reliability** : (1) valid without restriction  
 Guideline study

14.09.2007

(42)

#### 5.4 REPEATED DOSE TOXICITY

**Type** : Sub-chronic  
**Species** : rat  
**Sex** : male/female  
**Strain** : other: Holtzman  
**Route of admin.** : oral feed  
**Exposure period** : 91 days, but subgroups sacrificed at 21, 47, 63 and 91 days  
**Frequency of treatm.** : daily

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**Post exposure period** : none  
**Doses** : 1 ppm; increased to 10 ppm after 4 wks; 2 ppm increased to 50 ppm after 4 wks  
**Control group** : yes, concurrent vehicle  
**Method** :  
**Year** : 1958  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : The purpose of these series of studies was to evaluate the safety of merphos and to establish a level at which this compound demonstrates no-effect on plasma or red blood cell cholinesterase activity when administered orally to rats for a period of 90 days.

Three groups of rats (25/sex/dose level) were used in this study according to the following design:

Group 1: Control - 25 male and 25 female rats received the basal laboratory diet only.

Group 2: 25 male and 25 female rats received the basal laboratory diet containing 1.0 ppm merphos. After 4 weeks of feeding the dietary level of merphos was increased to 10 ppm.

Group 3: 25 male and 25 female rats received the basal laboratory diet containing 2.0 ppm merphos. After 4 weeks of feeding the dietary level of merphos was increased to 50 ppm.

The basal laboratory diet consisted of Purina Laboratory Chow to which the test material was added on a weight/weight basis to provide the above dietary levels. Fresh diets were prepared weekly. Animals were housed individually. Body weights and food consumption were recorded weekly. General physical appearance and behavior of each animal were recorded.

Five male and five female rats from each group, including the controls, were sacrificed at 21, 47, 63 and 91 days of feeding for plasma, red blood cell and brain cholinesterase activity determinations. The electrometric method of Michel, as modified by Frawley, was used to make these determinations.

Gross necropsies were performed on all animals which died during the study or were sacrificed for cholinesterase activity determinations. At termination liver and kidneys from the surviving 10 rats of each sex in each group were weighed, and organ/body weight ratios determined. The following tissues from three male and three female animals from each group were preserved for possible future histopathological examination: thyroid, lung, heart, liver, spleen, kidney, adrenal, stomach, pancreas, large and small intestine, urinary bladder, gonads, and bone marrow.

**Result** : Survival, physical appearance, behavior, appetite, body weights and food consumption were within normal limits throughout the study. The female rats fed 50 ppm showed liver weights and liver/body weight ratios significantly greater than controls. The 50 ppm level produced significant depression in plasma and red blood cell cholinesterase activity. Brain cholinesterase activity was significantly depressed in the male rats after 91 days of feeding and in the female rats after 63 days of feeding. The female rats fed 10 ppm exhibited significant inhibition of plasma and red blood cell cholinesterase activity only after 63 days of feeding. Brain cholinesterase activity was unaffected.

**Reliability** : (2) valid with restrictions  
Provides basic data

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(23)

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**Type** : Sub-chronic  
**Species** : rat  
**Sex** : male/female  
**Strain** : other: Holtzman  
**Route of admin.** : oral feed  
**Exposure period** : 7 and 13 weeks  
**Frequency of treatm.** : daily  
**Post exposure period** : subgroup subjected to a 5-week recovery period  
**Doses** : 100 and 500 ppm  
**Control group** : yes, concurrent vehicle  
**Method** :  
**Year** : 1958  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : The purpose of these series of studies was to evaluate the safety of merphos and to establish a level at which this compound demonstrates no-effect on plasma or red blood cell cholinesterase activity when administered orally to rats for a period of 90 days.

Three groups of rats were used in this study according to the following design:

Group 4: Control - 5 male and 5 female rats received the basal laboratory diet only.

Group 5: 25 male and 25 female rats received the basal laboratory diet containing 100 ppm merphos for 7 weeks.

Group 6: 25 male and 25 female rats received the basal laboratory diet containing 500 ppm merphos for 13 weeks; a subgroup was subjected to a 5-week recovery period. The test material was excluded from the basal diet after 13 weeks of feeding.

The basal laboratory diet consisted of Purina Laboratory Chow to which the test material was added on a weight/weight basis to provide the above dietary levels. Fresh diets were prepared weekly. Animals were housed individually. Body weights and food consumption were recorded weekly. General physical appearance and behavior of each animal were recorded.

Five male and five female rats from each test group were sacrificed at 24 and 42 days of feeding for plasma, red blood cell and brain cholinesterase activity determinations. Group 5 was terminated after 49 days of feeding and cholinesterase activity determinations were performed on five male and five female rats from this group. After 62 days of feeding five male and five female rats from Group 6 were sacrificed for cholinesterase activity determinations. After 91 days of feeding five male and five female rats from Group 4 (control) and five male and five female rats from Group 6 were sacrificed for cholinesterase activity determinations.

Gross necropsies were performed on all animals which died during the study or were sacrificed for cholinesterase activity determinations. The liver and kidney ratios were determined. Tissues were taken for histological examination from three male and three female animals from Group 4 and Group 6, including thyroid, lung, heart, liver, spleen, kidney, adrenal, stomach, pancreas, large and small intestine, urinary bladder, gonads, and bone marrow.

At 91 days the surviving male and female rats from Group 6 were placed on the basal laboratory diet; these animals were sacrificed after 32 additional days, and gross necropsies were performed on each animal. Cholinesterase activity for each animal was evaluated at termination to

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**Result** : determine whether recovery from inhibition had occurred.  
: Apparent growth suppression was noted in both groups during the first three weeks of feeding, prior to the sacrifice of any animals. Survival, physical appearance, behavior and food consumption were comparable to the control groups. Cholinesterase activity determinations were performed only on the control and high level rats. Complete inhibition of plasma and red blood cell cholinesterase activity in both male and female rats was noted and brain cholinesterase activity was also markedly depressed.

The average liver/body weight ratios for the rats of both sexes fed 500 ppm were significantly greater than those of the control groups. The average kidney/body weight ratios for the female rats were significantly greater than those of the control rats.

Gross necropsies of the rats fed 500 ppm in their diets revealed no pathological findings which could be associated with the ingestion of merphos.

Microscopic examination of tissues from animals receiving 500 ppm in the diet for 90 days revealed no evidence of cellular or tissue change which could be associated with the test article. All of the tissues from the experimental animals are similar to those of the controls. They are, therefore, considered to be within normal limits.

**Test substance** : Test article 651 identified as:  
Merphos technical: 98.5% a.i. %w/%w  
(tributyl phosphorotrithioite - 96)  
(tributyl phosphorotrithioate - 2.5)  
Acetic anhydride: 0.5%

**Reliability** : (2) valid with restrictions  
Provides basic data

05.12.2007

(24) (25)

**Type** : Sub-chronic  
**Species** : rat  
**Sex** : male/female  
**Strain** : other: Holtzman  
**Route of admin.** : oral feed  
**Exposure period** : 49 days  
**Frequency of treatm.** : daily  
**Post exposure period** : 25 days  
**Doses** : 20 ppm  
**Control group** : yes, concurrent vehicle  
**Method** :  
**Year** : 1958  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : The purpose of these series of studies was to evaluate the safety of merphos and to establish a level at which this compound demonstrates no-effect on plasma or red blood cell cholinesterase activity when administered orally to rats.

Two groups of rats (25/sex/dose level) were used in this study according to the following design:

Group 7: Control - 25 male and 25 female rats received the basal laboratory diet only.

Group 8: 25 male and 25 female rats received the basal laboratory diet containing 20 ppm merphos. The test material was excluded from the basal diet after 7 weeks of feeding.

**Result**

The basal laboratory diet consisted of Purina Laboratory Chow to which the test material was added on a weight/weight basis to provide the above dietary levels. Fresh diets were prepared weekly. Animals were housed individually. Body weights and food consumption were recorded weekly. General physical appearance and behavior of each animal were recorded.

Five male and five female rats from each group were sacrificed at 21 and 42 days of feeding for plasma, red blood cell and brain cholinesterase activity determinations. Gross necropsies were performed on all animals. The liver and kidneys from each animal sacrificed were weighed and organ/body weight ratios were determined. Tissues were taken for histological examination from three male and three female animals from each group sacrificed at 42 days and preserved in neutral formalin for possible examination, including thyroid, lung, heart, liver, spleen, kidney, adrenal, stomach, pancreas, large and small intestine, urinary bladder, gonads, and bone marrow.

After 49 days the size of each group was reduced (by sacrifice) to 5 males and 5 females and the compound was excluded from the diet of Group 8. The study was terminated after 25 more days of feeding. At this time cholinesterase activity determinations were performed on each rat to determine whether recovery occurred. Gross necropsies were performed on each animal.

The criteria chosen for statistical evaluation were mortality, body weights at termination, food consumption over the entire experimental period, organ weights and organ/body weight ratios at sacrifice, and plasma, red cell and brain cholinesterase activity at various time intervals.

: Survival, physical appearance, behavior and food consumption of the rats of both sexes were unaffected by the inclusion of merphos in their diets. Body weight gains for the female rats were within normal limits throughout the study; however, the values for the male rats were lower than the control group during the recover period, although no differences were noted during the 7-week feeding period.

Plasma and red blood cell cholinesterase activity was depressed in the rats of both sexes during the first 49 days of the study. During the recovery period, plasma and red blood cell cholinesterase activity returned to normal limits. Brain cholinesterase activity was unaffected during the course of the entire study.

Average liver weight and liver/body weight ratios of the female rats were significantly greater than those of the control group after 21 days of feeding. The kidney/body weight ratios for the male and female rats were significantly greater than those of the respective control groups after 21 days. This relationship remained for the female rats only, after 42 days of feeding.

Histopathologic evaluation of the three males and three females from Groups 7 and 8 revealed changes in the adrenal cortical cells, particularly in the zona fasciculation, which are considered to be the effect of prolonged stimulation (stress). Specifically these changes are an increase in the overall amount of fine or medium uniform vacuolization of the cytoplasm which is generally taken to indicate the lipid content of the cell; and the formation of larger vacuoles which sometimes compress the nucleus to one side and may occur in clusters with occasional loss of cell outline, and are taken to be the result of prolonged stimulation. These changes were found particularly in the female test group.

However, the changes are of a mild to moderate degree and their significance is decreased by the presence of similar findings in the female control group, even though to a lesser degree in the latter. The animals

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also showed some individual variation in the amount of vacuolization. The cytologic changes in the adrenal must be considered in relation to the size of the gland before it can be said that atrophy or hypertrophy has occurred. In this series of animals there was no significant variation in the width of the zonas so that as well as can be determined from histology alone, there was no evidence of change in gland size.

