AKZO NOBEL

Phosphorus Chemicals

August 28, 2001

Ms. Christine T. Whitman, Administrator
United States Environmental Protection Agency
P. O. Box 1473
Merrifield, VA 22116

re: High Production Volume (HPV) Challenge

Akzo Nobel Functional Chemicals LLC (ANFC), Phosphorus Chemicals Sub-business Unit (registration number), originally committed to sponsor twelve (12) chemical substances to the HPV Challenge Program per the letter of March 12, 1999. This sponsorship schedule was revised to include thirteen (13) chemical substances; letter of August 1, 2001 enclosed.

We hereby revise the attached table to reference the correct CAS Number, 220352-35-2, for Butylated triphenyl phosphate.

I trust this information is sufficient for your needs. If we can be of further assistance, please contact myself at 914/674-5394 or Dave Brandwene at 914/674-5546.

Very truly yours,

William F. Gentit
Manager, Regulatory Affairs

Enclosure:

c. Mr. Jim Keith - American Chemistry Council
D. Brandwene - Akzo Nobel Chemicals Inc./SHERA

Akzo Nobel Functional Chemicals LLC
5 Livingstone Avenue
Dobbs Ferry, New York 10522-3407
Tel. (914) 674 5000
Fax (914) 693 4497

CAS Number	Chemical	Start Year
13674-87-8	2-Propanol, 1,3-dichloro phosphate (3:1)	2001
1330-78-5	Tricresyl phosphate (mixed isomers) co-sponsored with Great Lakes Chemical Corp.	2001
25155-23-1	Trixylyl phosphate (mixed isomers) co-sponsored with Great Lakes Chemical Corp.	2001
115-86-6	Triphenyl phosphate co-sponsored with Bayer Corp. for ICCA/OECD Initiative	2001
220352-35-2	Butylated triphenyl phosphate co-sponsored with Great Lakes Chemical Corp.	2001
68937-41-7	Propylated triphenyl phosphate co-sponsored with Great Lakes Chemical Corp.	2001
125997-21-9	Phosphoryl Chloride, polymer with resorinol phenyl ester	2001
1241-94-7	Phosphoric Acid, 2-ethylhexyl, diphenyl ester co-sponsored with Ferro Corp.	2002
29761-21-5	Isodecyl diphenyl phosphate co-sponsored with Ferro Corp.	2002
2781-11-5	Diethyl-N,N-bis(2-hydroxyethyl aminomethyl phosphonate	2002
78-51-3	Ethanol, 2-butoxy-, phosphate (3:1) through TBEP CONSORTIUM with Great Lakes Chemical Corp Rhodia Inc.	2002
1779-48-2	Phosphinic acid, phenyl- through BPD/BPA COALITION with Avecia Inc. Ferro Corp.	2002
756-79-6	Phosphonic acid, methyl-, dimethyl ester through DMMP CONSORTIUM with Rhodia Inc.	2003

AR201-13275A

TEST PLAN

And

ROBUST SUMMARIES

For

PHOSPHORYL CHLORIDE, POLYMER WITH RESORCINOL PHENYL ESTER

CAS No. 125997-2 I-9

Prepared by

Akzo Nobel Functional Chemicals LLC
5 Livingstone Avenue
Dobbs Ferry, NY 10522

October 26, 2001

TEST PLAN

PHOSPHORYL CHLORIDE, POLYMER WITH
RESORCINOL PHENYL ETHER
(CAS #125997-21-9)

Study Type	Data Available	Data Acceptable	Testing Required
Physical/Chemical Characteristics			
Melting Point	NA	NA	No
Boiling Point	No	NA	Yes
Vapor Pressure	Yes	Yes	No
Partition Coefficient	No	NA	Yes
Water Solubility	Yes	Yes	No
Environmental Fate			
Photodegradation	No	NA	Yes
Stability in Water	Yes	Yes	No
Biodegradation	Yes	Yes	No
Fugacity	No	NA	Yes
Acute Toxicity to Fish	Yes	Yes	No
Acute Toxicity to Aquatic Invert.	Yes	Yes	No
Toxicity to Aquatic Plants	Yes	Yes	No
Human Health Effects			
Acute Toxicity	Yes	Yes	No
General Toxicity (Repeated Dose)	Yes	Yes	No
Genetic Toxicity	Yes	Yes	No
Reproductive Toxicity	Yes	Yes	No
Developmental Toxicity	Yes	Yes	No

NA = Not Applicable

IUCLID

Data Set

Existing Chemical	: ID: 125997-21-g
CAS No.	: 125997-21-9
TSCA Name	: Phosphoryl chloride, polymer with resorcinol phenyl ester

Producer Related Part

Company	: Akzo Nobel Functional Chemicals
Creation date	: 01.10.2001

Substance Related Part

Company	: Akzo Nobel Functional Chemicals
Creation date	: 01.10.2001

Memo

Printing date	: 26.10.2001
Revision date	
Date of last Update	: 26.10.2001
Number of Pages	: 18
Chapter (profile)	: Chapter: 1, 2, 3, 4, 5, 7
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

1.0.1 OECD AND COMPANY INFORMATION

Type	: cooperating company
Name	: Akzo Nobel Functional Chemicals
Partner	
Date	
Street	: 5 Livingstone Avenue
Town	: 10522 Dobbs Ferry, NY
Country	: United States
Phone	: 914-674-5394
Telefax	: 914-693-4487
Telex	
Cedex	