**Test substance** : Test article 651 identified as:  
Merphos technical: 98.5% a.i. %w/%w  
(tributyl phosphorotrithioite - 96)  
(tributyl phosphorotrithioate - 2.5)

**Reliability** : Acetic anhydride: 0.5%  
(2) valid with restrictions  
Provides basic data

05.12.2007

(26) (28)

**Type** : Sub-chronic  
**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : oral feed  
**Exposure period** : up to 112 days  
**Frequency of treatm.** : daily  
**Post exposure period** : subgroup subjected to a 12 day recovery period  
**Doses** : 2, 5, 750, 1000, 1250, 1500, and 2000 ppm  
**Control group** : yes, concurrent vehicle  
**NOEL** : = 5 ppm  
**Method** :  
**Year** : 1960  
**GLP** : no  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : Five groups of rats (25/sex/dose level) were used in this study according to the following design:

Group	Experimental Days		Level (ppm)
	Males	Females	
1	0-112	0-112	0
2	0-92	0-92	2.0
3	0-92	0-92	5.0
4	0-98	0-98	750
5	0-21	0-21	1000
	22-42	22-42	1250
	43-63	43-63	1500
	64-110	64-110	2000
	101-112	101-112	0

The basal laboratory diet consisted of Purina Laboratory Chow to which the test material was added on a weight/weight basis to provide the above dietary levels. Fresh diets were prepared weekly. Control rats received the basal laboratory diet only. Animals were housed individually. Body weights and food consumption were recorded weekly. General physical appearance and behavior of each animal were recorded.

Five male and five female rats from each group, including the control, were sacrificed on the 22nd, 43rd, and 64th days, and plasma, red blood cell and brain cholinesterase activity determinations were performed. The electrometric method of Michel, as modified by Frawley, J.P. et al., was used for these determinations. Five males from Group 2, five males from Group 3 and five untreated stock adult male rats of the same strain were sacrificed on the 76th day for plasma cholinesterase determinations. These determinations were performed by the manometric method of Nachmansohn and Rothenberg. Five male and five female rats from each

group were sacrificed on the 92nd day. Red blood cell and brain cholinesterase determinations for each animal were performed by the electrometric method. Plasma cholinesterase determinations for the male rats were performed by both the electrometric and the manometric method. Five female rats each from Groups 1, 2, and 3 were sacrificed on the 98th day and plasma cholinesterase determinations were performed by the manometric method. On the 101st day the test material was withdrawn from five male and five female rats from Group 5. These animals, together with five males from Group 1, were maintained on the basal laboratory diet for a period of 11 days. Upon completion of the recovery period on the 112th, these animals were sacrificed and plasma, red blood cell, and brain cholinesterase determinations were performed by the electrometric method.

Gross necropsies were performed on each rat used in the study with the exception of five male and five female rats of Group 4, which were sacrificed on the 99th day. The weights of liver and kidneys from each animal sacrificed on the 22nd, 43rd, 64th, 92nd, 98th and 112th days were recorded and organ/body weight ratios were determined. The following tissues from each rat in Groups 1 and 5 sacrificed at the various time intervals, each rat in Group 4 with the exception of five males and five females sacrificed on the 99th day, and from each rat in Groups 2 and 3 sacrificed on the 92nd day were preserved in 10% Formalin: thyroid, lungs, heart, liver, spleen, kidney, adrenal, stomach, pancreas, large and small intestine, urinary bladder, gonads, bone and bone marrow. The above tissues from all males and females in Groups 1 and 5 sacrificed at 92 days were examined microscopically. In addition, the adrenals from the rats in Group 4 which were sacrificed at 92 days, and the rats in Group 5 sacrificed after the 12-day recovery period were also examined microscopically.

The criteria chosen for statistical evaluation were body weight gains from 0-6, 6-9, 9-13, and 13-16 weeks; food consumption 0-6, 0-9 and 0-13 weeks; terminal body weights, organ weights, organ/body weight ratios and cholinesterase activity values determined at 22, 43, 64, 92, 98 and 112 days.

**Result**

- : No deaths occurred in the control or any of the test groups. The gross appearance and behavior of the test rats in Groups 2, 3, and 4 fed merphos at dietary levels of 2, 5, and 750 ppm, respectively, were comparable to those of the controls throughout the entire study. A moderate incidence of respiratory involvement was noted in the above test groups, as well as in the control group. The rats in Group 5, which were fed the test compound at levels which were gradually increased from 1000 to 2000 ppm, appeared thin and exhibited signs of marked respiratory involvement, rough coats, paleness of the extremities, urine stains on the abdomen, and excitability during the final four experimental weeks.

Body weight gains for the males in Groups 2 and 3 were comparable to those of the male controls; slight growth suppression was noted in the females in the above groups, as compared to the female controls. Food consumption for Groups 2 and 3 was comparable to that for the respective controls. Body weight gains and food consumption from 0-9 weeks for rats in Group 4, and from 0-13 weeks for rats in Group 5 were significantly lower than those for the respective controls. Body weight gains for the males on the recovery study were significantly higher than those for the male controls during the 12-day period.

Plasma, red blood cell, and brain cholinesterase activity was measured in male and female rats at all levels, including the controls, at various intervals during the course of the study using the electrometric method. Certain determinations were repeated using the manometric technique. No significant plasma, red blood cell or brain cholinesterase depression was

noted in animals of Groups 2 and 3. Marked plasma, red blood cell, and brain cholinesterase activity depression was observed consistently through the course of the study in Groups 4 and 5. Plasma, red blood cell, and brain cholinesterase activity were rapidly regenerated when the rats of Group 5 were placed on the control diet for 12 days after completion of the feeding study.

Gross necropsies performed on the male and female test rats sacrificed at various times, revealed thickened intestinal walls and catarrhal exudate in the lumen of the small intestine, and pale, chalky-colored adrenals in a number of rats from Groups 4 and 5, including the recovery group.

Sections of thyroid, lung, heart, liver, spleen, kidney, small intestine, large intestine, pancreas, testis, ovary and bone marrow of all test and control rats were within normal limits.

Adrenal glands from 10 animals, five males and five females from Group 4 showed mild (+) to moderate (2+) vacuolation of the cord cells of the zona fasciculata in adrenal cortex of 5 out of 5 sections from male rats. The adrenal sections from the five female rats were comparable to the control adrenal sections.

The results from adrenal sections of five male and five female rats from Group 5 showed slight (+/-) to marked (3+) vacuolated cord cells in the zona fasciculata of the adrenal cortex in all rats examined. After a 12-day recovery period, slight to severe vacuolation of the cord cells of the zona fasciculata was observed in five out of five adrenal sections taken from the males and three out of five adrenal sections taken from females.

Organ weights and organ/body weight ratios for the test rats in Groups 2 and 3 were comparable to those for the controls; significantly lower terminal body weights and liver and kidney weights and significantly higher liver and kidney/body weight ratios as compared to the controls were determined for the test rats in Groups 4 and 5.

It was concluded that dosages of 5 ppm of merphos in the diet of rats is a no-effect level.

A reevaluation of the histopathology of the adrenal sections was conducted several months later, with the following conclusions: Microscopic examination of the adrenal sections from the group composed of ten rats receiving 2000 ppm of merphos (Group 5) shows a marked degree of hypertrophy of the cells throughout the zona fasciculata. This hypertrophy extends into the zona glomerulosa where it practically obliterates a well demarcated zone, and also extends down into the zona reticularis leaving but a very small amount of this layer present. All of the hypertrophic cells show considerable granularity of the cytoplasm of a normal, regular-size nucleus with normal staining characteristics. In some of these the medullary cells also appear to be slightly hypertrophied. No evidence of any increased granularity of these cells is seen and there is no evidence of any marked change in the nuclear pattern. Compared with the control adrenal slides, there is a distinct difference in the size of the entire cortex in that the experimental animals are definitely of a hypertrophic nature.

Adrenals from the ten animals of Group 4 were examined. Three males and one female from this group show a similar process of hypertrophy in the layers of the cortex of the medulla, but the degree is much less than is present in the Group 5 animals. The most prominent hypertrophy in these four animals appears to be in the zona fasciculata. Here the zonae glomerulosa and reticularis are much more distinct and are somewhat similar to those seen in the controls, indicating the degree of hypertrophy is much less. The adrenal glands of the other rats in Group 4 were



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comparable to controls.

Reevaluation of the Group 5 animals placed on a 12-day recovery period showed a very slight degree of hypertrophy of cells, especially in the zona fasciculata. Two of the animals show a very slight degree of vacuolation of the cells. The zonae glomerulosa and reticularis in practically all of the animals are quite distinct and somewhat similar to those of the controls.

In reviewing the slides which were done in 1958 from rats which received 500 ppm merphos, the adrenals in this group of eight animals are practically normal. In one male and the three females, there is a very, very slight suggestion of hypertrophy of some of the cells of the zona fasciculata. The degree of hypertrophy is very slight and must be look for carefully and compared with the controls to recognize it. The other animals of this group showed no evidence of any hypertrophy.

It would appear, therefore, that the greatest degree of hypertrophy of the cortico layer of the adrenal of these experimental animals takes place in the zona fasciculata, then in the zona glomerulosa, and then in the zona reticularis. This hypertrophy does away with the blood vessels which are entirely collapsed by pressure. The most marked degree is in the 2000 ppm level, the second is in the 750 ppm level, and the slightest or least effect of hypertrophy is seen in the 500 ppm levels. This is apparently the result of a stress picture since the degree of hypertrophy seems to be in proportion to the length of tie and the concentration of dosage of the test material. It is concluded that this reaction is a perfectly normal, physiological response of the animal to an abnormal type of stimulation.

**Test substance** : Merphos (tributyl phosphorotrithioite); purity 95%  
**Reliability** : (2) valid with restrictions  
Provides basic data

13.12.2007

(27) (29)

**Type** : Sub-acute  
**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : gavage  
**Exposure period** : 5 days  
**Frequency of treatm.** : daily  
**Post exposure period** : none  
**Doses** : 88, 131, 197, 296, 444, 666, and 1000 mg/kg  
**Control group** : no  
**LD50** : = 452 mg/kg bw  
**Method** :  
**Year** : 1980  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : The test article was administered neat to groups of three fasted male/female Sprague-Dawley rats at dose levels from 88 to 1000 mg/kg. Doses were administered daily for five successive days. Animals were observed for mortality and toxic signs over five days. The oral LD50 was calculated by linear regression by the method of Litchfield and Wilcoxon.

**Result** : Daily Mortality

Dose mg/kg	Sex	Dead/Dosed	Days to Death
88	M	0/1	NA
	F	0/2	NA
131	M	0/2	NA
	F	0/1	NA
197	M	0/1	NA
	F	0/2	NA

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296	M	0/2	NA
	F	1/1	Day 3
444	M	0/1	NA
	F	2/2	Day 3
666	M	1/2	Day 2
	F	1/1	Day 3
1000	M	0/1	NA
	F	2/2	Days 2,3

Toxic signs observed included decreased activity, ocular/nasal/oral discharge, perianal discharge, diarrhea, hunching, dehydration, emaciation, prostration, rough coat, decreased body temperature, aggressiveness, hyperactivity and diuresis. The oral LD50 (combined sexes) of the test article was 452 mg/kg for the neat material (95% confidence: 187 - 1092).

**Reliability** : (2) valid with restrictions  
Provides basic data

05.12.2007

(59)

**Type** : Sub-acute  
**Species** : rat  
**Sex** : male/female  
**Strain** : Sprague-Dawley  
**Route of admin.** : gavage  
**Exposure period** : 5 days  
**Frequency of treatm.** : daily  
**Post exposure period** : none  
**Doses** : 88, 131, 197, 296, 444, 666, and 1000 mg/kg  
**Control group** : no  
**LC50** : = 375 mg/kg bw  
**Method** :  
**Year** : 1980  
**GLP** : no data  
**Test substance** : as prescribed by 1.1 - 1.4

**Method** : The test article was administered at 50% v/v in corn oil neat to groups of three fasted male/female Sprague-Dawley rats at dose levels from 88 to 1000 mg/kg. Doses were administered daily for five successive days. Animals were observed for mortality and toxic signs over five days. The oral LD50 was calculated by linear regression by the method of Litchfield and Wilcoxon.

**Result** : Daily Mortality

Dose mg/kg	Sex	Dead/Dosed	Days to Death
88	M	0/2	NA
	F	0/1	NA
131	M	0/1	NA
	F	0/2	NA
197	M	0/2	NA
	F	0/1	NA
296	M	0/1	NA
	F	1/2	Day 4
444	M	0/2	NA
	F	1/1	Day 3
666	M	1/1	Day 3
	F	2/2	Days 3,4
1000	M	2/2	Days 4,5
	F	1/1	Day 3

Toxic signs observed included decreased activity, ocular/nasal/oral discharge, perianal discharge, diarrhea, hunching, dehydration, emaciation, prostration, rough coat, decreased body temperature, aggressiveness, hyperactivity and diuresis. The oral LD50 (combined sexes) of the test

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<b>Reliability</b>	:	article at 50% v/v in corn oil was 375 mg/kg (95% confidence: 114 - 1230). It was judge from the data that the corn oil dilution had no effect on the oral toxicity of technical merphos in rats. (2) valid with restrictions Provides basic data	
05.12.2007			(59)
<b>Type</b>	:	Chronic	
<b>Species</b>	:	rat	
<b>Sex</b>	:	male/female	
<b>Strain</b>	:	Fischer 344	
<b>Route of admin.</b>	:	oral feed	
<b>Exposure period</b>	:	two years	
<b>Frequency of treatm.</b>	:	daily	
<b>Post exposure period</b>	:	no	
<b>Doses</b>	:	0, 4, 40 or 320 ppm	
<b>Control group</b>	:	yes	
<b>NOAEL</b>	:	4 ppm	
<b>LOAEL</b>	:	40 ppm	
<b>Method</b>	:	other	
<b>Year</b>	:	1992	
<b>GLP</b>	:	yes	
<b>Test substance</b>	:	other TS	
<b>Method</b>	:	<p>The chronic toxicity and oncogenic potential of technical grade tribufos was examined in the Fischer 344 rat. The test substance was administered continuously in the diet on the basis of the active ingredient (AI) at nominal concentrations of 0, 4, 40 or 320 ppm to a one-year interim sacrifice/chronic toxicity group and a two-year oncogenicity group, consisting of at least 10 and 50 animals/dose/sex, respectively. In addition to ophthalmological and electroretinographic exams, hematologic, clinical chemistry and urinalysis parameters were measured at periodic intervals as were body weight, body temperature, clinical signs and food consumption. A complete necropsy was performed on all animals of the chronic/oncogenic groups with all gross lesions and tissues collected being examined histologically. In addition, histopathological examinations were conducted on specific neurological tissue obtained from separate one- and two-year sacrifice groups, which were included in the study.</p> <p>The test was conducted in accordance with:</p> <ol style="list-style-type: none"><li>1. US-EPA-FIFRA, Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, Guideline 83-5, November 1984;</li><li>2. US-EPA-TSCA, Health Effects Testing Guidelines, 40 CFR Section 798.3320, revised July 1988;</li><li>3. OECD Guidelines for Testing of Chemicals, Section 4, Guideline 453, May 1981; and</li><li>4. Japan, Ministry of Agriculture, Forestry and Fisheries, Guidance on Toxicology Study Data for Application of Agriculture Chemical Registration, 59 NohSan No. 4200, January 1985.</li></ol>	
<b>Result</b>	:	<p>Average monthly body weight gain, based on the entire two years of exposure, was determined to be ~95 and 100% of controls for low-dose males and females, respectively, ~95% of controls for mid-dose males and females, and ~73% of controls for high-dose males and females.</p> <p>Food consumption remained unaffected in both males and females up to and including a dose of 40 ppm. Average daily food consumption per animal, based on the entire two years of exposure, declined slightly in 320 ppm males. When averaged over the same time period, but on the basis of daily food consumed per kg body weight, a slight increase in the rate of food consumption (8-9%) was measured in both sexes of the 320 ppm group.</p>	

Clinical signs attributed to administration of tribufos were principally noted in the high-dose group of both sexes. These included an increased incidence relative to control animals of paleness, eye opacity zones, rough coat, rashes and raised zones, urine stain and diarrhea.

Survival was comparable between treated and control animals of each sex.

Body temperature was not affected by the administration of tribufos.

Ophthalmologic and electroretinographic changes attributed to the test substance were observed only in the 320 ppm group.

Clinical pathology changes attributed the test substance were:

- a. Declines in erythrocyte counts, hemoglobin and hematocrit in 40 and 320 ppm animals;
- b. Declines in total protein, globulin, cholesterol and calcium in 320 ppm males and/or females and in cholesterol and calcium in 40 ppm males;
- c. Increases in blood urea nitrogen in 320 ppm males and females;
- d. Decreases in ALP and ALT activity in 40 ppm males and 320 ppm males and females; and
- e. Declines in PChe and RChe activity in 40 and 320 ppm males and females and in BChe activity in 320 ppm males and females.

Gross Pathology and Organ weight changes attributed to the test substance were:

- a. A discolored and abnormal consistency to the small intestine in one and two-year 40 and 320 ppm males and females;
- b. An enlarged adrenal gland in one- and two-year 320 ppm males and females;
- c. Opacity of the eye in 320 ppm males;
- d. Declines in absolute spleen and kidney weight in two-year 40 and 320 ppm males;
- e. An increase in absolute testicular weight in two-year 320 ppm males; and
- f. An increase in absolute and relative adrenal weight in one- and two year 320 ppm males and females.

Micropathological evidence of tribufos-induced neurotoxicity was not found in this study; however, the following micropathological changes were attributed to the test substance:

- a. Diffuse, bilateral retinal atrophy in one- and two-year 320 ppm males and females;
- b. Increases in optic nerve atrophy and cataract in two-year 320 ppm males and females (Both lesions were considered secondary to the retinal changes noted in this study.);
- c. Hyperplasia in two-year 40 and 320 ppm animals and vacuolation in one- and two-year 40 and 320 ppm animals of the mucosa of the proximal small intestine; and
- d. Increased vacuolation of the cortex of the adrenal in 320 ppm two year males and females.

For the Fischer 344 rat, dosed orally in the feed with technical grade tribufos for two years, a systemic no-observed-effect level (NOEL) of 4 ppm (0.2

mg tribufos/kg body weight/day) was established. In addition, the marked decline in body weight gain in 320 ppm animals (~73% of controls), which was accompanied by a slight increase in the daily rate of food consumption relative to controls (8-9%) , indicate a maximum tolerated dose (MTD) for tribufos was established and possibly exceeded in this study.

**Test substance**  
**Reliability**

: technical grade tribufos  
: (1) valid without restriction

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10.01.2008	Guideline study	(47)
<b>Type</b>	: Sub-acute	
<b>Species</b>	: rat	
<b>Sex</b>	: no data	
<b>Strain</b>	: no data	
<b>Route of admin.</b>	: oral unspecified	
<b>Exposure period</b>	: 43 days continuously	
<b>Frequency of treatm.</b>	:	
<b>Post exposure period</b>	:	
<b>Doses</b>	:	
<b>Control group</b>	:	
<b>Method</b>	:	
<b>Year</b>	: 2002	
<b>GLP</b>	: no data	
<b>Test substance</b>	: other TS	
<b>Result</b>	: Toxic Effects: P28 - BLOOD - Changes in serum composition (total protein, bilirubin, cholesterol, etc.); Y01 - BIOCHEMICAL EFFECTS - Enzyme inhibition, induction, or change in blood or tissue levels - True cholinesterase	
<b>Reliability</b>	: (4) not assignable Original study not reviewed	
10.01.2008		(4)

### 5.5 GENETIC TOXICITY 'IN VITRO'

<b>Type</b>	: Ames test
<b>System of testing</b>	: Salmonella typhimurium TA98, TA100, TA1535, TA1537 and TA1538.
<b>Test concentration</b>	: 667, 1000, 3333, 6667 and 10,000 ug/plate
<b>Cycotoxic concentr.</b>	: > 10,000 ug/plate
<b>Metabolic activation</b>	: with and without
<b>Result</b>	: negative
<b>Method</b>	: EPA OPP 84-2
<b>Year</b>	: 1989
<b>GLP</b>	: yes
<b>Test substance</b>	: other TS
<b>Method</b>	: DEF Technical was tested in the Salmonella/Mammalian-Microsome Plate Incorporation Mutagenicity Assay using the plate incorporation method. The test article was tested at five dose levels (667, 1000, 3333, 6667 and 10,000 ug/plate) along with appropriate vehicle and positive controls on tester strains TA98, TA100, TA1535, TA1537 and TA1538 in the presence and absence of S-9 mix. Following an approximate 48 hour incubation at 37 +/-2 deg C, revertant colonies per plate were counted. All dose levels of test article, vehicle controls and positive controls were plated in triplicate. A dose range-finding study was conducted in which ten dose levels (10, 33, 67, 100, 333, 667, 1000, 3333, 6667 and 10,000 ug/plate) of the test article were plated, one plate per dose, with an overnight culture of TA100 on selective minimal agar in both the presence and absence of S-9. The vehicle used to deliver DBF Technical to the test system was dimethylsulfoxide (DMSO). Liver microsomal enzymes were prepared from male Sprague-Dawley rats that had been injected with Aroclor 1254. Positive controls used in the study included 2-aminoanthracene (TA 98, TA100, TA 1535, TA 1537, TA 1538 at 0.5 ug/plate in the presence of S9), 2-nitrofluorene (TA 98 at 1.0 ug/plate and TA 1538 at 0.5 ug/plate in the absence of S9), sodium azide (TA 100 and TA 1535 at 0.5 ug/plate), and ICR-191 (TA 1537 at 2.0 ug/plate).