01.10.2001

1.0.2 LOCATION OF PRODUCTION SITE

Name of Plant	: Akzo Nobel Functional Chemicals LLC
Street	: P.O. Box 1721
Town	: 25515-5721 Gallipolis Ferry, WV
Country	: United States
Phone	: 304-675-I 150
Telefax	
Telex	
Cedex	

01.10.2001

1.0.3 IDENTITY OF RECIPIENTS

1.1 GENERAL SUBSTANCE INFORMATION

Substance type	: organic
Physical status	: liquid
Purity	: = 95 - 99 % wlw
Reliability	: (1) valid without restriction

02.10.2001

1.1.0 DETAILS ON TEMPLATE

1.1.1 SPECTRA

1.2 SYNONYMS

Phosphoryl chloride, polymer with 1,3-benzenediol, phenyl ester

Reliability	: (1) valid without restriction

02.10.2001

RDP
02.10.2001

Resorcinol bis(diphenyl phosphate)

02.10.2001

1.3 **IMPURITIES**

CAS-No : 115-86-6
EINECS-No : 204-I 12-2
EINECS-Name : triphenyl phosphate
Contents : = 1 - 5 % w/w
Reliability : (1) valid without restriction
0210.2001

1.4 **ADDITIVES**

1.5 QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.7 USE PATTERN

Type : industrial
Category : Basic industry: basic chemicals
Reliability : (1) valid without restriction
0210.2001

1.7.1 TECHNOLOGY PRODUCTION/USE

Type : Production
Reliability : (1) valid without restriction
02.10.2001

1.8 **OCCUPATIONAL EXPOSURE LIMIT VALUES**

1.9 SOURCE OF EXPOSURE

Memo : During production and use
Reliability : (1) valid without restriction
02.10.2001

1.10.1 RECOMMENDATIONS/PRECAUTIONARY MEASURES

Type : Handling
Remark : Wear protective clothing including chemical goggles and rubber gloves when handling this product to avoid eye and skin contact. Avoid inhalation of vapor or mist. Wash thoroughly after handling.

Reliability : (1) valid without restriction
02.10.2001

Type : Storage
Remark : Store away from foodstuff and animal feed. Containers should be stored in a cool, dry, well-ventillated area away from flammable or oxidizing materials. Keep away from sources of flame or heat.
Reliability : (1) valid without restriction
02.10.2001

Type : Fire
Remark : This product is not classified as flammable or combustible. It is self-extinguishing once the source of ignition is removed. It may decompose under fire conditions, to produce carbon monoxide, carbon dioxide, and phosphorus oxides.
Reliability : (1) valid without restriction
02.10.2001

1.10.2 EMERGENCY MEASURES

Type accidental spillage
Remark Isolate spill area and restrict access of nonessential personnel. Stop source of spill if possible. Dike area to prevent spill from spreading. Soak up product with a suitable absorbant such as clay, sawdust or kitty litter. Sweep up material and place in a chemical waste container for disposal. Caution, spill area may be slippery. Cover spill area with slurry of household detergent and water. Use stiff brush to work slurry into cracks and crevices. Allow to stand for 2 or 3 minutes and then flush with water. Dike wash water for disposal. Do not allow contaminated water to enter waterways or sewers.
Reliability : (1) valid without restriction
02.10.2001

Type injury to persons (skin)
Remark Remove contaminated clothing. Thoroughly wash all affected areas with soap and water. Get medical attention if irritation occurs and persists.
Reliability (1) valid without restriction
02.10.2001

Type injury to persons (eye)
Remark Immediately flush eyes with plenty of water. If wearing contact lenses, remove them. Hold eyelids apart during the flushing to ensure rinsing of the entire surface of the eye and lids with water. Get medical attention if irritation occurs.
Reliability (1) valid without restriction
02.10.2001

Type injury to persons (oral)
Remark Get medial attention or call a poison control center immediately. Do not induce vomiting unless directed to do so by medical personnel. If vomiting occurs, keep head below hips.
Reliability (1) valid without restriction
02.10.2001

Type injury to persons (inhalation)
Remark If inhaled, remove victim to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.
Reliability (1) valid without restriction
02.10.2001

1.11 PACKAGING

Memo : Shipped in carbon steel bulk and drum containers.
Reliability : (1) valid without restriction
02.10.2001

1.12 POSSIB. OF RENDERING SUBST. HARMLESS

1.13 STATEMENTS CONCERNING WASTE

Memo : Any amount not used should be disposed of in accordance with all applicable regulations.
Remark : This product does not meet EPA's criteria of a hazardous waste.
02.10.2001

1.14.1 WATER POLLUTION

1.14.2 MAJOR ACCIDENT HAZARDS

1.14.3 AIR POLLUTION

1.15 ADDITIONAL REMARKS

1.16 LAST LITERATURE SEARCH

1.17 REVIEWS

1.18 LISTINGS E.G. CHEMICAL INVENTORIES

Type : TSCA
Additional info
Reliability : (1) valid without restriction
02.10.2001

2. Physico-Chemical Data

Id 125997-21-9
Date 26.10.2001

2.1 **MELTING POINT**

2.2 **BOILING POINT**

2.3 **DENSITY**

Type : bulk density
Value : = at °C
02. 10.2001

2.3.1 **GRANULOMETRY**

2.4 **VAPOUR PRESSURE**

Value : < .1 hPa at 38° C
Decomposition : no
Method
Year
GLP : no
Test substance
Decomposition no
Reliability : (2) valid with restrictions
02.20.2001

2.5 **PARTITION COEFFICIENT**

2.6.1 WATER SOLUBILITY

Value : < 10 mg/l at 25 ° C
Qualitative
Pka : at 25 ° C
PH at and ° C
Reliability : (2) valid with restrictions
02.10.2001

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 **AUTO FLAMMABILITY**

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

Result : not explosive
Reliability : (1) valid without restriction
02.10.2001

2.11 OXIDIZING PROPERTIES

2.12 ADDITIONAL REMARKS

3.1 .1 PHOTODEGRADATION

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	= 11 day at 20 degree C
t1/2 pH7	:	= 17 day at 20 degree C
t1/2 pH9	:	= 21 day at 20 degree C
Deg. **Product**		
Method	:	OECD Guide-line 111 “Hydrolysis as a Function of pH"
Year	:	2000
GLP	:	**yes**
Test substance	:	as prescribed by 1 .1 - 1.4
Reliability	:	(1) valid without restriction
03.10.2001		

3.1.3 STABILITY IN SOIL

3.2 MONITORING DATA

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	activated sludge, domestic
Concentration		2.7mg/l related to Test substance
Contact time		56 day
Degradation	:	= 66 % after 56 day
Result		inherently biodegradable
Deg. Product		
Method		Directive 84/449/EEC, C.6 “Biotic degradation - closed bottle test”
Year		1996
GLP		yes
Test substance		as prescribed by 1.1 - 1.4
Method		The biodegradability of Fyrolflex RDP was determined in secondary activated sludge obtained from a plant that treats predominantly domestic waste water. In this Closed Bottle Test, 10 bottles contained only innoculum, 10 bottles contained innoculum and test substance, and an additional 10 bottles contained innoculum and sodium acetate. The test substance was added at 2.0 mg/l and sodium acetate at 6.7 mg/l. The innoculum was diluted to 2 mg dry weight/l. The bottles were closed and incubated at 21 degrees C in the dark. Duplicate bottles were withdrawn

for analysis of dissolved oxygen concentration on days 7, 14, 21, and 28. The test was extended to day 56. Biodegradation was calculated as the ratio of the biochemical oxygen demand (BOD) to the theoretical oxygen demand (ThOD).

Result

The theoretical oxygen demand of Fyrolflex RDP is 1.75 mg/mg. To assess possible toxicity to the microorganisms, Fyrolflex RDP was added to innoculums containing well-degradable sodium acetate to see if it inhibits the degradation of this chemical, No inhibition was observed, indicating Fyrolflex RDP is not toxic to the microorganisms. The pH was 6.8 at the start of the test and was 7.0 on day 28. The temperature ranged from 22 to 24 degrees C. In this test, Fyrolflex RDP was degraded 37% in 28 days and 66% by day 56. It is thus classified as inherently biodegradable.

Reliability

(1) valid without restriction

08.102001

(2)

3.6 **BOD5, COD OR BOD5/COD RATIO**

3.7 **BIOACCUMULATION**

3.8 **ADDITIONAL REMARKS**

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	: semistatic
Species	: Brachydanio rerio (Fish, fresh water)
Exposure period	: 96 hour(s)
Unit	: mg/l
Analytical monitoring	: **yes**
NOEC	: m = 3.04
LC50	: m = 12.37
Method	: OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	: 1996
GLP	: **yes**
Test substance	: as prescribed by 1 .1▪ 1.4
Method	: The acute lethal toxicity of Fyrolflex RDP was determined in the freshwater fish Brachydanio rerio (zebra fish) by continuously exposing the fish for 96 hours in a semi-static system. Behavioral changes and other signs of toxicity were also recorded during the test. Seven fish, averaging about 1.9 cm in length and about 0.12 grams, were used per dose level. Oxygen concentration and pH were measured daily. As a semi-static test, the fluids were renewed after 48 hours of testing. Water temperature was maintained at about 23 degrees C. Mortality and behavioral changes were recorded at 24, 48, 72, and 96 hours. Based on results from a preliminary rangefinding test, the following nominal concentrations were used in the definitive test: 3.04, 6.69, 14.71, 32.34, and 71.20 mg/l. A control group also contained 7 fish. Water samples were taken for analysis at 0, 48, and 96 hours, and were analyzed in duplicate.
Result	: The oxygen concentration varied from 8.1 to 8.9 mg/l. The pH varied from 7.7 to 8.2. Analysis of the water at the start of the study showed recovery in the range of 56 to 76% of the nominal concentration, primarily due to precipitation of the test substance which was clearly visible. At the end of the test recovery was in the range of 87 to 108% of the nominal concentrations. The 96 hour LC50 for Fyrolflex RDP is 12.37 mg/l and the NOEC is 3.04 mg/l for sublethal effects and 6.69 mg/l for mortality.
Reliability	: (1) valid without restriction

08.10.2001 (3)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	: flow through
Species	: Daphnia magna (Crustacea)
Exposure period	: 48 hour(s)
Unit	: mg/l
Analytical monitoring	: **yes**
NOEC	: m < .43
EC50	: m = .76
Method	: EPA OPPTS 850.1010
Year	: 1999
GLP	: **yes**
Test substance	: as prescribed by 1 .1▪ 1.4
Method	: Two replicate chambers were used for each of the five test concentrations. Each chamber contained 10 daphnids. Replicate control chambers were included in the study. The nominal test concentrations were 0.65, 1 .1, 1.8, 3.0, and 5.0 mg/l. Concentrations in the chambers were measured at the start and end of the test and were found to be 0.43, 0.64, 1.5, 2.2, and 3.2 mg/l. Observations of mortality/immobility were made a 1, 24, and 48 hours after test initiation. EC50 values were determined for 24 and 48 hours. Dimethylformamide was used as the diluent so solvent control

chambers were included in the study. The test chambers were maintained at a temperature of 20 degrees C. The pH, hardness, alkalinity, and total organic carbon were measured at the start and end of the test.