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- Result** : The results of the Salmonella/Mammalian-Microsome Plate Incorporation Mutagenicity Assay indicate that under the conditions of this study, DEF Technical did not cause a positive response on any of the tester strains either in the presence or absence of microsomal enzymes prepared from Aroclor induced rat liver. The positive controls performed as anticipated, indicating that the test was sensitive and valid.
- Test substance** : Identification: Technical Grade DEF  
Percent Active Ingredient: 98.5 S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)
- Reliability** : (1) valid without restriction  
Guideline study
- 13.09.2007 (40)
- Type** : Ames test  
**System of testing** : TA98, TA100, TA1535, TA1537 and TA1538  
**Test concentration** : 10, 50, 100, 1000, and 5000 ug/plate  
**Cycotoxic concentr.** : > 5000 ug/plate  
**Metabolic activation** : with and without  
**Result** : negative  
**Method** : EPA OPP 84-2  
**Year** : 1991  
**GLP** : yes  
**Test substance** : other TS
- Method** : DEF Technical was tested in the Salmonella/Mammalian-Microsome Plate Incorporation Mutagenicity Assay using the plate incorporation method. The study was conducted using the reductive modification to the preincubation procedure, in which the bacteria, the modified metabolic activation system (with 30% hamster liver S-9 and reductive cofactors) or buffer, and the test article are allowed to incubate at 30°C for 30 minutes prior to the addition of the top agar. The test article was tested at five dose levels (10, 50, 100, 1000, and 5000 ug/plate) along with appropriate vehicle and positive controls on tester strains TA98, TA100, TA1535, TA1537 and TA1538 in the presence and absence of S-9 mix. Following an approximate 48 hour incubation at 37 deg C, revertant colonies per plate were counted. All dose levels of test article, vehicle controls and positive controls were plated in triplicate. A dose range-finding study was conducted in which six dose levels (10, 50, 100, 500, 1000 and 5000 ug/plate) of the test article were plated, one plate per dose, with an overnight culture of TA 98 on selective minimal agar in both the presence and absence of metabolic activation containing 30% S9 and reductive cofactors. The vehicle used to deliver DBF Technical to the test system was dimethylsulfoxide (DMSO). Liver microsomal enzymes were prepared from uninduced male hamster livers.
- The following positive control chemicals are used:  
" Sodium azide (CAS No. 26628-22-8) at 5 ug/plate for the base-pair substitution mutants TA1535 and TA100;  
" 9-Aminoacridine hydrochloride (CAS No. 52417-22-8) at 50 ug/plate for the frameshift mutant TA1537;  
" 2-Nitrofluorene (CAS No. 607-57-8) at 5 ug/plate for the frameshift mutants TA1538 and TA98;  
" 2-Anthramine (CAS No. 613-13-8) at 1 ug/plate for strains TA98 and TA100 in the presence of metabolic activation are used to ensure the efficacy of the standard activation system;  
" Congo red (CAS No. 573-58-0) is used as a control to test the reductive procedures. Congo red is tested at 100 ug/plate with strain TA98 in the presence and absence of the modified and standard metabolic activation systems.
- Result** : Range-finding study: Toxicity was observed in the presence of the modified S9 mix at 1000 and 5000 ug as slight thinning of the background lawn.

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Definitive study: No dose-related increase in the number of histidine revertants was observed. Toxicity was again noted with strain TA98 in the presence of the modified S-9 mix as slight background lawn thinning. A second assay was conducted using the same assay conditions. As in the first assay, there was no dose-related increase in the number of histidine revertant colonies. In contrast with the previous assays, toxicity was not observed with strain TA98 in the presence of S9; however, the fluctuation in toxicity may be due to slight variations in the daily bacterial culture and metabolic activation system or minor differences in the concentration of dosing solutions DEF. Technical was not detected as being mutagenic as tested according to the procedures used in this study. The positive controls performed as anticipated, indicating that the test was sensitive and valid.

**Test substance** : Identification: Technical Grade DEF  
Percent Active Ingredient: 98.1 S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)

**Reliability** : (1) valid without restriction  
Guideline study

13.09.2007 (65)

**Type** : Cytogenetic assay  
**System of testing** : Chinese hamster ovary cells  
**Test concentration** : -S9: 0.004, 0.007, 0.013, 0.025 and 0.05 ul/ml; +S9: 0.007, 0.013, 0.025, 0.05 and 0.1 ul/ml  
**Cycotoxic concentr.** : -S9: 0.025 and 0.05 ul/ml; +S9: 0.05 and 0.1 ul/ml  
**Metabolic activation** : with and without  
**Result** : negative  
**Method** : EPA OPP 84-2  
**Year** : 1989  
**GLP** : yes  
**Test substance** : other TS

**Method** : Also in accordance with 40 CFR Part 158 and US-EPA-FIFRA, Section 158.340

The test article, DEF Technical, was tested in the chromosome aberration assay using Chinese hamster ovary cells. Dose levels for the chromosome aberration assay were selected following a preliminary toxicity test based upon reduction in mitotic index after treatment relative to the solvent control. CHO cells were exposed to solvent alone and to nine concentrations of test article ranging from 0.0005 ul/ml to 5 ul/ml in the absence and presence of an S-9 reaction mixture. After neutralization, the test article was insoluble in solvent at 5 ul/ml and insoluble in test medium at concentrations above 0.05 ul/ml. The osmolality of the highest concentration tested, 5 ul/ml, was 398 mOsm/kg. Based upon the findings of the range-finding toxicity study, dose levels of 0.004, 0.007, 0.013, 0.025 and 0.05 ul/ml, non-activated system, and 0.007, 0.013, 0.025, 0.05 and 0.1 ul/ml, S-9 activated system, were selected for the definitive study. Due to the test article induced delay in cell cycle kinetics observed in the toxicity study, the harvest time was set at 20 hours in order to assure that cells were evaluated in first division metaphase after treatment. The test article was dissolved in dimethylsulfoxide (DMSO), CAS 67-68-5. The S9 was prepared according to established procedures using livers from adult male Sprague Dawley rats induced by Aroclor 1254. Positive controls included triethylenemelamine (TEM; used in the non-activated study at a final concentration of 0.5 ug/ml) dissolved and diluted in distilled water and cyclophosphamide (CP; used in the activated study at a final concentration of 50 ug/ml) dissolved and diluted in distilled water.

**Result** : Dose levels 0.025 and 0.05 ul/ml tested in the non-activated study and dose levels 0.05 and 0.1 ul/ml tested in the S-9 activated study indicated toxic effects induced by the test article. In addition, the S-9 activated study was limited by the solubility of the test article in medium. Metaphase cells

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were collected at 20 hours after treatment for microscopic evaluation in both the non-activated and S-9 activated test systems. The harvest time was delayed because of cell cycle delay observed in the toxicity study.

No statistically significant increase in chromosome aberrations was observed in the non-activated or S-9 activated test systems. The positive and negative controls fulfilled the requirements for a valid test. DEF Technical was concluded to be negative in the CHO cytogenetics assay.

**Test substance** : Identification: Technical Grade DEF  
Percent Active Ingredient: 98.5 S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)

**Reliability** : (1) valid without restriction  
Guideline study

13.09.2007

(39)

**Type** : Unscheduled DNA synthesis  
**System of testing** : rat primary hepatocytes  
**Test concentration** : 0.0001, 0.0003, 0.001, 0.003, and 0.006 ul/ml  
**Cycotoxic concentr.** : >0.1 ul/ml  
**Metabolic activation** :  
**Result** : negative  
**Method** : EPA OPP 84-2  
**Year** : 1989  
**GLP** : yes  
**Test substance** : other TS

**Method** : The purpose of the study was to evaluate the test article, DEF Technical, for its ability to induce unscheduled DNA synthesis in rat primary hepatocytes as measured by autoradiographic methods. The test article was dissolved and diluted in dimethylsulfoxide (DMSO). The positive control compound, 7,12- dimethylbenz(a)anthracene (DMBA) was dissolved in DMSO.

A preliminary cytotoxicity test was performed to establish an appropriate dose range for the test article. Ten doses ranging from 0.0003 to 10 ul/ml were tested. Replicate cultures of rat hepatocytes were washed with complete medium and refed with serum-free medium 90-180 minutes after seeding. The cultures were then treated with test article. Eighteen to twenty hours later, an aliquot of culture fluid was removed, centrifuged, and the level of lactic acid dehydrogenase (LCH) activity in the culture fluid determined. Two replicate plates were used for IIF measurement at each dose level. The relative toxicities were obtained by comparing the LCH activity in the treated cultures to the LCH activities in the solvent control cultures.

UDS test: Based on the results of the preliminary cytotoxicity test, the test article, DEF Technical, was tested at eight dose levels. Three replicate glass dishes seeded with  $1 \times 10^6$  rat hepatocytes/dish were treated with 0.00003 to 0.03 ul/ml of test article. DMBA, at 3.0 and 10 ug/ml, was used as the positive control. Each test article and control dish received 3H-thymidine at a final concentration of 10 uCi/ml. In parallel with the test plates, three cultures per dilution were treated with the test article and control compounds for a parallel toxicity test. The cells were treated for 18-20 hours. The parallel toxicity plates were harvested by removal of a portion of the medium for LDH determinations as described in the initial cytotoxicity test to obtain the relative survivals and relative toxicities. After eighteen to twenty hours of exposure, the cells in the Unscheduled DNA Synthesis assay plates were washed in serum-free WME, swelled in 1% sodium citrate and fixed in ethanol-glacial acetic acid fixative. The coverslips were air-dried, mounted cell side up on glass slides, and allowed to dry. The slides were coated with Kodak NIB emulsion and stored in a refrigerator for ten days in light tight boxes with desiccant. The slides were



then developed, fixed, and stained.

The slides were read "blind" on an automated colony counter. Nuclear grains were counted in 50 cells in random areas on each of three coverslips per treatment where possible. For each treatment slide, the net nuclear counts were averaged and the standard deviation (S.D.) determined and recorded. Also reported are the grand mean and S.D. for each dose level as well as the percent of cells in repair (cells with > 5 net nuclear grains).