Result : The pH was maintained at about 8.3 and the dissolved oxygen at 8.5 mg/l. At 48 hours the hardness, alkalinity, and total organic carbon were determined to be 132, 178, and <1.0 mg/l. The 48 hour EC50 was determined to be 0.76 mg/l. The 95% confidence limits were 0.63 and 0.80 mg/l.

Reliability : (1) valid without restriction
03.10.2001

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

Species	Selenastrum capricornutum (Algae)
Endpoint	growth rate
Exposure period	96 hour(s)
Unit	mg/l
Analytical monitoring	yes
NOEC	m = 24.32
LOEC	m = 48.64
Method	OECD Guide-line 201 “Algae, Growth Inhibition Test”
Year	1995
GLP	yes
Test substance	as prescribed by 1.1-1.4
Method	The toxicity of Fyrolflex RDP to freshwater green alga was determined by measuring the effect of five dose levels of the test substance on alga growth in 96 hours. Cell growth was measured spectrophotometrically at 536 nm and quantified using a standard curve showing extinction and cell density. Three replicates were used at each dose level. The control group contained 6 replicates. Analysis of the test substance in the growth falsks was carried out, in duplicate, at the start and end of the study. Temperature and pH were measured during the study. The nominal doses were 0. 3.04, 6.08, 12.16, 24.32, and 48.64.
Result	Exponential growth was confirmed in the control flasks which showed an extinction increase of 57 times, within 72 hours, substantially higher than the 16-fold minimum required for a valid test. The pH showed a maximum increase of 1.4 pH units (7.7 to 9.1) and the temperature varied from 23.5 to 24.5 degrees C. Doses used in the definitive test were based on the results of a dose rangefinding test. In the definitive test, the alga growth rate was only slightly inhibited in response to the highest dose of 48.64 mg/l. Because of the low toxicity, it was not possible to accurately calculate the EC10 and EC50 values. The NOEC is 24.32 mg/l and the LOEC is 48.64 mg/l.
Reliability	(1) valid without restriction

08.10.2001 (1)

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 SOIL DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO OTHER NON-MAMM. TERRESTRIAL SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.1.1 ACUTE ORAL TOXICITY

Type	LD50
Species	rat
Strain	Sprague-Dawley
Sex	male/female
Number of animals	20
Vehicle	
Value	> 5000 mg/kg bw
Method	EPA OTS 798.1175
Year	1993
GLP	yes
Test substance	as prescribed by 1.1 - 1.4
Method	Ten male and 10 female Sprague-Dawley rats received a single oral gavage dose of 5 g/kg. The rats were observed for 14 days. Clinical signs of toxicity were recorded. Blood was drawn from each rat 7 days prior to dosing, 24 hours after and at the end of the 14 day observation period via the retro-orbital sinus specifically to measure monocyte nonspecific esterase (MNSE) activity. All of the animals were necropsied at the end of the 14 day observation period and underwent gross examination of the internal organs.
Result	No treatment-related clinical signs were observed in any of the animals. No rats died during the study. While there was no decrease in MNSE activity 24 hours after dosing, MNSE activity was significantly decreased in both male and female animals 14 days after treatment. All of the rats gained weight and the necropsy findings were normal. The acute oral LD50 in male and female rats is greater than 5 g/kg.
Reliability	(1) valid without restriction

25.10.2001 (7)

5.1.2 ACUTE INHALATION TOXICITY

Type		LC50
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	20
Vehicle	:	
Exposure time	:	4 hour(s)
Value	:	> 4.14 mg/l
Method	:	EPA OPPTS 870.1300
Year	:	1994
GLP	:	yes
Test substance		as prescribed by 1.1 - 1.4
Method		Aerosolized Fyrolflex RDP was administered to 10 male and 10 female Sprague-Dawley rats for 4 hours by a nose-only inhalation exposure system. The exposure concentration was determined by analyzing samples taken from the system. The aerosol MassMedian Aerodynamic Diameter was measured. After exposure, the animals were observed for 14 days. Mortality and clinical signs were recorded.
Result		No rats died during the study. The Mass Median Aerodynamic Diameter was 1.63 um with a standard deviation of 2.84. This is well within the respirable range of the rat. Sample analysis showed the rats were exposed to 4.14 mg/l. Clinical signs were observed in 8 of the 20 rats and included ptosis, salivation, and discharge around the eyes and nose. All of the rats gained weight during the 14 day observation period, and all were symptom free at 14 days. The acute inhalation LC50 is greater than the

highest attainable concentration of 4.14 mg/l.

Reliability : (1) valid without restriction
09.10.2001

(5)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	20
Vehicle		
Value	:	> 2000 mg/kg bw
Method	:	EPA OPPTS 870.1200
Year	:	1994
GLP	:	**yes**
Test substance	:	as prescribed by 1.1-1.4
Method	:	Fyrolflex RDP was applied undiluted to the shaved backs of 10 male and IO female Sprague-Dawley rats at a dose of 2 g/kg. The test sites were wrapped and the animals were collared to prevent oral ingestion of the test substance. After 24 hours, the test substance was removed. The animals were observed daily for mortality and clinical signs of toxicity.
Result	:	No treatment-related clinical signs were observed during the 14 day observation period. There was no mortality. All of the rats gained weight during the study. Necropsy findings for all rats were within normal limits. Therefore, the acute dermal LD50 for Fyrolflex RDP is greater than 2 g/kg.
Reliability	:	(1) valid without restriction