Criteria for Evaluation of Test Results: The results of this study were evaluated according to the following criteria. If the mean net nuclear count was increased by at least five counts over the control, the results for a particular dose level were considered significant. A test article was judged positive if it induced a dose-related response and at least one dose produced a significant increase in the average net nuclear grains when compared to that of the control. In the absence of a dose response, a test article which showed a significant increase in the mean net nuclear grain count in at least two successive doses was considered positive. If a test article showed a significant increase in the net nuclear grain count at one dose level without any dose response, the activity of the test article was considered to be equivocal. The test article was considered negative if no significant increase in the net nuclear grain counts at any dose level was observed.

Criteria of a Valid Test: The test was considered valid if positive control compound induced a significant increase in the net nuclear grain count, the proportion of cells in repair in the negative (solvent) control was less than 15% and the net nuclear grain count of the solvent control was less than one.

The test article was tested at eight dose levels ranging from 0.00003 to 0.03 ul/ml, and was fully evaluated at five dose levels of 0.0001, 0.0003, 0.001, 0.003, and 0.006 ul/ml.

**Result** : Slides treated with DEF Technical or DMBA were compared to the appropriate solvent control. According to the criteria set for evaluating the test results, both doses of the positive control, DMBA, induced a significant increase in the average net nuclear count of silver grains. None of the test article doses caused a significant increase in the mean net nuclear counts. All criteria for a valid test were met.

The results of the UDS assay indicate that under the test conditions, the test article did not cause a significant increase in the mean number of net nuclear grain counts (i.e., an increase of at least 5 counts over the solvent control), at any dose level. Therefore, the test article is considered negative in this study.

**Test substance** : Identification: DEF Technical  
Percent Active Ingredient: 98.5% S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)

**Reliability** : (1) valid without restriction  
Guideline study

06.12.2007

(41)

## 5.6 GENETIC TOXICITY 'IN VIVO'

**Type** : Micronucleus assay  
**Species** : mouse  
**Sex** : male/female  
**Strain** : CD-1  
**Route of admin.** : gavage

## 5. Toxicity

Id 150-50-5

Date 10.01.2008

**Exposure period** : 24, 48, and 72 hours  
**Doses** : 60, 125, and 250 mg/kg bw  
**Result** : negative  
**Method** : EPA OPP 84-2  
**Year** : 1991  
**GLP** : yes  
**Test substance** : other TS

**Method** : A range-finding assay was performed to determine the doses to be used in this study. Mice (3/sex/dose group) were treated with a single dose of DEF Technical suspended in corn oil at 0, 10, 50, 100, 500, 1000, and 2000 mg/kg body weight. Surviving animals were sacrificed approximately 72 hours after the dose. The number of RNA positive erythrocytes [polychromatic erythrocytes (PCE)] in a field of 200 red blood cells (RBC) was determined. Deaths occurred in all animals of both sexes at 1000 and 2000 mg/kg, and in 3 of 3 males and 2 of 3 females at 500 mg/kg. Only slight PCE suppression was observed in the remaining female mouse at 500 mg/kg BW. Based on the incidence of deaths from the range-finding assay, the doses selected for the definitive assay were 60, 125, and 250 mg/kg BW. The positive control selected for the definitive assay was benzene (500 mg/kg).

Definitive assay: Mice (5/sex/dose) were dosed by oral gavage with the test article in corn oil at dose levels of 0, 60, 125, and 250 mg/kg bw. The volume of dose solution administered was 10 ml/kg BW. A solvent control (corn oil) and positive control (benzene) were also included, each with 5/sex. Mice were sacrificed approximately 24, 48, or 72 hours after the dose administration. Blood was collected by plasma and erythrocyte cholinesterase activities. The right femur from each mouse was removed and slides prepared for the evaluation of micronucleus. Bone marrow smears were evaluated using epifluorescence microscopy. Two parameters were determined: (1) the number of micronucleated RNA-positive erythrocytes among a total of 1000 RNA positive erythrocytes per animal, which provides an index of chromosomal damage; and (2) the number of RNA-positive erythrocytes in 200 erythrocytes per animal, which provides an index of bone marrow cytotoxicity. The ratio of RNA-containing erythrocytes to mature erythrocytes (RBC) was based on the number of RNA-positive cells among approximately 200 erythrocytes.

**Result** : Mice treated with the vehicle control at 24, 48, or 72 hours in the definitive assay yielded a MN frequency of 0.04, 0.02, and 0.10%, respectively, for males and 0.08, 0.06, and 0.08%, respectively, in females. Doses of 60, 125, and 250 mg/kg BW of DEF Technical at 24, 48, or 72 hours prior to sacrifice yielded MN of 0.12% or less. None of these increases was statistically significant. In contrast, the positive control, benzene, at 24, 48, or 72 hours after treatment yielded 2.58, 0.55, and 0.10% PCE with MN, respectively, for males and 1.17, 0.30, and 0.10%, respectively, for females. On the basis of these data, DEF Technical does not induce an increase in micronuclei in bone marrow erythrocytes.

**Test substance** : Identification: DEF Technical  
Percent Active Ingredient: 98.1 S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)

**Reliability** : (1) valid without restriction  
Guideline study

14.09.2007

(63)

**Type** : Unscheduled DNA synthesis  
**Species** : mouse  
**Sex** : male/female  
**Strain** : CD-1  
**Route of admin.** : gavage  
**Exposure period** : 2 or 16 hours

## 5. Toxicity

Id 150-50-5

Date

**Doses** : 75, 150 and 300 mg/kg  
**Result** : negative  
**Method** : EPA OPP 84-2  
**Year** : 1991  
**GLP** : yes  
**Test substance** : other TS

**Method** : Conducted in accordance with 40 CFR Part 158 US-EPA-FIFRA, Section 158.340 and Guideline 84-4.

A range-finding assay (0, 10, 50, 100, 500, 1000, and 2000 mg/kg bw) was performed to determine the doses for a micronucleus assay. Male and female mice, three per group, were dosed on Day 1 and sacrificed on Day 4. Male mice from the 500, 1000, and 2000 mg/kg dose groups all died from the toxicity of the test article. Two of the three female mice from the 500 mg/kg dose group and all female mice from the 1000 and 2000 mg/kg dose groups died from the toxicity of the test article. Clinical signs in male and female mice included diarrhea, lacrimation, tremors, weakness, and rough fur.

Dose levels chosen for the definitive study were 75, 150, and 300 mg/kg bw DEF Technical for both male and female mice (3/sex/dose group). Corn oil served as the vehicle. The vehicle (negative) control mice received corn oil 2 or 16 hr before sacrifice. The positive control mice received dimethylnitrosamine (DMN; 10 mg/kg BW) in water 2 or 16 hr before sacrifice. Two experiments were performed for the definitive assays, one with male mice and the other with female mice.

**Result** : Clinical signs in male and female mice dosed with 150 or 300 mg/kg bw DEF Technical included diarrhea, lacrimation, tremors, weakness, and rough fur. Slides obtained from four female mice and one male mouse were not scorable because of lack of cell attachment or insufficient quality of the cells attached to the slides.

Male CD-1 mice treated with DEF Technical or the vehicle control yielded a mean of < -6.1 net grains/nucleus (NG) and < 2% of cells in repair (% IR). In contrast, 2- and 16-hr positive control mice yielded 8.7 and 8.6 mean NG with 53 and 40% IR, respectively.

Female mice treated with DEF Technical or the vehicle control yielded < -8.2 mean NG and <= 2% IR. In contrast, 2- and 16-hr positive control mice yielded 15.0 and 18.0 mean NG with 67 and 72% IR, respectively.

Based on the data obtained from the in vivo-in vitro hepatocyte DNA repair assays, we conclude that DEF Technical did not induce UDS under the conditions of this study following oral administration to male or female CD-1 mice. These results suggest that DEF Technical is not a genotoxic agent in the livers of male or female CD-1 mice following in vivo treatment.

**Test substance** : Identification: DEF Technical  
Percent Active Ingredient: S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)  
Purity: 98.1%

**Reliability** : (1) valid without restriction  
Guideline study

13.12.2007

(64)

### 5.7 CARCINOGENICITY

#### 5.8.1 TOXICITY TO FERTILITY

## 5. Toxicity

Id 150-50-5

Date

<b>Type</b>	:	Two generation study
<b>Species</b>	:	rat
<b>Sex</b>	:	male/female
<b>Strain</b>	:	Sprague-Dawley
<b>Route of admin.</b>	:	oral feed
<b>Exposure period</b>	:	ten week prior to mating of F0 through lactation of F2 offspring
<b>Frequency of treatm.</b>	:	daily
<b>Premating exposure period</b>		
<b>Male</b>	:	ten weeks
<b>Female</b>	:	ten weeks
<b>Duration of test</b>	:	Through lactation of F2 offspring
<b>No. of generation studies</b>	:	2
<b>Doses</b>	:	0, 4, 32 and 260 ppm
<b>Control group</b>	:	yes, concurrent vehicle
<b>NOAEL parental</b>	:	= 4 ppm
<b>NOAEL F1 offspring</b>	:	= 32 ppm
<b>NOAEL F2 offspring</b>	:	= 32 ppm
<b>Method</b>	:	EPA OPP 83-4
<b>Year</b>	:	1991
<b>GLP</b>	:	
<b>Test substance</b>	:	other TS
<b>Method</b>	:	<p>The study was conducted in accordance with:</p> <ol style="list-style-type: none"><li>1) US-EPA-FIFRA, Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, Guideline 83-4, November 1984.</li><li>2) US-EPA-TSCA, Health Effects Testing Guidelines, 40 CFR Section 798.4700.</li><li>3) OECD Guidelines for Testing of Chemicals, Section 4, Guideline 416, May 1983.</li><li>4) Japan, Ministry of Agriculture, Forestry and Fisheries, Guidance on Toxicology Study Data for Application of Agricultural Chemical Registration, 59 NohSan No. 4200, January 1985.</li></ol> <p>Technical grade tribufos was administered via the diet to CD Sprague-Dawley rats for two generations to test for potential reproductive effects. The test compound was administered at nominal dose levels of 0, 4, 32 and 260 ppm (actual doses were 4.0, 30.2 and 260 ppm). The F0 and F1 parents were comprised of 30 rats/sex/group. The F0 and F1 parents received tribufos in the diet throughout the entire study, beginning at eight weeks of age for the F0 parents and at weaning for the F1 parents. Prior to breeding, the animals received treated feed for a ten week period. F0 parents were mated to produce F1a litters and F1 parents (randomly selected F1a pups) were mated to produce F2a litters. During the study, adult animals were evaluated for the effect of the test compound on body weight, food consumption, clinical signs, cholinesterase activity, estrous cycling, mating, fertility, gestation length, and litter size. The offspring were evaluated for compound-related effects on sex ratio, pup viability, body weight gain, clinical signs, and cholinesterase activity. Gross necropsy evaluations were performed on all adults and pups. Histopathologic evaluation of reproductive organs, the pituitary, and gross lesions was performed on all adults.</p>
<b>Result</b>	:	<p>The following outline summarizes the findings in this study:</p> <ol style="list-style-type: none"><li>1. A marked increase in the cannibalization and related signs of pups (due to a compound effect on the dams) was observed in the high-dose group. No other treatment-related clinical signs were observed in the adults or pups.</li><li>2. Treatment-related lower body weights were observed in the F1 high-dose group males and females during the pre-mating period. The lower F1 body</li></ol>

weights were due to a decrease in pup body weight gain during the Fla lactation period (Fla pups = FI adults).

3. During the Fla and F2a lactation phases, treatment-related lower body weights were observed in the F0 and FI high-dose group females. A significantly lower weight change was also observed in the F0 high-dose group. The food consumption during the Fla and F2a lactation phases were also reduced in the high-dose group.

4. The only effect on adult reproductive parameters was a slight, but treatment-related, increase in the gestation length for the F0 and FI high-dose groups.

5. In the high-dose group, there was a treatment-related increase in the number of FO and FI dams with stillborn pups.

6. There was a reduction in pup viability in the high-dose group during the Fla and F2a lactation periods.

7. In the high-dose group, a treatment-related decrease in pup weight gain was observed during the Fla and F2a lactation periods.

8. The cholinesterase no-observable-effect level (NOEL) in adult male and female rats was 4 ppm.

9. A biologically significant cholinesterase depression occurred in the plasma and red blood cell cholinesterase of high-dose group 21-day pups; no biologically significant changes occurred in the four-day pup cholinesterase levels.

10. No treatment-related pathologic effects were observed, other than a treatment-related increase in pup cannibalization and related lesions in the high-dose group for the Fla and F2a pups.

The reproductive NOEL for tribufos in this study was 32 ppm. This is based on an increase in gestation length, the cannibalization of pups, a reduction in pup viability and a decrease in pup body weight gain during the lactation period in the high-dose group. The overall NOEL for tribufos in adult males and females based on cholinesterase data was 4 ppm.

**Test substance** : Identification: DEF Technical  
Percent Active Ingredient: S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)  
Purity: 98%

**Reliability** : (1) valid without restriction  
Guideline study

13.12.2007 (43)

### 5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

**Species** : rat  
**Sex** : female  
**Strain** : other: Charles River CrI:CD@(SD)BR  
**Route of admin.** : gavage  
**Exposure period** : Gestation Day 6 to Day 15  
**Frequency of treatm.** : daily  
**Duration of test** : Gestation Day 20  
**Doses** : 1, 7, or 28 mg/kg  
**Control group** : yes, concurrent vehicle  
**NOAEL maternal tox.** : < 1 mg/kg bw  
**NOAEL teratogen.** : > 28 mg/kg bw

## 5. Toxicity

Id 150-50-5

Date 10.01.2008

**Result** : no evidence of test article-related embryotoxicity, fetotoxicity, or teratogenicity

**Method** : OECD Guide-line 414 "Teratogenicity"

**Year** : 1986

**GLP** : yes

**Test substance** : other TS

**Method** : This study was conducted in accordance with EPA New and Revised Health Effects Test Guidelines (1984), IRLG Recommended Guidelines (1981), and OECD Guidelines (1981).

DEF Technical was prepared as a 0.2% w/v emulsion in an aqueous CMC vehicle (0.5% w/v carboxymethylcellulose and 0.4% w/v polysorbate 80 in distilled water), analyzed, and administered orally to 3 groups of 33 inseminated female Charles River CrI:CD@(SD)BR rats (dams) at doses of 1, 7, or 28 mg/kg. A fourth group of 33 dams received the vehicle alone and served as the control. Each group of 33 dams was subdivided into 2 termination phases: Phase I was comprised of 5 dams terminated on Day 16 of gestation and Phase II was comprised of 28 dams terminated on Day 20 of gestation. All dams were dosed, following nidation, on Days 6 through 15 of gestation. On Day 16 of gestation, 24 hours after the tenth and final dose of the test or control article, Phase I dams were weighed and sacrificed. Intact brains were removed and blood samples were obtained from these dams for determination of brain, plasma, and erythrocyte cholinesterase (ChE) activity. On Day 20 of gestation, 5 days after the final dose of the test or control article, Phase II dams were sacrificed.

Parameters measured for Phase II dams included body weight; food consumption; maternal erythrocyte, plasma, and brain ChE activity; pregnancy rates; dams with live progeny; corpora lutea; implantations; resorptions; litter size; fetal weights and viability; placental weights; uterine weights; fetal sex ratios; and pre- and postimplantation loss. Each dam was examined for gross external and visceral changes. In addition, fetuses were sexed and examined for gross external, visceral, and skeletal treatment-related dysmorphogenesis. Fetal brain ChE was determined for representative fetuses from each group.

**Result** : There was a toxicologically relevant (> 20%) inhibition of maternal plasma ChE activity on Day 16 that was statistically significant ( $p < 0.05$ ) for the mid- and high dose levels; only a borderline inhibition occurred in plasma ChE activity for the low dose level. There was also a toxicologically relevant and statistically significant inhibition of maternal erythrocyte ChE activity (mid- and high dose) and maternal brain ChE activity (high dose) on Day 16. By Day 20, ChE activity for high dose plasma, erythrocyte, and brain and middose erythrocyte, while indicating that recovery was occurring when compared to Day 16, continued to be inhibited at toxicologically relevant and, except for high dose plasma, statistically significant levels. Inhibition of plasma ChE activity for the low dose was neither statistically significant nor toxicologically relevant on Day 20. Fetal brain ChE activity, measured on Day 20, remained unchanged for all groups when compared with the control. Also observed was salivation in 2 animals and a statistically significant ( $p < 0.05$ ) reduction in overall maternal body weight gain during gestation for the high dose group. There was no evidence of test article-related embryotoxicity, fetotoxicity, or teratogenicity at any dose level tested.

**Test substance** : Identification: DEF Technical  
Percent Active Ingredient: S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)  
Purity: 98%

**Conclusion** : DEF Technical was maternally toxic at doses of 1, 7, and 28 mg/kg. However, there was no evidence of test article-related embryotoxicity, fetotoxicity, or

## 5. Toxicity

Id 150-50-5

Date 10.01.2008

teratogenicity at doses up to and including 28 mg/kg. Based on the results of this study, 28 mg/kg is considered the no-effect dose in terms of reproductive liability.

**Reliability** : (1) valid without restriction  
Guideline study (49)

15.10.2007

**Species** : rabbit  
**Sex** : female  
**Strain** : other: American Dutch  
**Route of admin.** : gavage  
**Exposure period** : Gestation Day 7 to Day 19  
**Frequency of treatm.** : daily  
**Duration of test** : Gestation Day 28  
**Doses** : 1, 3, or 9 mg/kg  
**Control group** : yes, concurrent vehicle  
**NOAEL maternal tox.** : < 1 mg/kg bw  
**NOAEL teratogen.** : > 9 mg/kg bw  
**Result** : devoid of any potential to promote embryotoxicity, fetotoxicity, and/or teratogenic effects

**Method** : EPA OPP 83-3  
**Year** : 1987  
**GLP** : yes  
**Test substance** : other TS

**Method** : DEF Technical was prepared as either a 0.022, 0.067, or 0.2% emulsion in an aqueous CMC vehicle (0.5% w/v carboxymethylcellulose and 0.4% w/v polysprbate 80 in distilled water), analyzed, and administered orally to 3 groups of American Dutch rabbits in doses of 1, 3, or 9 mg/kg. A fourth group received the aqueous CMC vehicle alone serving as the control. Doses were selected based on a range finding study. Each group was comprised of 17 artificially inseminated does. The day of insemination was considered Day 0 of gestation. All does received the test or control article from Day 7 to Day 19, during the stages of embryogenesis and early fetation. Doe body weights were obtained on Days 0, 7, 10, 14, 19, 21, and 28 of gestation and all does were observed daily for overt changes in appearance and behavior. On Day 20 of gestation approximately 24 hours after the last dose of DBF), blood samples were obtained from the auricular artery for the purpose of determining plasma and erythrocyte (RBC) cholinesterase activities. Once again on Day 28, blood samples were obtained (by cardiac puncture) for cholinesterase determinations. In addition, at doe termination on Day 28, the brain was removed, divided into two sagittal sections, and one-half was immediately frozen on dry ice. Brain, plasma, and RBC cholinesterase activities were determined using Ellman's Reagent, with acetylthiocholine as the substrate. On the twenty-eighth day of gestation, all does were sacrificed. The abdomen was opened, ovaries excised, and corpora lutea were counted and recorded. The uterine horns were transected at the cervix, removed, and weighed. Each uteri was longitudinally opened along the antimesometrial surface and the amniotic sacs displaced to one side to facilitate inspection of the uterine walls for the presence of resorptions. All fetuses and resorptions were removed and each implant was noted. The abdominal and thoracic viscera from the does were scrutinized and gross anatomical changes were recorded. Each fetus was given a complete external and internal examination.

Parameters evaluated included: maternal cholinesterase (plasma, brain, erythrocyte) activity, doe weights, food consumption, pregnancy rates, does with live progeny, corpora lutea, implantations, resorptions, litter size, fetal weights and viability, placental weights, fetal sex ratio, and pre- and post-implantation loss. Fetuses were examined for gross external, visceral, and skeletal dysmorphic changes.

## 5. Toxicity

Id 150-50-5

Date 10.01.2008

**Result** : The DEF test article promoted a statistically significant ( $p \leq 0.01$ ) reduction in body weight gain and a slight but not statistically significant reduction in food consumption during the treatment period for the high dose group. The test article also produced a statistically significant ( $p < 0.05$ ) and toxicologically meaningful ( $>20\%$ ) inhibition of plasma and erythrocyte (RBC) cholinesterase activity on Day 20 of gestation for all treatment groups; by Day 28 only RBC enzyme was significantly reduced for all groups. The reduction was less, however, indicating recovery for this parameter. By Day 28, plasma enzyme was no longer meaningfully reduced and there was no inhibition of brain cholinesterase for any treatment group. The test article had no adverse effects on any maternal reproductive parameter, all values were comparable between the three treatment groups and the control group. The test article did not augment resorption, promote late gestational death, or reduce fetal weight. In addition the test article did not elicit any evidence of teratogenicity. External, visceral, and skeletal evaluation of the fetuses disclosed no alterations in development which could be attributable to test article administration.