25.10.2001

(8)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

52.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	**100%**
Exposure	:	Semiocclusive
Exposure time	:	4 hour(s)
Number of animals	:	3
PDII		
Result	:	not irritating
EC classification	:	not irritating
Method	:	Directive 84/449/EEC, 8.4 “Acute toxicity (skin irritation)”
Year	:	1989
GLP	:	**yes**
Test substance	:	as prescribed by 1.1-1.4
Method	:	Three adult female albino rabbits each received 0.5 ml of the test substance applied to a gauze patch which was attached to the right flank of each animal. The right flank was covered with the same semi-occlusive dressing and acted as the control flank. After a 4 hour exposure, the test substance was removed using tissues and tap water. The application sites were observed at 45 minutes and at 24, 48, and 96 hours after removal of the patches for signs of edema and erythema. Any irritation observed was to be graded according to Draize.
Result	:	There was no sign of dermal irritation at the application site of any of the three animals. The primary skin irritation index is therefore zero (0). The substance is non-irritating to the skin.
Reliability	:	(1) valid without restriction

25.10.2001 (13)

52.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	100%
Dose	:	.1 ml
Exposure Time		
Comment		.
Number of animals	:	3
Result	:	slightly irritating
EC classification	:	irritating
Method	:	Directive 84/449/EEC, B.5 "Acute toxicity (eye irritation)"
Year		1989
GLP	:	yes
Test substance	:	as prescribed by 1.1-1.4
Method	:	The left eye of three albino rabbits received 0.1 ml of test substance, after which the lids were held together for about two seconds. The non-treated right eye of each animal served as a control. The eyes were observed immediately after treatment, at 60 minutes, and at 24, 48, and at 72 hours for effects on the cornea, iris, and conjunctiva. The eyes were scored according to the method of Kay and Calandra. About 24 hours after treatment, a solution of 2% fluorescein was applied to both eyes of each animal and the eyes were examined for corneal damage.
Resu lt		About 60 minutes after application of the test substance to the eyes, one treated eye showed slight conjunctival redness and chemosis. The other two treated eyes showed no irritation. The slight irritation was no longer present at the 24 hour observation. There was no adverse effect to the cornea or iris in any of the 3 rabbits. The Draize score of 3.3 at 60 minutes indicates the test substance should be classified as minimally irritating.
Reliability		(1) valid without restriction

25.10.2001 (14)

5.3 **SENSITIZATION**

5.4 **REPEATED DOSE TOXICITY**

Species	:	rat
Sex	:	male/female
Strain		Sprague-Dawley
Route of admin.	:	inhalation
Exposure period	:	28 Days
Frequency of treatment	:	Daily, 5 days per week
Post obs. period		60 day recovery group
Doses		0, 0.1, 0.5, and 2.0 mg/l
Control group		yes, concurrent no treatment
NOAEL		= .1 mg/l
LOAEL	:	= .5 mg/l
Method	:	EPA OTS 798.2450
Year	:	1996
GLP	:	yes
Test substance	:	as prescribed by 1.1-1.4
Method	:	To determine the effects of repeated inhalation exposure to Fyrolflex RDP, groups of 10 male and 10 female Sprague-Dawley rats were exposed to 0, 0.1, 0.5, or 2.0 mg/l of the test material for 6 hours per day, 5 days per week, for 4 weeks via a nose-only exposure system. Another group of 10

male and 10 female rats received the high dose and were held for 60 days after exposure ceased, to examine recovery. The animals were observed daily for clinical signs of toxicity. Body weights and food consumption were measured. Chamber aerosols of the test material were generated using a Laskin nebulizer. The concentration of Fyrolflex RDP in the chambers was measured gravimetrically and by HPLC. Aeorosol particle size was measured several times during the exposure. The animals were observed twice daily for mortality and morbidity. Hematology and clinical chemistry parameters were measured pre-test, at the end of the 28 day exposure, and 60 days later in the recovery groups. Monocyte nonspecific esterase and plasma and erythrocyte cholinesterase activities were measured. At termination, gross necropsies were conducted on all animals. The liver, kidneys, lungs, spleen, adrenal glands, heart, brain, testes with epididymides, ovaries, pituitary, thymus, and thyroid glands were removed and processed for microscopic examination.

Resu lt : The mean median aerosol diameter ranged from 1.39 to 1.70 urn, which is well within the respirable range of the rat. There were no deaths and no treatment-related clinical signs observed during the study. The mean body weight and food consumption of the high dose males was significantly decreased when compared to controls. There was no effect on hematology or clinical chemistry parameters. Plasma cholinesterase was significantly inhibited in high dose males (15%) and females (64%) at the end of the 28 day exposure, and was still present in the high dose females at the end of the 60 day recovery period. There was no efect on erythrocyte cholinesterase activity. Monocyte nonspecific esterase activity was no inhibited by treatment. Gross pathology was limited to white foci in the lungs of the high dose animals after exposure, and in 80% of the high dose animals after the recovery period. Lung histopathology showed alveolar histiocytosis in the mid and high dose groups. This progressed to chronic foreign body inflammation in the high dose animals in the recovery group. This response is characteristic of a noncytotoxic, water insoluble foreign material that reaches the alveolar region of the lung. While the lung changes were exposure related, they were not considered to reflect a specific toxic response to Fyrolflex RDP. No exposure-related gross or microscopic pathology was identified in any organ in any of the exposed animals. The NOEL in this study is 0.1 mg/l.