**Test substance** : Identification: DEF Technical  
Percent Active Ingredient: S,S,S-Tributyl phosphorotrithioate (CAS Registry Number: 78-48-8)  
Purity: 98%

**Conclusion** : DBF Technical, when administered to gravid rabbits at doses of 1, 3, and 9 mg/kg, doses which were maternally toxic to the does, was devoid of any potential to promote embryotoxicity, fetotoxicity, and/or teratogenic effects. A dose of 9 mg/kg should be considered the no-effect level for developmental toxicity.

**Reliability** : (1) valid without restriction  
Guideline study

15.10.2007

(46)

**Species** : rat  
**Sex** : female  
**Strain** : no data  
**Route of admin.** : oral unspecified  
**Exposure period** : gestation day 6 - 15  
**Frequency of treatm.** : daily  
**Duration of test** :  
**Doses** :  
**Control group** :  
**other: TDLo** : = 70 mg/kg bw  
**Method** :  
**Year** : 1998  
**GLP** : no data  
**Test substance** : other TS

**Result** : TDLo = Toxic Dose Low  
Reproductive Effects: Maternal Effects:  
T12 - REPRODUCTIVE INCLUDING EMBRYOTOXIC, NEONATAL AND TERATOGENIC; Maternal Effects - Other effects

**Reliability** : (4) not assignable  
Original study not reviewed

15.10.2007

(3)

**Species** : rat  
**Sex** : female  
**Strain** : no data  
**Route of admin.** : oral unspecified  
**Exposure period** : 0 day preg to 21 day post  
**Frequency of treatm.** : daily  
**Duration of test** :  
**Doses** :



## 5. Toxicity

Id 150-50-5

Date 10.01.2008

**Control group** :  
**other: TDLO** : = 430 mg/kg bw  
**Method** :  
**Year** : 2002  
**GLP** : no data  
**Test substance** : other TS

**Result** : Reproductive effects: Specific Developmental Abnormalities:  
T53 - REPRODUCTIVE INCLUDING EMBRYOTOXIC, NEONATAL AND  
TERATOGENIC - Specific Developmental Abnormalities - Urogenital  
system;  
T59 - REPRODUCTIVE INCLUDING EMBRYOTOXIC, NEONATAL AND  
TERATOGENIC - Specific Developmental Abnormalities - Other  
developmental abnormalities

**Reliability** : (4) not assignable  
Original study not reviewed

15.10.2007

(4)

**Species** : rat  
**Sex** : female  
**Strain** : no data  
**Route of admin.** : oral unspecified  
**Exposure period** : 0 day preg to 11 day post  
**Frequency of treatm.** :  
**Duration of test** :  
**Doses** :  
**Control group** :  
**other: TDLo** : = 330 - mg/kg bw  
**Method** :  
**Year** : 2002  
**GLP** : no data  
**Test substance** : other TS

**Result** : Reproductive effects: Specific Developmental Abnormalities: T41 -  
REPRODUCTIVE INCLUDING EMBRYOTOXIC, NEONATAL AND  
TERATOGENIC - Specific Developmental Abnormalities - Central nervous  
system

**Reliability** : (4) not assignable  
Original study not reviewed

15.10.2007

(4)

### 5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

### 5.9 SPECIFIC INVESTIGATIONS

### 5.10 EXPOSURE EXPERIENCE

### 5.11 ADDITIONAL REMARKS

**Type** : Neurotoxicity

**Method** : GLP: No data

Eleven groups of laying hens (*Gallus gallus domesticus*, mixed breed) were given a single oral dose of 100 - 2000 mg/kg merphos in gelatin capsules.

## 5. Toxicity

Id 150-50-5

Date 10.01.2008

### Result

Hens given 200 mg/kg or higher dosages of merphos were treated with 30 mg/kg atropine sulfate just prior to dosing with the organophosphorus pesticide, and this treatment was continued daily for 2 days. Controls were composed of four groups (three birds each) of orally treated hens that were given (1) empty gelatin capsules, (2) 500 mg/kg TOCP, (3) 10 mg/kg parathion (with 30 mg/kg atropine sulfate), or (4) 300 mg/kg atropine sulfate. Body weights were monitored and hens were examined daily for signs of toxicity. Surviving birds were killed by heart puncture at the end of the 90-day test period. Tissues from the nervous system were taken for histopathological examination shortly after death in birds that died during the experiment and in surviving birds killed by heart puncture at the end of the test period. Sciatic, tibial, and peroneal nerves, and spinal cord were excised and prepared for histopathological analysis.

: Administration of a single oral dose of merphos resulted in initial loss of weight. Most of the birds that survived had regained lost weight by the end of the observation period. Hens treated orally with single doses of TOCP showed loss of weight which increased as the clinical condition of these hens progressed to paralysis. Hens treated with parathion initially showed some loss of weight, all of which was regained at the end of administration. Atropine sulfate controls showed a slight loss of weight. Birds given empty gelatin capsules with acetone gained weight.

The atropine sulfate treatment was stopped after 2 days because most hens treated with a single oral dose of merphos recovered from the initial weakness observed shortly after administration. Although no last cholinergic effects were seen in most hens, one hen dosed with 2000 mg/kg and one dosed with 800 mg/kg died on days 4 and 23, respectively. Most hens given a single oral dosage of 400 - 2000 mg/kg showed mild ataxia 5 -15 days after administration. Hens given 200 mg/kg showed no abnormalities at any time during the experiment. All hens given a single 500 mg/kg oral dosage of TOCP developed ataxia with near paralysis state 71-79 days after administration. Hens given 10 mg/kg parathion showed weakness at first, but recovered within a few days of treatment. All hens given atropine sulfate or gelatin capsules remained normal.

Brain tissues showed no histopathological changes. No histopathological alterations were detected in any of the tissues taken from hens given single oral doses of merphos. Nerve tissues from controls treated with parathion, atropine sulfate alone, or gelatin capsule were also normal. One hen, given a single oral dosage of 500 mg/kg TOCP and killed 90 days after treatment, showed unequivocal degeneration of the spinal cord, and another TOCP hen exhibited equivocal changes, which consisted of occasional swollen axons without obvious fragmentation or phagocytosis of the axons and unaccompanied by myelin loss. Although this type of lesion may represent the earliest histopathologic alteration in delayed neurotoxicity, it was designated "equivocal" degeneration change since it has been occasionally observed in the spinal cord of normal hens. The spinal cord of the third TOCP-treated hen as well as the peripheral nerves of hens given a single oral dose of TOCP showed no degeneration.

Reliability  
10.10.2007

: (2) valid with restrictions

(5)

Type

: Neurotoxicity

Method

: Single topical dosages of 1000 mg/kg merphos were applied with a micropipet on the combs of a group of six hens (*Gallus gallus domesticus*, mixed breed). Three groups of hens (three each) served as controls. One group received topical treatment with 500 mg/kg TOCP. A second group was treated with 10 mg/kg parathion given in 0.1 ml acetone solution (with 30 mg/kg oral dose of atropine sulfate). The third group was treated with an equal volume of acetone. Body weights were monitored and hens were examined daily for signs of toxicity. Surviving birds were killed by heart

**Result**

puncture at the end of the 90-day test period. Tissues from the nervous system were taken for histopathological examination shortly after death in birds that died during the experiment and in surviving birds killed by heart puncture at the end of the test period. Sciatic, tibial, and peroneal nerves, and spinal cord were excised and prepared for histopathological analysis.

: Topical application of a single dose of merphos caused loss of weight which continued in the hens that developed ataxia and paralysis. Hens treated topically with single doses of TOCP showed loss of weight which increased as the clinical condition of these hens progressed to paralysis. Hens treated with parathion initially showed some loss of weight, all of which was regained at the end of administration. Atropine sulfate controls showed a slight loss of weight. Birds treated topically with acetone gained weight.

Topical application of a single 1000 mg/kg dosage produced delayed neurotoxicity in all treated hens. Five of these hens developed severe ataxia, one of which died after 16 days and another progressed to paralysis. None of these hens developed signs of late acute effect. All hens given a single 500 mg/kg topical dosage of TOCP developed paralysis within 16 days following the administration. Parathion-treated hens developed initial weakness but recovered within a few days. Hens treated with a topical dose of acetone remained normal.

Degeneration of the anterior columns in the spinal cord was identical to that found in tri-o-cresyl phosphate treated hens and was the most consistent histopathologic change. Topical administration of merphos caused a more prolonged inhibition of plasma butyrylcholinesterase activity than the orally administered compound. Orally administered merphos was rapidly metabolized in the gastrointestinal tract directly to nBM or following its oxidation to S,S,S-tributyl phosphorotrithioate. nBM apparently cause the late acute toxic effect. Topically administered merphos, which was not metabolized in the gastrointestinal tract, caused delayed neurotoxicity but did not produce a late acute effect.

Brain tissues showed no histopathological changes. Nerve tissues from controls treated with parathion, atropine sulfate alone, or acetone were also normal. No histopathological changes were seen in peripheral nerves of hens given a single topical dosage of 1000 mg/kg, unequivocal alterations were exhibited in the spinal cord. Degeneration of the anterior columns in the spinal cord was identical to that found in tri-o-cresyl phosphate treated hens and was the most consistent histopathologic change.

**Reliability**  
10.10.2007

: (2) valid with restrictions

(5)

**Type**

: Neurotoxicity

**Method**

: Groups of mixed breed hens (5/group) were given a daily oral dose of 0.1, 0.5, 1.0, 2.5, 5.0, 10, 20, 40 or 80 mg/kg of merphos in gelatin capsules for 3 months. Hens at the highest two doses were given 10 to 30 mg/kg/day atropine sulfate (4 to 7 days) as protection against cholinergic effects. Controls consisted of four groups of five hens treated orally with either empty gelatin capsules; 10 mg/kg/day tri-o-cresyl phosphate (positive control); or 1 mg/kg/day parathion (negative control) for 3 months. Another group of three hens was given a daily oral dose of 30 mg/kg of atropine sulfate for 34 to 90 days as an atropine sulfate control. At the end of the treatment period, the birds were observed for 1 month then sacrificed and tissues from the central and peripheral nervous systems were taken for histological examination.