Reliability : (1) valid without restriction
26.10.2001 (12)

Species : mouse
Sex : female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 28 Days
Frequency of treatment : daily
Post obs. period
Doses : 500, 1500, and 5000 mg/kg/day
Control group : yes, concurrent no treatment
NOAEL : = 5000 mg/kg
Method : other: lmmunotoxicity Evaluation
Year : 1996
GLP : yes
Test substance : as prescribed by 1.1 - 1.4
Method : A repreated dose study was conducted to determine the immunotoxicity of resorcinol bis(diphenylphosphate). Groups consisting of 50 female B6C3F1 mice received either 500, 1500 or 5000 mg/kg of the test substance daily for 28 days by oral gavage. Animals in the control group were sham dosed. Additional groups received the same doses for 28 days and were then held through a 60 day recovery period. Positive control groups were included for certain endpoints. Body weights were determined weekly. Necropsies were conducted on all animals. Thymus and spleens

were weighed at necropsy. The following tissues were removed, processed through histology and examined microscopically: thymus, spleen, representative lymph nodes, and all gross lesions. At necropsy, blood was collected via the retro-orbital sinus and erythrocyte cholinesterase and plasma pseudocholinesterase activity was measured. Immune system endpoints measured in this study include: lymphoid organ cellularity and cell viability, splenic natural killer cell activity, splenic T-lymphocyte blastogenesis, macrophage numbers and phagocytic activity, antibody forming cell response, and host susceptibility to Listeria infection.

Result : No treatment-related clinical signs were seen in any of the animals and no animals died during the study. There was no effect on body weights or on spleen and thymus weights or in cellularity. There were no adverse necropsy findings and no histopathologic changes in thymus, spleen, or lymph nodes. After 28 days of exposure, all treatment groups showed a significant decrease in erythrocyte cholinesterase activity and plasma pseudocholinesterase activity, but both enzyme activities returned to control levels at the end of the 60 day recovery period. There were no treatment related changes in peritoneal cell numbers or cell types, peritoneal macrophage phagocytic activity, or host susceptibility to infection. Splenic natural killer cell activity, lymphocyte blastogenesis, antibody forming cell function were also unaffected by treatment. All animals that received positive control chemicals demonstrated a significant effect in the respective tests. In this comprehensive validated battery of immune function tests, resorcinol bis(diphenylphosphate) did not cause immunotoxicity following daily oral exposure to doses up to 5000 mglkglday for 28 days.

Reliability : (1) valid without restriction
26.10.2001 (6)

5.5 **GENETIC TOXICITY 'IN VITRO'**

Type	:	Ames test
System of testing	:	Salmonella typimurium and Escherichia coli
Concentration	:	5000, 2500, 1000, 333, 100. and 33.3 ug/plate
Cycotoxic conc.	:	No cytotoxicity observed in any dose group
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 471 "Genetic Toxicology: Salmonella thyphimurium Reverse Mutation Assay"
Year	:	1998
GLP	:	yes
Test substance	:	as prescribed by 1.1- 1.4
Reliability	:	(1) valid without restriction

08.10.2001 (4)

Type	:	Chromosomal aberration test
System of testing	:	Cultured human lymphocytes
Concentration	:	625, 500, 375, 312,250, 187, 125, and 50 ug/ml
Cycotoxic conc.	:	
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 473 "Genetic Toxicology: In vitro Mammalian Cytogenetic Test"
Year	:	1989
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Stimulated human peripheral lymphocytes were exposed to resorcinol bis(diphenylphosphate), both with and without metabolic activation, for up to 96 hours. Following treatment and incubation of the cells, cell division was arrested in metaphase stage of the cell cycle by the addition of the

spindle poison colchicine. The chromosome metaphase spreads were examined microscopically for the presence of aberrations such as breaks, gaps, fragments, dicentrics, and exchange figures.

Result : The positive control chemicals (mytomycin C without activation and cyclophosphamide with metabolic activiation) both produced statistically significant in the frequency of aberrant cells. In contrast, the test material did not induce chromosomal aberrations either with or without metabolic activation.

Reliability : (1) valid without restriction

26.10.2001 (15)

5.6 GENETIC TOXICITY 'IN VIVO'

Type	: Micronucleus assay
Species	: mouse
Sex	: male/female
Strain	: **Swiss**
Route of admin.	: gavage
Exposure period	:
Doses	: 5000 mg/kg
Result	: negative
Method	: OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year	: 1988
GLP	: **yes**
Test substance	: as prescribed by 1.1 - 1.4

Method : Five male and 5 female mice per sampling time received a single oral gavage dose of 5,000 mg/kg. Additional groups received the positive control chemical cyclophosphamide. Bone marrow was extracted at 24, 48, and 96 hours after dosing with test substance and at 48 hours for the positive control animals. Slides were prepared containing bone marrow smears. The number of micronuclei were counted in 1000 polychromatic erythrocytes to determine whether treatment with the test chemical causes an increase in the number of micronuclei.

Result : No increase in micronuclei was observed in any of the groups of mice treated with the test substance. In contrast, the animals treated with the positive control chemical showed a significant increase in the number of micronuclei.

Reliability : (1) valid without restriction

26.10.2001 (16)

5.7 CARCINOGENITY

5.8 TOXICITY TO REPRODUCTION

Type	: Two generation study
Species	: rat
Sex	: male/female
Strain	: Sprague-Dawley
Route of admin.	: oral feed
Exposure period	: 31 Weeks
Frequency of treatment	: Daily
Premating exposure period	
Male	: 10 Weeks
Female	: 10 Weeks
Duration of test	: 31 Weeks

Doses	0, 1,000, 10,000, or 20,000 ppm
Control group	yes, concurrent no treatment
NOAEL Parental	> 20000 ppm
NOAEL F1 Offspr.	> 20000 ppm
NOAEL F2 Offspr.	> 20000 ppm
Method	EPA OPPTS 870.3800
Year	1996
GLP	**yes**
Test substance	as prescribed by 1.1 - 1.4
Method	To determine the effects of Fyrolflex RDP on reproduction and fertility, four groups of 30 Sprague-Dawley rats each received eFyrolflex RDP in their diet at either 0, 1000, 10,000, or 20,000 ppm. Treated diets were prepared weekly and analyzed to confirm dietary concentration. Each group was fed the appropriate diet for 10 weeks prior to mating, through the 2 week mating period, through gestation and lactation, up until sacrifice. Vaginal smears were taken from each female rat 3 weeks prior to mating to ensure cyclicity. Twenty-five sperm positive females per group were used to produce the first generation (F1). This was also true for the second generation (F2). Females were allowed a natural parturition, at which time the pups were counted, sexed, and examined grossly for anomalies. All rats were observed once daily for mortality, morbidity, and behavioral effects. Anogenital distance was measured in the F1 generation. Body weight, body weight gain, and food consumption was measured. Vaginal smears were collected from all females 3 weeks prior to mating. After mating, the right testis and epididymis from at least 25 males per group were removed, trimmed of excess fat and weighed. Sperm samples were collected from each epididymis and evaluated for motility. Sperm morphology and sperm count was assessed. The uterus, vagina, ovaries, cervix, testes, epididymis, prostate, and seminal vesicles from the high dose group and control group were collected, weighed, and examined microscopically for treatment-related anomalies.
Result	There was no treatment-related effect on litter survival. Body weights were significantly lower in the treated animals as compared to the control group during week 1 due to an initial taste aversion. Anogenital distance was similar in the control and high dose groups, whereas vaginal opening and preputial separation were delayed in the 10,000 and 20,000 ppm groups, and were considered secondary to the reduction in F1 body weights. Neither parents nor offspring showed any treatment-related clinical signs of toxicity. Vaginal cytology and cyclicity and male reproductive functions (sperm count, motility, morphology) were unaffected by treatment. Mating performance was similar in the treated and control groups. No treatment-related lesions were observed in the reproductive organs. Thus, there were no adverse effects on reproductive performance or fertility parameters associated with the administration of Fyrolflex RDP in the diet through 31 weeks.
Reliability	(1) valid without restriction

08.10.2001 (11)

5.9 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	rabbit
Sex	female
Strain	New Zealand white
Route of admin.	gavage
Exposure period	Gestation days 6 to 28
Frequency of treatment	Daily
Duration of test	29 days
Doses	50, 200, or 1000 mg/kg/day
Control group	yes, concurrent vehicle

NOAEL Maternalt.	: > 1000 mg/kg bw
NOAEL Teratogen	: > 1000 mg/kg bw
Method	: **EPA OPPTS 870.3700**
Year	: 1996
GLP	: **yes**
Test substance	: as prescribed by 1.1-1.4
Method	: This study was conducted to evaluate the potential of Fyroflex RDP to alter fetal development following oral administration to pregnant New Zealand rabbits during organogenesis (gestation days 6-28). Twenty-seven rabbits per group received either 0, 50, 200, or 1000 mglkglday of Fyrolflex RDP by oral gavage from gestation day 6 through gestation day 28. A corn oil control group, also consisting of 27 animals, was included in the study, Animals were observed daily for signs of treatment-related effects. Body weights and food consumption were measured on study days 0, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, and 29. The pregnant animals were humanely euthanized and subjected to cesarean section and gross necropsy to determine their pregnancy status and the condution of the fetuses. The liver, spleen, kidneys, uterine horns, fetuses and ovaries were removed from each rabbit, trimmed where necessary and weighed. The number of corpora lutea in each ovary were counted and recorded. Each fetus received a gross external examination. All fetuses underwent wet visceral examinations and one-third of the heads were removed and examined by the Wilson technique. All fetuses were processed for skeletal examination. All anomalies were classified as to variety and were given a severity score.
Result	: There were no treatment-related clinical signs of toxicity. There were no effects on maternal food consumption, body weight, body weight gain, or on uterus, liver, kidney, and spleen weights. Fetal body weights and viability , as well as developmental endpoints, were unaffected by treatment with Fyroflex RDP. Thus, exposure of pregnant rabbits to doses ranging from 50 to 1000 mglkglday during periods of major organogenesis and histogenesis did not result in any toxic or teratogenic/developmental effect in the pregnant animals or in their fetuses.
Reliability	: (1) valid without restriction

26.10.2001 (10)

5.10 OTHER RELEVANT INFORMATION

Type	: other: Comparative Metabolism and Toxicokinetics
Method	: The metabolism and toxicokinetics of resorcinol bis(dipnenylphosphate) was determined after exposue of rats and monkeys to 14-C-resorcinol bis(diphenylphosphate) via intravenous, inhalation, oral, or dermal routes. The metabolism was also determined in mice, by fewer routes of administration. Male and female B6C3F1 mice, male and female Sprague-Dawley rats, and male and female cynomolgus monkeys received a single target dose of 100 mg/kg with a target radioactive dose of between 50 and 150 uCi/animal, depending on the species and route of administration. Blodd, urine, and feces samples were collected at specified times for the quantification of 14-C levels. Expired air was collected from the rats. Excreta samples were quantitatively extracted. Metabolite profiles of urinary and fecal metabolites were generated for several animals from each group. The major metabolites were isolated, purified, and structurally characterized by HPLC-mass spectrometry (MS, MS-MS, and MS-MS-MS techniques).
Result	: The metabolic profile in all 3 species is complex, with certain urine or feces extracts showing over 30 HPLC peaks associated with 14-C radioactivity. There was very little inter-animal variation, and no differences were seen between species or sexes with regard to metabolite profiles. The major fecal metabolites were resorcinol diphenylphosphate (the half ester), hydroxy-resorcinol diphenylphosphate, dihydroxy-resorcinol

diphenylphosphate, and hydroxylated parent compound. The major urinary metabolites were identified as resorcinol, resorcinyl glucuronide, and resorcinyl sulfate. A small amount of labeled carbon dioxide was expired. This study confirms that the test substance is metabolized in an identical manner by rats, mice, and primates, and that the rat and mouse are appropriate surrogates in which to assess the toxicityof resorcinol bis(diphenylphosphate). In both rats and primates, the highest peak plasma concentration (Cmax) and greatest area under the curve (AUC) was obtained with intravenous administration. In rats, the Cmax for inhalation, oral, and dermal exposures were 42%, 10%, and 1%, respectively. The AUC values for the 3 routes were 60%, 58%, and 15% of the intravenous AUC. Approximatey 20% of the dermal dose was absorbed in the rat whereas primates absorbed only 10% of the applied dermal dose. Tissue accumulation and retention was minimal indicating complete clearance of the administered dose.

Reliability : (1) valid without restriction
26.10.2001 (9)

5.11 EXPERIENCE WITH HUMAN EXPOSURE

(1) Akzo Nobel Central Research Center, Study No. RGL F95084. Toxicity of Fyrolflex RDP to the Freshwater Alga Selenastrum capricornutum. 1995.

(2) Akzo Nobel Central Research Center, Study No. RGL F95141. Biodegradability of Fyrolflex RDP in the Closed Bottle Test. 1996.

(3) Akzo Nobel Central Research Center, Study No. RGL F96053, Acute Toxicity of Fyrolflex RDP to the Freshwater Fish Brachydanio rerio. 1996.

(4) Covance Laboratories Inc., Study No. 19494-0-409OECD. Mutagenicity Test with Fyrolflex RDP in the Salmonella - Escherichia coli Mammalian Microsome Reverse Mutation Assay with a Confirmatory Assay. Conducted for Akzo Nobel Chemicals Inc., 1998.

(5) IIT Research Institute, Study No. L08465-SN1. Acute Nose-Only Inhalation Toxicity Study of Fyrolflex RDP in Rats. Conducted for Akzo Nobel Chemicals Inc. 1994.

(6) IIT Research Institute, Study No. L08488-2, Immunotoxicity Study in Mice of Fyrolflex RDP. Study conducted for Akzo Nobel Chemicals Inc. 1992. Study published in the International Journal of Toxicology 19:265-275, 2000.

(7) IIT Research Institute, Study No. L08489-1, Acute Oral Toxicity of Fyrolflex RDP in Rats (Limit Test), conducted for Akzo Nobel Chemicals Inc., 1994.

(8) IIT Research Institute, Study No. L08489-SN2. Acute Dermal Toxicity Study of Fyrolflex RDP in Rats. Study conducted for Akzo Nobel Chemicals Inc. 1994.

(9) IIT Research Institute, Study No. L08530-1, 14-C-Resorcinol Bis(diphenylphosphate: Comparative Metabolism and Toxicokinetics in the Rat, Mouse, and Monkey. Study was conducted for Akzo Nobel Chemicals. 1997. This study was published in the International Journal of Toxicology 19:233-242, 2000.

(10) IIT Research Institute, Study No. LO8588-4, A Developmental Toxicity Study of Orally Administered Fyrolflex RDP in Rabbits. Study conducted for Akzo Nobel Chemicals Inc. 1996. Study published in the International Journal of Toxicology 19:257-264, 2000.

(11) IIT Research Institute, Study No. LO8588-5. Two Generation Oral Reproductive Toxicity Study of Resorcinol Bis-Diphenylphosphate in Rats. Study conducted for Akzo Nobel Chemicals Inc. 1996.

(12) IIT Research Institute, Study No. LO8588-6. Twenty-Eight Day Nose Only Inhalation Toxicity Study of Resorcinol Bis-Diphenylphosphate (Fyrolflex RDP) in Rats. Study conducted for Akzo Nobel Chemicals Inc. 1996. Study published in the International Journal of Toxicology 19:223-231, 2000.

(13) RCC NOTOX B.V., study No. 114911494. Primary Skin irritation/Corrosion Study of CR 733-S in the Rabbit. Study was conducted for GE Plastics Europe. 1989.

(14) RCC NOTOX B.V., Study No. 1149/1495. Acute Eye Irritation/Corrosion Study of CR 722-S in the Rabbit. Conducted for GE Plastics Europe. 1989.

(15) RCC NOTOX B.V., Study No. 1149/ECH169. Evaluation of the Ability of CR 733-S to Induce Chromosomal Aberrations in Cultured Peripheral Human Lymphocytes. Study conducted for GE Plastics Europe. 1989.

(16) RCC NOTOX, Study No. 1149/MN 1520. Evaluation of the Mutagenicity of CR 733-S in the Micronucleus Test in the Mouse. The study was conducted for GE Plastics Europe. 1988.

7.1 END POINT SUMMARY

7.2 HAZARD SUMMARY

7.3 RISK ASSESSMENT