**Result**

: Hens receiving 20-80 mg/kg/day lost weight and developed severe ataxia and delayed neurotoxicity that progressed to paralysis. Mortality also occurred at these dose levels. Hens receiving doses of 0.5 - 10 mg/kg/day lost weight, but regained it by the end of the observation period. These

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- Reliability**  
10.10.2007 : hens also showed mild to gross ataxia, and equivocal or negative histopathological changes in the spinal cord and peripheral nerves. (2) valid with restrictions (5)
- Type** : Neurotoxicity
- Method** : Daily topical dosages of 20 and 40 mg/kg merphos were applied with a micropiet on the combs of two groups of three hens each (*Gallus gallus domesticus*, mixed breed). Three groups of hens (three each) served as controls. One group received topical treatment with daily dosages of 20 mg/kg TOCP. A second group was treated with 1 mg/kg parathion (given in 0.1 ml of acetone solution). The third group was treated with equal volumes of acetone. The birds were treated for 90 days and the surviving birds were kept for observation for another 30 days. Body weights were monitored and hens were examined daily for signs of toxicity. Surviving birds were killed by heart puncture at the end of the 90-day test period. Tissues from the nervous system were taken for histopathological examination shortly after death in birds that died during the experiment and in surviving birds killed by heart puncture at the end of the test period. Sciatic, tibial, and peroneal nerves, and spinal cord were excised and prepared for histopathological analysis.
- Result** : Topical application of daily doses of merphos caused loss of weight which continued in the hens that developed ataxia and paralysis. Hens treated topically with daily doses of TOCP showed loss of weight which increased as the clinical condition of these hens progressed to paralysis. Hens treated with parathion initially showed some loss of weight, all of which was regained at the end of administration. Atropine sulfate controls showed a slight loss of weight. Birds treated topically with acetone gained weight.
- Topical administration of daily doses of merphos caused delayed neurotoxicity in a dose-dependent fashion. A daily topical dosage of 20 mg/kg merphos caused gross ataxia. One of three hens treated daily with 40 mg/kg developed severe ataxia with near paralysis. The third hen developed paralysis and died after 41 days of treatment. None of these hens developed signs of the late acute effect that was observed in hens given a daily oral dosage of 80 mg/kg merphos. Two of the three hens treated daily with a topical dosage of 20 mg/kg TOCP developed ataxia with near paralysis and the third hen progressed to paralysis during the observation period. Parathion-treated hens recovered from an initial paralysis shortly after the topical application of 1 mg/kg/day parathion had been stopped. Hens treated daily with a topical dose of acetone were normal.
- Brain tissues showed no histopathological changes. Nerve tissues from controls treated with parathion, atropine sulfate alone, or acetone were also normal. Hens treated with a daily topical 20 mg/kg dosage of merphos showed no histopathologic changes in the spinal cord or peripheral nerve. A daily 40 mg/kg topical dosage of merphos caused axons and myelin degeneration of the peripheral nerves of hens.
- Reliability**  
10.10.2007 : (2) valid with restrictions (5)
- Type** : Neurotoxicity
- Method** : The method for the screening test for the paralytic effect of the test article was conducted in White Leghorn chickens. The test chickens were each given atropine sulfate in water solution by the oral route at a dosage level of 15 mg/kg to protect them against the acute effect of the test article. Fifteen minutes later the test article was administered in peanut oil solution of suspension by subcutaneous injection under the right wing. The chickens were checked daily for signs of paralysis by placing them on the

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- Result** : ground and observing their ability to walk.  
: Merphos:  
Lowest lethal dose tested = 600 mg/kg  
Neurotoxic effect:  
Highest ineffective dose tested = 400 mg/kg  
Lowest effective dose tested = 600 mg/kg  
Duration: > 90 days\*
- DEF:  
Lowest lethal dose tested = 200 mg/kg  
Neurotoxic effect:  
Highest ineffective dose tested = --  
Lowest effective dose tested = 200 mg/kg  
Duration: > 30 days\*
- \* = Onset of leg weakness delayed 14-28 days after dosing with DEF and 3-21 days after dosing with Merphos.
- Test substance** : Merphos and DEF were technical grade  
05.12.2007 (20)
- Type** : other: ECETOC working group technical report
- Remark** : Organophosphorus pesticides (OPPs) have been used for decades. In view of their potent biological effects, these agents are subject to toxicological scrutiny aimed at the recognition of potential hazards and their risk management. In addition to the "classical" hazards of acute toxicity and delayed neuropathy, termed organophosphorus-induced delayed neuropathy (OPIDN), other specific types of organophosphorus neurotoxicity, such as "intermediate syndrome", ocular "Saku disease" and more recently "chronic syndrome" have been allegedly associated with OPP exposure. It has been claimed that even low-level apparently asymptomatic chronic exposure could cause long-term adverse effects on the nervous system. This prompted ECETOC to review the existing epidemiological data and toxicological testing protocols for the development and registration of OPPs, with respect to their sensitivity and reliability for detecting such effects.
- The present report reviews studies relating to long-term effects in humans, discriminating between chronic effects of acute or repeated exposure strong enough to produce clinical signs and symptoms (symptomatic exposure) and the effects of chronic, low-level, apparently asymptomatic exposure. These two fundamentally different situations are often confused in the literature. In addition, chronic, low-level exposure may have been associated in some studies with undocumented episodes of acute intoxication and the signs, symptoms and sequelae of acute exposure mistakenly interpreted as effects of chronic exposure. Some epidemiological studies demonstrate the absence of adverse effects in cohorts exposed but protected (by protective clothing) and thus confirm the possibility of using OPPs safely. Others report adverse effects that vary but are predominantly either psychological, neurological or ophthalmological. Unfortunately, both the "positive" and the "negative" epidemiological studies often lack sufficient details of the conditions, levels of exposure and compounds involved and data are frequently confounded by the spontaneous occurrence of changes related to aging and underlying diseases. Moreover, most studies are retrospective and methods of examination have not been standardised, are frequently subjective and rarely appropriately controlled. Therefore, at present, the evidence for the alleged chronic effects arising from low-level exposure appears insufficient. In most studies, there are no specific complaints about oculotoxicity resulting from chronic exposure. This is of interest in that oculotoxicity was previously suspected and special animal tests for this effect were required. This report also reviews experimental and mechanistic studies focused on

chronic OPp effects. It concludes that animal experiments, aimed at further characterising neurotoxicity induced by specific OPps, confirm acute and protracted effects on cognitive functions but have not demonstrated the alleged effects of prolonged, low-level exposure. Kinetic data demonstrate that inhibition of cholinesterase (ChE) by multiple low doses increases only during the initial phase of exposure and thereafter reaches a steady state, so that there is no long-range cumulative inhibition. No convincing explanation of how chronic, low-level exposure could possibly culminate in chronic dysfunction has been provided. Several mechanisms have been proposed, such as changes in receptors or neurotransmission, potential non-cholinergic effects of ChE or of OPps, or inhibition of other proteins/enzymes. However, in the absence of a demonstration that such effects really do occur at doses too small to cause acute or sub-acute effects, these hypotheses cannot be used as a foundation for the understanding of OPp neurotoxicity. The testing protocols used in animal safety studies have been reviewed with respect to their ability to identify OPp effects. The effects known or alleged to occur in humans have been compared to the toxicological "end-points" observed in animals. This comparison has demonstrated good predictability of the acute and delayed neuropathic effects. Although some chronic effects can be predicted from animal studies, there are restrictions caused by the short natural lifespan of experimental animals and by the restricted capability of animal experiments to test for exclusively-human mental performance. For the sake of completeness and to facilitate the comprehensive understanding of OPp toxicology, an Appendix to the report has been provided, with reviews of experimental and clinical data related to acute effects, intermediate syndrome, and OPIDN.

The Task Force has arrived at the following conclusions:

**Acute and intermediate effects.** The primary neurotoxic effects of OPps on humans and animals are well understood. Such effects are well understood. Such effects are generally reversible. Nevertheless, acute poisoning due to severe overdose can produce persistent changes. The acute toxicity of OPps is appropriately assessed in regulatory animal safety studies, well documented in humans, and clinically manageable. The intermediate syndrome is always associated with prior acute effects and the number of reported cases is limited. Risk from such hazards can be managed by minimising exposure. Neuropathic effects (OPIDN). The potential to induce OPIDN can be reliably detected by monitoring neuropathy target esterase (NTE) inhibition and by adequate neuropathological examination in delayed neurotoxicity studies in hens. It is unlikely that chronic low-level inhibition of NTE could cause neuropathy, because OPIDN is a threshold event. In any case such effects would have been observed in sub-chronic and chronic safety studies in rats and dogs had they occurred. Most cases of OPIDN have been caused by nonpesticidal organophosphorus compounds such as triorthocresyl phosphate (TOCP).

**Long-term effects.** There is no pharmacokinetic evidence for cumulative effects of chronic exposures to OPps at levels which are not acutely toxic. With prolonged substantial exposure the sensitivity to OPps decreases owing to the development of tolerance, and the effects are reversible after cessation of exposure. Based on well-established pharmacological and toxicokinetic principles, irreversible sequelae of low level exposure are considered unlikely. Tolerability studies in human volunteers conducted with a number of specific OPps indicate the absence of sequelae from daily, low-level asymptomatic exposure lasting for several weeks. There is insufficient evidence in the epidemiological literature that there is a "chronic syndrome" resulting from chronic, apparently asymptomatic exposure. To resolve the question of whether or not such a syndrome does exist, surveillance of the exposed populations is considered more appropriate

than additional animal studies. The described features of "chronic syndrome" resemble the complaints and changes sometimes seen in the general population and known to be linked to other societal and socio-economic factors. Interpretation of epidemiological observations should take such confounding factors into consideration. Some of the toxic effects claimed to constitute the alleged "chronic syndrome" can be detected in general regulatory safety studies and in special neurotoxicity studies within the constraints of inter- species extrapolation. There are human mental capabilities which are not testable in animals. Therefore; and in the absence of-hard evidence of the key features of 'chronic syndrome' in humans with low-level, asymptomatic exposure, it is not feasible to propose modifications of present regulatory animal studies.

Oculotoxicity. Review of reported complaints indicates that oculotoxicity does not appear to be a hazard of chronic OPp exposure. Persistent ocular effects are not observed in most epidemiological studies. In animal studies, ophthalmoscopy and biomicroscopy, supported by adequate pathology examination, provide sufficient sensitivity for detecting adverse effects in standard animal regulatory safety studies.

15.10.2007

(17)

**6.1 ANALYTICAL METHODS**

**6.2 DETECTION AND IDENTIFICATION**



**7.1 FUNCTION**

**7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED**

**7.3 ORGANISMS TO BE PROTECTED**

**7.4 USER**

**7.5 RESISTANCE**

**8.1 METHODS HANDLING AND STORING**

**8.2 FIRE GUIDANCE**

**8.3 EMERGENCY MEASURES**

**8.4 POSSIB. OF RENDERING SUBST. HARMLESS**

**8.5 WASTE MANAGEMENT**

**8.6 SIDE-EFFECTS DETECTION**

**8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER**

**8.8 REACTIVITY TOWARDS CONTAINER MATERIAL**

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT