

# S I D S

# D o s s i e r

OECD HPV Chemical Programme, SIDS Dossier approved at SIAM 28 (15-17 April 2009)

**Printing Date** 2011-04-11 14:36:45 KST

**Restriction of specific regulatory purposes**

EU: BPD, EU: PPP, EU: REACH, CA: CEPA, CA: PCPA, JP: CSCL, OECD: HPVC, US: EPA HPVC, US: FIFRA, US: TSCA, other:

**Confidentiality**

CBI, IP, no PA

**Name** Phosphoric acid

**Legal entity owner** National Institute of Environmental Research / Incheon / Korea, Republic Of

**Substance: Phosphoric acid**

UUID IUC5-f844f4ba-7a8f-4651-974f-b65937105df4

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-12-09 10:49:21 KST

Remarks

**0 Related Information****0.1 Templates****0.2 Categories****0.3 Mixtures****1 General Information****1.1 Identification****Substance identification**

Chemical name Phosphoric acid

**[IP] OECD: HPVC**Legal entity [National Institute of Environmental Research / Incheon / Korea, Republic Of](#)**[IP] OECD: HPVC****Role in the supply chain****[IP] OECD: HPVC**Role: ☐ Manufacturer ☐ Importer ☐ Only representative ☐ Downstream user**Reference substance**Reference substance [Phosphoric acid / Phosphoric Acid / Phosphoric Acid / 7664-38-2](#)

EC number EC name

CAS number CAS name

7664-38-2 Phosphoric Acid

IUPAC name

Phosphoric Acid

**Type of substance**

Composition mono constituent substance

Origin inorganic

**Contact person**Person flags **[IP] OECD: HPVC**

Organisation NIER (National Institute of Environmental Research)

Department Risk Assessment Division

Title Senior Researcher

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Address Environmental Research Complex, Kyungseo-dong, Seo-Gu, Incheon

Postal code 404-708

Town Incheon

Region / State Kyungseo-dong, Seo-Gu

Country Korea, Republic Of

**1.2 Composition****Substance composition**

Name	Phosphoric acid
Brief description	99.999%, 85 wt. % in H <sub>2</sub> O, Colorless liquid
Degree of purity	

**[IP] OECD: HPVC**

99.999 % (v/v)

**Impurities****[IP] OECD: HPVC**

Typical concentration &lt; 20 ppm

Remarks total metallic

Name Phosphoric acid

Brief description 99.999 + % based on trace metal analysis, White crystals

**Degree of purity****[IP] OECD: HPVC**

&gt; 99.999 % (w/w)

**1.3 Identifiers****1.4 Analytical information****1.5 Joint submission****1.6 Sponsors****Sponsors****[IP] OECD: HPVC**

Name National Institute of Environmental Research (NIER)

Type member state

**Contact information**

Address National Institute of Environmental Research (NIER)

Address Kyongseodong, Seogu, Incheon, 404-708, Korea

Postal code 404-708

Town Incheon

Region / State Kyongseodong, Seogu

Country

Phone +82-(0)32-560-7169

Fax +82-(0)32-568-2037

E-mail iceom@korea.kr

Web site http://www.nier.go.kr

**Contact persons**

Organisation	National Institute of Environmental Research (NIER)
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Last name	EOM
Phone	+82-(0)32-560-7169
Mobile	+82-(0)10-7129-6162
Fax	+82-(0)32-568-2037
E-mail	iceom@korea.kr
Address	Environmental Research Complex, Kyungseo-dong, Seo-gu
Postal code	404-708
Town	Incheon
Region / State	Kyungseo-dong, Seo-gu
Country	Korea, Republic Of

**2 Classification and Labelling****2.1 GHS****2.2 DSD - DPD****3 Manufacture, use and exposure****3.1 Technological process**

## Technological process

### [IP] OECD: HPVC

**Methods of manufacture** The Republic of KOREA, Phosphoric acid is manufactured by the compound fertilizer or feed process. The whole processes are below;

Raw materials input → Screening and pulverization → Hemi-gypsum decomposition reaction process → Hemi-gypsum filtration → Di-gypsum conversion process → Di-gypsum filtration → Products store and shipment

Hemi-gypsum decomposition reaction process. There are two reactions in this stage.

Reaction 1 :  $\text{Ca}_3(\text{PO}_4)_2 + \text{H}_3\text{PO}_4 \rightarrow 3\text{CaHPO}_4$

Reaction 2 :  $2\text{CaHPO}_4 + 2\text{H}_2\text{SO}_4 + \text{H}_2\text{O} \rightarrow 2\text{CaSO}_4 \cdot \frac{1}{2}\text{H}_2\text{O} + 2\text{H}_3\text{PO}_4$

Di-gypsum conversion process.

Reaction :  $\text{Ca}_3(\text{PO}_4)_2 + 3\text{H}_2\text{SO}_4 + 6\text{H}_2\text{O} \rightarrow 3\text{CaSO}_4 \cdot 2\text{H}_2\text{O} + 2\text{H}_3\text{PO}_4$

Reference: National Institute of Environmental Research (NIER), Survey on circulation volume and use pattern of phosphoric acid, Republic of Korea.

### [IP] OECD: HPVC

**Methods of manufacture** Phosphoric acid is manufactured by the wet process or the furnace(thermal) process. The wet process acid, produces directly from phosphate ores, has a high production volume, low cost, and low purity. It is used mostly for the production of fertilizers. Phosphoric acid manufactured by the furnace or thermal process is produced from elemental phosphorus. It is produced in much smaller quantities for uses other than fertilizer applications, such as metal treatment, refractories, catalysts, and food and beverages

Reference : Hudson, R. B. ; Dolan, M. J. (1982), Phosphoric acids and phosphates. In: Grayson, M.; Ecroth, D., eds. Kirk-Othmer encyclopedia of chemical technology; v. 17, peroxides and peroxy compounds, inorganic to piping systems. 3rd ed. New York, NY; John Wiley & Sons; pp.428-472

## 3.2 Estimated quantities

### Estimated quantities

#### [IP] OECD: HPVC

Tonnage 837431 Own use 442152

#### [IP] OECD: HPVC

**Remarks** Estimated production of phosphoric acid in the United States for 1987 was 10,473 thousand tons. Estimated production in 1988 was 11,717 thousand tons, an increase of 11.9 percent from 1987.

Reference : Reisch, M. S. (1989) Top 50 chemicals production reaches record high. Chem. Eng. News 67(15); 11-14

## 3.3 Sites

## 3.4 Form in the supply chain

## 3.5 Identified uses and exposure scenarios

### Overall use and exposure

### Uses and exposure

#### Main use category

- (X) Industrial use
- (X) Professional use
- (X) Consumer use

#### Specification for industrial and professional use

- (X) Used in closed system

( ) Use resulting in inclusion into or onto matrix

( ) Non-dispersive use

(X) Dispersive use

### Significant routes of exposure

#### Human exposure

(X) Oral

(X) Dermal

(X) By inhalation

#### Environmental exposure

(X) Water

(X) Air

( ) Solid waste

(X) Soil

#### Pattern of exposure

( ) Accidental / infrequent

( ) Occasional

(X) Continuous / frequent

### Identified uses and exposure scenarios

#### Identified use

<b>Brief description</b>	fertilizers, cleaning and washing agents, anti-freezing agents, surface-active agents, absorbents, adsorbents, Corrosion inhibitors, colouring agents, pH-regulating agents etc. The manufacture of fertilizers is the largest use of phosphoric acid.
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#### Exposure scenario

### 3.6 Uses advised against

### 3.7 Waste from production and use

### 3.8 Exposure estimates

#### Exposure estimates

[IP] OECD: HPVC

#### Exposure related to production

**Working environment** The Republic of Korea, in the production facilities, phosphoric acid is produced in a closed system. It is well regulated by the following controls, which are being applied in all facilities in Republic of Korea. Engineering controls were washing dust collector. Administration controls were regulation of industrial safety and health and safe work practices within a company. Inhalation exposure are expected to be minimal as personal protective equipments(PPEs) such as dust mask, gas mask, gloves and protective goggles. According to the available monitoring data, the 8hr-TWA(Time Weighted Average) concentrations of the phosphoric acid ranged from 0.002 mg/m<sup>3</sup>, which were below the occupational exposure limit of 1 mg/m<sup>3</sup>.(Reference : National Institute of Environmental Research (NIER), Survey on circulation volume and use pattern of phosphoric acid, Republic of Korea).

There are occupational exposure standard limit values for phosphoric acid as follows;  
 OSHA standards : Permissible Exposure Limit(PEL) : 8hr-Time Weighted Average(TWA) : 1 mg/cm<sup>3</sup>  
 Threshold Limit Values(TLV) : 8hr-Time Weighted Average(TWA) : 1 mg/cm<sup>3</sup> ; 15min Short Term Exposure Limit (STEL) : 3 mg/m<sup>3</sup>  
 NIOSH Recommendations : Recommended Exposure Limit(REL) : 10hr-Time Weighted Average(TWA) : 1mg/cm<sup>3</sup> ; 15min Short Term Exposure Limit(STEL) : 3 mg/m<sup>3</sup>(Reference : <http://toxnet.nlm.nih.gov/>, Hazardous Substance Data Bank(HSDB), US National Library of Medicine)

**Environment** Environmental release to the atmosphere may occur during manufacturing or processing such as loading of phosphate rock, transfer, reaction, filtration etc. Phosphoric acid from manufacturing or processing are controlled by dust collector in the each transfer tower(Reference: National Institute of Environmental Research (NIER), Survey on circulation volume and use pattern of phosphoric acid, Republic of Korea).

#### Exposure related to use

**Consumers** Phosphoric acid can be found in soft drinks(e.g. Coca-cola), food(e.g. jellies, preserves), animal food(e.g. cat food), some cleaning agents. It can be absorbed into the body by inhalation of its aerosol and ingestion. The consumer may be exposed to small quantities of phosphoric acid in the consumption of food and soft drinks and by using some cleaning agents(Reference : National Pollutant Inventory, Australian Government Department of the Environment and Heritage)

### 4 Physical and chemical properties

**Physical and chemical properties**

UUID IUC5-72420c03-8323-4d49-b3c8-4fcad6ef97f2

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-08 17:25:39 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

**Discussion**

Summary of physico-chemical properties for phosphoric acid.

Property	Value	Reference
Physical state	liquid (colourless clear syrupy liquid)	Budavari et al, 1998
Melting point	42.4 °C	Lide, 2004
Boiling point	407 °C	Lide, 2004
Density	1.87 g/cm <sup>3</sup> at 25 °C	Budavari et al, 1998
Vapour pressure	2.75x10 <sup>-9</sup> Pa at 25 °C	ACGIH, 1991
Solubility in water	5480 g/L at 20 °C	Lide, 2004

**4.1 Appearance/physical state/colour*****Appearance/physical state/colour-1 [2] (Budavari et al., 1998)***

UUID IUC5-30c96745-f26c-45f3-b4cf-7f870c1f4667

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-24 17:38:28 KST

Remarks

**Administrative Data****[IP] OECD: HPVC**

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type other: handbook

Reliability 2 (reliable with restrictions)

Rationale for reliability (2g) Data from handbook or collection of data

**Data source****Reference**

Reference type review article or handbook

Author Budavari S, O'Neil M, Smith A, Heckelman P, and Kinnary J

Year 1998

Title The Merck Index, An Encyclopedia of Chemicals, Drugs and Biologicals, 12th Edition on CD-ROM Version 12:2

**Bibliographic source**

Testing laboratory

Report no.

Owner company Chapman &amp; Hall /CRC

Company study no.

Report date

**Data access**

data published

**Materials and methods****GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name Identity

phosphoric acid **Results and****discussion****Physical state at 20°C and 1013 hPa**

liquid clear syrupy liquid

solid orthorhombic crystals

**Colour**

clear

**Substance type**

inorganic

**Appearance/physical state/colour-2 [2] (Lewis, 2002)**

UUID IUC5-6ce9368a-4e73-4f9c-b10c-35dea30f289c

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-24 15:54:42 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type other:

Reliability 2 (reliable with restrictions)

Rationale for reliability (2g) Data from handbook or collection of data

**Data source****Reference**

Reference type review article or handbook

Author Lewis RJ Year 2002

Title Hawley's Condensed Chemical Dictionary 14th ed.

Bibliographic source ISBN 0-471-05532-8

Testing laboratory Report no.

Owner company John Wiley & Sons, Inc., New York

Company study no. Report date

**Data access**

data published

**Materials and methods****Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name Identity

Phosphoric Acid **Results and**

**discussion****Physical state at 20°C and 1013 hPa**

solid

liquid sparkling liquid

**Form**

crystalline

**Colour**

colorless

**Odour**

odourless

**Substance type**

inorganic



**4.2 Melting point/freezing point****Melting point-1 [2] (Budavari et al., 1998 and CRC-handbook, 2004)**

UUID IUC5-de5944b3-5aac-4299-ad65-efc4c690c605

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-24 19:58:55 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type other:

Reliability 2 (reliable with restrictions)

Rationale for reliability (2g) Data from handbook or collection of data

**Data source****Reference**

Reference type review article or handbook

Author Budavari S, O'Neil M, Smith A, Heckelman P, and Kinnary J Year 1998

Title The Merck Index, An Encyclopedia of Chemicals, Drugs and Biologicals, 12th Edition on CD-ROM Version 12:2

Bibliographic source

Testing laboratory Report no.

Owner company Chapman & Hall /CRC

Company study no. Report date

Reference type review article or handbook

Author Lide DR Year 2004

Title CRC HANDBOOK of CHEMISTRY and PHYSICS on CD-ROM, Version 2004

Bibliographic source ISBN 0-8493-2108-5

Testing laboratory Report no.

Owner company CRC PRESS

Company study no. Report date

Reference type review article or handbook

Author Lewis RJ Year 2002

Title Hawley's Condensed Chemical Dictionary 14th ed.

Bibliographic source ISBN 0-471-05532-8

Testing laboratory Report no.

Owner company John Wiley & Sons, Inc., New York

Company study no. Report date

**Data access**

data published

**Materials and methods****Test materials**

Test material equivalent to submission substance identity

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

**Results and discussions****Melting / freezing point**

Melt./Freez. 42.4  
pt.

Atm.  
pressure

Decomposition

Decomp.  
temp.

Sublimation

Subl.  
temp.

Remarks solid, 100%

**Remarks on results including tables and figures**

**Melting point-2 [2] (NPI, 2010)**

UUID IUC5-80dbfc7d-6186-41a7-890d-8c1ec92dc068

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-24 20:49:31 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type other:

Reliability 2 (reliable with restrictions)

Rationale for reliability (2g) Data from handbook or collection of data

**Data source****Reference**

Reference type other:

Author (NPI)National Pollutant Inventory Year 2010

Title Fact sheets: Phosphoric acid

Bibliographic source <http://www.npi.gov.au/substances/phosphoric-acid/index.html>

Testing laboratory Report no.

Owner company Department of the Environment, Water, Heritage and the Arts, Australia

Company study no. Report date

**Data access**

data published

**Materials and methods****Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity Phosphoric Acid

**Results and discussions****Melting / freezing point**

Melt./Freez. pt. 42 °C

Atm. pressure

Decomposition

Decomp. temp.

Sublimation

Subl. temp.

Remarks 100%

Melt./Freez. pt. 21 °C

Atm. pressure

Decomposition

Decomp. temp.

Sublimation

Subl.  
temp.

Remarks 85%

Melt./Freez.  
pt. 18

Atm.  
pressure

Decomposition

Decomp.  
temp.

Sublimation

Subl.  
temp.

Remarks 75%

**4.3 Boiling point*****Boiling point-1 [2] (NPI, 2010)***

UUID IUC5-f62508f5-0a31-4523-96c9-d787942904ed

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-24 20:48:32 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type other:

Reliability 2 (reliable with restrictions)

Rationale for reliability 2g-Data from handbook or collection of data

**Data source****Reference**

Reference type other:

Author NPI (National Pollutant Inventory) Year 2010

Title Fact sheets: Phosphoric acid

Bibliographic source <http://www.npi.gov.au/substances/phosphoric-acid/index.html>

Testing laboratory Report no.

Owner company Department of the Environment, Water, Heritage and the Arts, Australia

Company study no. Report date

**Data access**

data published

**Materials and methods****Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

**Any other information on materials and methods incl. tables****Results and discussions****Boiling point**

Boiling pt. 260

Atm. pressure

Decomposition

Decomp. temp.

Remarks 100%

Boiling pt. 154 °C

Atm. pressure

Decomposition

Decomp. temp.

Remarks 85%

Boiling pt. 135 °C

Atm. pressure

**Decomposition****Decomp.  
temp.****Remarks** 75%**Remarks on results including tables and figures**

**4.4 Density****Density-1 [2] (Budavari et al., 1998)**

UUID IUC5-326272a2-46fe-4137-8328-1df2e214c683

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-08 17:26:48 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type other:

Reliability 2 (reliable with restrictions)

Rationale for reliability (2g) Data from handbook or collection of data

**Data source****Reference**

Reference type review article or handbook

Author Budavari S, O'Neil M, Smith A, Heckelman P, and Kinnary J

Year 1998

Title The Merck Index, An Encyclopedia of Chemicals, Drugs and Biologicals, 12th Edition on CD-ROM Version 12:2

Bibliographic source

Testing laboratory

Report no.

Owner company Chapman & Hall /CRC

Company study no.

Report date

**Data access**

data published

**Materials and methods****Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

**Any other information on materials and methods incl. tables****Results and discussion****Density**

Type density

Density 1.87

Temp. 25 °C

Type density

Density 1.68

Temp. 25 °C

**Remarks on results including tables and figures**

Density at 25 °C

1.8741 (100% solution)

1.6850 (85% solution)

1.3334 (50% solution)

1.0523 (10% solution)

**4.6 Vapour pressure*****Vapour pressure-1 [2] (SRC, 2010)***

UUID IUC5-29f9d19d-aa39-4024-b830-8acc660ace56

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-26 15:39:40 KST

Remarks

**Administrative Data**

[IP] OECD: HPV

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type other: database

Reliability 2 (reliable with restrictions)

Rationale for reliability (2g) Data from handbook or collection of data

**Data source****Reference**

Reference type other: database

Author SRC Year 2010

Title Data From SRC PhysProp Database : Phosphoric acid

Bibliographic source <http://www.syrres.com/what-we-do/databaseforms.aspx?id=386>

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Materials and methods****Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

**Any other information on materials and methods incl. tables****Results and discussions****Vapour pressure**

0.00000275 kPa at 25 °C

Remarks Estimated Data, Ref: MEYLEA, WM & HOWARD, PH (1985)

**Remarks on results including tables and figures**



**4.7 Partition coefficient*****Partition coefficient***

UUID IUC5-c847c085-084b-403a-a3a5-93a21d56327c

Dossier UUID 0

Author nier1 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2009-03-18 14:42:45 KST

Remarks

**Administrative Data****[IP] OECD: HPV**C**Short description of key information**

The Octanol-water partition coefficients are not relevant for inorganic substances.

**4.8 Water solubility*****Water solubility-1 [2] (Lide, 2004)***

UUID IUC5-c3536ee1-3131-4776-9ddd-f0b6a638746b

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-26 15:44:44 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type other:

Reliability 2 (reliable with restrictions)

Rationale for reliability (2g) Data from handbook or collection of data

**Data source****Reference**

Reference type review article or handbook

Author Lide DR Year 2004

Title CRC HANDBOOK of CHEMISTRY and PHYSICS on CD-ROM, Version 2004

Bibliographic source ISBN 0-8493-2108-5

Testing laboratory Report no.

Owner company CRC PRESS

Company study no. Report date

**Data access**

data published

**Materials and methods****Test materials**

Test material equivalent to submission substance identity

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

**Results and discussions****Water solubility**

5480 g/L

Temp. 20 °C

pH

Remarks on results including tables and figures

**4.13 Flammability*****Flammability***

UUID IUC5-ed7ee812-7577-4018-baf6-00508c0900d8

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2009-01-02 16:09:41 KST

Remarks

**Administrative Data****[IP] OECD: HPVC****Key parameter (optional)**

Flammability non flammable

**4.16 Oxidation reduction potential*****Oxidation reduction potential***

UUID IUC5-4803f51c-31be-4f9c-a90b-d506465f6cde

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-08 17:27:29 KST

Remarks

**Administrative Data****[IP] OECD: HPVC****Discussion**

There is no information available.

**4.21 Dissociation constant*****Dissociation constant-1 [2] (Budavari et al., 1998)***

UUID IUC5-606e233e-ac8c-41b8-92ac-c1b641476b63

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-26 15:46:25 KST

Remarks

**Administrative Data**

OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type other:

Reliability 2 (reliable with restrictions)

Rationale for reliability (2g) Data from handbook or collection of data

**Data source****Reference**

Reference type review article or handbook

Author Budavari S, O'Neil M, Smith A, Heckelman P, and Kinnary J

Year 1998

Title The merck index

Bibliographic source The Merck Index, An Encyclopedia of Chemicals, Drugs and Biologicals, 12th Edition on CD-ROM Version 12:2, Chapman & Hall /CRC

Testing laboratory

Report no.

Owner company

Company study no.

Report date

**Data access**

data published

**Materials and methods****Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity Phosphoric Acid

**Results and discussions****Dissociation constant**

No. #1 pKa 2.15 at

Remarks

No. #2 pKa 7.09 at

Remarks

No. #3 pKa 12.32 at

Remarks

**5 Environmental fate and pathways****5.1 Stability****5.1.1 Phototransformation in air*****Phototransformation in air***

UUID IUC5-ace3d97d-dde2-4918-b89a-4e227e84577a

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-08 17:28:00 KST

Remarks

**Administrative Data****[IP] OECD: HPVC****Discussion**

The photodegradation is not applicable to inorganic substances like phosphoric acid. In the aquatic environment, phosphoric acid will dissociate and release  $\text{H}^+$ ,  $\text{H}_2\text{PO}_4^-$  and  $\text{HPO}_4^{2-}$  ions. The dissociated ions will not be subject to photodegradation.

**5.1.2 Hydrolysis*****Hydrolysis***

UUID IUC5-c7b5dc22-90b7-4474-a9e6-32d5068ae271

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-08 17:28:19 KST

Remarks

**Administrative Data****[IP] OECD: HPVC****Discussion**

Phosphoric acid dissociates in water into its respective ions ( $\text{H}^+$ ,  $\text{H}_2\text{PO}_4^-$  and  $\text{HPO}_4^{2-}$ ). Standard hydrolysis studies are not relevant.

**5.2 Biodegradation*****Biodegradation***

UUID IUC5-17235b7e-f300-4128-8e56-d9c82e817806

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-08 17:28:31 KST

Remarks

**Administrative Data****[IP] OECD: HPVC****Discussion**

Standard biodegradation tests are not applicable to inorganic substances because the methods are based on carbon oxidation.



### **5.3 Bioaccumulation**

#### ***Bioaccumulation***

UUID IUC5-f3229c21-eee7-43ab-b81d-6df6446d1daa

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-08 17:28:42 KST

Remarks

#### **Administrative Data**

**OECD: HPV**

#### **Discussion**

The bioaccumulation potential seems to be low based on a BCF value of 3.162 estimated with BCFWIN (from the US EPA EPI Suite).

Bioaccumulation is not anticipated for inorganic compounds that are miscible with water such as phosphoric acid.

## 5.4 Transport and distribution

### 5.4.1 Adsorption / desorption

#### Adsorption / desorption-1 [2] (Environment Canada, 1981)

UUID IUC5-ab324df2-1b28-4cc6-9b05-4ba73a7c5bd4

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-08 17:29:15 KST

Remarks

## Administrative Data

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type other:

Reliability 2 (reliable with restrictions)

Rationale for reliability (2g) Data from handbook or collection of data

## Data source

### Reference

Reference type other: database

Author Environment Canada Year 1981

Title Tech Info for Problem Spills: Phosphoric Acid (Draft). In: HSDB

Bibliographic source p. 51

Testing laboratory Report no.

Owner company

Company study no. Report date

### Data access

data published

## Materials and methods

### Test materials

#### Test material equivalent to submission substance identity

yes

#### Test material identity

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity Phosphoric Acid

## Overall remarks, attachments

### Overall remarks

When spilled onto soil, phosphoric acid will infiltrate downward, the rate being greater with lower concentration because of reduced viscosity. During transport through the soil, phosphoric acid will dissolve some of the soil material, in particular, carbonate-based materials. The acid will be neutralized to some degree with adsorption of the proton and phosphate ions also possible. However, significant amounts of acid will remain for transport down toward the groundwater table. Upon reaching the groundwater table, the acid will continue to move in the direction of groundwater flow. A contaminated plume will be produced with dilution and dispersion serving to reduce the acid concentration.

## 5.6 Additional information on environmental fate and behaviour

### *Additional information on environmental fate and behaviour-1 [2] (US EPA, 2000)*

**UUID** IUC5-ba04d3e2-785d-4455-b688-f49386b45e5f  
**Dossier UUID** 0  
**Author** nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
**Date** 2011-04-08 17:29:36 KST  
**Remarks**

#### Administrative Data

[IP] OECD: HPVC

**Purpose flag** supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS  
**Study result type** other:  
**Reliability** 2 (reliable with restrictions)  
**Rationale for reliability** (2g) Data from handbook or collection of data

#### Data source

##### Reference

<b>Reference type</b>	review article or handbook		
<b>Author</b>	US EPA(United State Environmental Protection Agency)	<b>Year</b>	2000
<b>Title</b>	Phosphoric Acid; Community Right-to-Know Toxic Chemical Release Reporting		
<b>Bibliographic source</b>	<a href="http://www.epa.gov/EPA-TRI/2000/June/Day-27/tri16182.htm">http://www.epa.gov/EPA-TRI/2000/June/Day-27/tri16182.htm</a>		
<b>Testing laboratory</b>		<b>Report no.</b>	
<b>Owner company</b>			
<b>Company study no.</b>		<b>Report date</b>	

#### Materials and methods

##### Test materials

##### Test material equivalent to submission substance identity

yes

##### Test material identity

**Identifier** CAS number  
**Identity** 7664-38-2  
**Identifier** IUPAC name  
**Identity** Phosphoric Acid

#### Overall remarks, attachments

##### Overall remarks

Phosphoric acid has an important eutrophication potential similar to that of inorganic phosphate. Eutrophication is the nutrient enrichment of waters resulting in stimulation of an array of undesirable symptomatic changes in the aquatic ecosystem. Therefore, phosphoric acid can reasonably be anticipated to cause significant adverse effects on the environment. Phosphoric acid, as well as other phosphates, has the potential to cause increased algal growth leading to eutrophication in the aquatic environment. Eutrophication may result when excessive phosphates enter into an aquatic ecosystem in the presence of sunlight and nitrogen. The phosphate ion is a plant nutrient and it can be a major limiting factor for plant growth in freshwater environments. When levels of phosphate are limited, plant growth is controlled. In excess, however, phosphate from phosphoric acid can cause extreme algal blooms. Toxic effects result from oxygen depletion as the algae die and decay. Toxic effects have also been related to the release of decay products or direct excretion of toxic substances from sources such as blue-green algae. In addition, phosphates in aquatic environments may encourage the growth of introduced plants to the detriment of native plants and thereby change plant distribution.

## **6 Ecotoxicological Information**

### **6.1 Aquatic toxicity**

#### ***Aquatic toxicity***

UUID IUC5-5a28f7f4-4cc1-4da7-bced-fbc43c6ff014

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-08 17:30:17 KST

Remarks

#### **Administrative Data**

[IP] OECD: HPVC

#### **Discussion**

##### **1. Short-term toxicity**

###### **1) Fish**

*Oryzias latipes*: 96-h LC<sub>50</sub> : 75.1 mg/L (between pH 4.45 and 3.39)

*L. macrochirus*: 96-h LC<sub>50</sub> : pH 3.5 ~ 3.0

*Aphanius dispar*: 96-h LC<sub>50</sub> : pH 3.5 ~ 3.25

Mosquito fish: 96-h TLm : 138 mg/L

###### **2) Aquatic invertebrate**

*Daphnia magna*: 48-h EC<sub>50</sub> : > 376 mg/L ( with adjustment of pH, between pH 7.95 and 7.53)

###### **3). Algae**

*Pseudokirchneriella subcapitata*: 72-h EC<sub>50</sub> : 77.9 mg/L (growth rate, between pH 5.61 and 3.4) and 32.0 mg/L (yield, between pH 7.48 and 5.61)

##### **2. Long-term toxicity**

No data are available to aquatic organisms.

**6.1.1 Short-term toxicity to fish*****Short-term toxicity to fish***

UUID IUC5-b953796c-a2f0-4e36-b41c-2e449e96a2d6

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-08 17:31:42 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

**Key parameter (optional)**

LC50 75.1  
for  
freshwater  
fish  
in  
mg/L

LC50  
for  
marine  
water  
fish  
in  
mg/L

**Discussion**

Table1. Summary of short-term toxicity to fish.

Species	Exposure time	LC <sub>50</sub> value
Red killifish, <i>Oryzias latipes</i>	96h	75.1 mg/L (between pH 4.45 and 3.39)
Bluegill, <i>L. macrochirus</i>	96h	Between pH 3.5 and pH 3.0
<i>Aphanius dispar</i>	96h	Between pH 3.5 and pH 3.25
Mosquito fish	96h	Other : TLm 138mg/L

1. The 96hr-LC<sub>50</sub> value of phosphoric acid to red killifish, *Oryzias latipes* was determined as 75.1 mg/L (between pH 4.45 and 3.39).
2. The concentration of hydrogen ions which caused 50% lethality in 96h (96h LC<sub>50</sub>) in the bluegill, *L. macrochirus*, was between pH 3.5 and 3.0 for phosphoric acid.
3. The hydrogen ion concentration of the phosphoric acid which cause 50% mortality of *Aphanius dispar* in 96h was between pH 3.5 and 3.25.
4. The 96hr-TLm of phosphoric acid to mosquito fish was 138mg/L.

**Short-term toxicity to fish.001**

UUID IUC5-9767a5ed-6f0e-4092-bc48-409f60516634

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 09:47:05 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result Study period June 20, 2005-July 8, 2005

Reliability 1 (reliable without restriction)

Rationale for reliability 1a- GLP guideline study

**Data source****Reference**

Reference type study report

Author National Institute of Environmental Research (NIER), Korea

Year 2005

Title Acute Toxicity Test of Phosphoric acid to Red Killifish, *Oryzias latipes*

Bibliographic source

Testing laboratory Korea Institute of Toxicology, Korea Research Institute of Chemical Technology(KRICT) Report no. EG05040

Owner company

Company study no.

Report date

**Data access**

data submitter is data owner

**Data protection claimed**

yes, but willing to share

**Materials and methods****Test guideline**

Qualifier according to

Guideline OECD Guideline 203 (Fish, Acute Toxicity Test)

Deviations no

**GLP compliance**

yes (incl. certificate)

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Details on test material**

Purity: 99.999%, 85 wt. % in H<sub>2</sub>O

Description: Colorless liquid Supplier:

Aldrich , Lot No. 09604TR

**Analytical monitoring**

yes

**Details on sampling**

Stability test of the test substance : Stability of the test substance in the test medium was determined during the test period using 100 mg/L test solution prepared at preliminary test. Total 30 mL (10 mL × 3 replicates) of each test solution was taken at 0, 24, 48, 72 and 96 hrs.

Analysis of the test substance in the test solution : The concentrations of the test substance were analyzed from all test solutions

at 0, 48 and 96 hrs of the test. Total 30 mL (10 mL x 3 replicates) of test solution was taken.

#### **Details on analytical methods**

ICP-AES analysis was performed.

#### **Details on test solutions**

Culturing and dilution water : Tap water was passed through a membrane filter (1µm).

Preparation of test solutions : 50 mL aliquot of stock solution (1200, 2000, 3500, 5900, and 10000 mg/L) was added to each 4,950 mL of dilution water to give the desired exposure concentration of 12, 20, 35, 59, and 100 mg/L. The control used dilution water only.

#### **Test organisms**

##### **Test organisms (species)**

Oryzias latipes

##### **Details on test organisms**

Name : Red killifish (Oryzias latipes)

Age : 3 month old

Length : 2.7 cm (SD = 0.1 cm)

Body weight : 0.16 g (SD = 0.02g)

Source : The ecotoxicology Research Team, Korea Institute of Toxicology (KIT), KRICT, Deajeon, Korea (origin: Laboratory of Freshwater Fish stocks, Bioscience Center, Nagoya University, Japan) Acclimation :

46 fish in a 40 L glass container for 7 days before the definitive test. Food supply :

No food during the 24 hour period immediately prior to exposure.

#### **Study design**

##### **Test type**

static

##### **Water media type**

freshwater

##### **Limit test**

no

##### **Total exposure duration**

96 h **Remarks**

#### **Test conditions**

##### **Hardness**

41.7 mg/L (as CaCO<sub>3</sub>)

##### **Test temperature**

23.6±0.2°C

##### **pH**

3.39~7.80

##### **Dissolved oxygen**

6.3~8.3 mg/L (75~97% of ASV)

##### **Nominal and measured concentrations**

Nominal test concentration: 0, 12, 20, 35, 59 and 100 mg/L

Mean measured test concentration: 0, 14.3, 23.6, 42.0, 70.5 and 120.0 mg/L

##### **Details on test conditions**

Experiment Design : Seven fish were exposed (not replicated).

The photoperiod : 16 hours light and 8 hours dark with 30 minute dawn and dusk transition period.

The intensity : 670~840 lux.

Food supply : No food and air

#### **Any other information on materials and methods incl. tables**

##### **The results of range-finding test showing the effects of pH in the 100mg/L of test solution**

Treatments	Initial pH	No. of fish tested	Cumulative No. of dead fish		
			0hr	24hr	48hr
100mg/L (pH adjustment to 7.00)	3.32	5	0	0	0
100mg/L (No pH adjustment)	3.34	5	0	5	5
10mg/L (No pH adjustment)	6.78	5	0	0	0

Test concentrations: No mortality was observed at 100mg/L with pH adjustment. However, 100% mortality was observed at 100mg/L while no mortality was observed at 10mg/L in the normal range-finding test. The definitive test was carried out without adjustment of pH.

##### **Statistical analysis and expression of the results**

LC<sub>50</sub> values and 95% confidence limits were calculated using the Moving-Average Angle Method (EPA/600/4 -85/013, 1985) since partial lethal concentrations were observed at less than two concentrations between 0% and 100% death concentration.

## Results and discussions

### Effect concentrations

Duration 24 h  
Endpoint LC50  
Effect conc. 75.1 mg/L

#### Nominal/Measured

Conc.  
based  
on  
Basis  
for  
effect  
Remarks  
(e.g.  
95%  
CL) 67.3~82.9

Duration 48 h  
Endpoint LC50  
Effect conc. 75.1 mg/L

#### Nominal/Measured

Conc.  
based  
on  
Basis  
for  
effect  
Remarks  
(e.g.  
95%  
CL) 67.3~82.9

Duration 72 h  
Endpoint LC50  
Effect conc. 75.1 mg/L

#### Nominal/Measured

Conc.  
based  
on  
Basis  
for  
effect  
Remarks  
(e.g.  
95%  
CL) 67.3~82.9

Duration 96 h  
Endpoint LC50  
Effect conc. 75.1 mg/L

#### Nominal/Measured

Conc.  
based  
on  
Basis  
for  
effect  
Remarks  
(e.g.  
95%  
CL) 67.3~82.9

### Details on results

There were no mortalities and adverse effects observed in any of the fish exposed to control group. However, 7 fish died in the 100 mg/L treatment groups during the test (Table 1). Some fish exposed to test substance were seen losing equilibrium (Table 3). All results are expressed in terms of mean measured concentration. The LC50 values, the highest test concentrations resulting in 0% mortality, the lowest test concentrations resulting 100% mortality, and no-observed effect levels of the test substance are in Table 4.

### Any other information on results incl. tables

Table 1. Cumulative mortality of *Oryzias latipes*



Mean measured concentration (mg/L)	Number of organisms tested	Cumulative number of dead fish			
		24 hrs	48 hrs	72 hrs	96 hrs
Control	7	0	0	0	0
14.3	7	0	0	0	0
23.6	7	0	0	0	0
42.0	7	0	0	0	0
70.5	7	0	0	0	0
120.0	7	7	7	7	7

Table 2. pH

Mean measured conc.(mg/L)	0hr	24hr	48hr	72hr	96hr
Control	7.80	7.40	7.39	7.30	7.21
14.3	6.75	7.01	7.18	7.12	7.16
23.6	6.46	6.67	7.07	7.00	7.04
42.0	6.05	6.29	6.71	6.66	6.66
70.5	4.19	4.25	4.48	4.44	4.45
120.0	3.39	-	-	-	-

Table 3. Symptoms of intoxication of the test substance to *Oryzias latipes*

Mean measured concentration (mg/L)	Symptoms of Intoxication			
	24 hrs	48 hrs	72 hrs	96 hrs
Control	NOR(7)	NOR(7)	NOR(7)	NOR(7)
14.3	NOR(7)	NOR(7)	NOR(7)	NOR(7)
23.6	NOR(7)	NOR(7)	NOR(7)	NOR(7)
42.0	NOR(7)	NOR(7)	NOR(7)	NOR(7)
70.5	NOR(7)	NOR(7)	NOR(6), LOE(1)	NOR(6), LOE(1)
120.0	-	-	-	-

(( ): No. of fish, NOR : Normal, LOE : Loss of equilibrium)

Table 4. Summary of test results

Exposure time	24 hrs	48 hrs	72 hrs	96 hrs
LC <sub>50</sub> value	75.1	75.1	75.1	75.1
95% confidence limits	67.3~82.9	67.3~82.9	67.3~82.9	67.3~82.9
Highest test concentration resulting in 0% mortality	70.5	70.5	70.5	70.5
Lowest test concentration resulting in 100% mortality	120.0	120.0	120.0	120.0
No-observed effect level	70.5	70.5	42.0	42.0

(Unit: mg/L, mean measured test concentration)

## Overall remarks, attachments

### Overall remarks

## Applicant's summary and conclusion

### Conclusions

The 96hr-LC<sub>50</sub> value of phosphoric acid to red killifish, *Oryzias latipes* was determined as 75.1 mg/L (between pH 4.45 and 3.49).

### Executive summary

The study was conducted to assess the acute toxicity of phosphoric acid (CAS No.7664-38-2) to red killifish (*Oryzias latipes*) under the static system.

The study was conducted in accordance with the OECD Guidelines for the Testing of Chemicals No. 203 Fish, Acute Toxicity Test (Adopted: 17 July,1992).

The toxicity test was performed in control, 14.3, 23.6, 42.0, 70.5, and 120.0 mg/L (mean measured concentration) of phosphoric acid. Seven adult fish were exposed to each treatment concentration. Observations were made on the number of dead fish and the incidence of sub-lethal effects after 24, 48, 72, and 96 hours of exposure.

The following values, expressed in terms of the mean measured concentrations, were obtained from the test.

(Unit : mg/L)

Time	48 hours	96 hours
LC <sub>50</sub>	75.1	75.1

95% confidence limits	67.3~82.9	67.3~82.9
Highest test concentration resulting in 0% mortality	70.5	70.5
Lowest test concentration resulting in 100% mortality	120.0	120.0
No observed effect level	70.5	42.0

All results were expressed in terms of the mean measured concentrations as the mean measured concentrations of test substance in the test solutions were ranged from 117% to 123% of nominal concentration throughout the test period.

**Short-term toxicity to fish.002**

UUID IUC5-accf4862-a619-480c-a9c2-06b806f73ea7

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 14:32:09 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 2 (reliable with restrictions)

Rationale for reliability 2e-Study well documented, meets generally accepted scientific principles, acceptable for assessment

**Data source****Reference**

Reference type publication

Author Ellgaard, E.G. and Gilmore III, J.Y. Year 1984

Title Effects of different acids on the bluegill sunfish, *Lepomis macrochirus* Rafinesque

Bibliographic source J. Fish Biol. 25(2): 133-137.

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Materials and methods****Test guideline**

Qualifier no guideline followed

Guideline

Deviations

**GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Analytical monitoring**

no

**Test organisms****Test organisms (species)**

*Lepomis macrochirus*

**Details on test organisms**

Name : Bluegill, *L. macrochirus*

Length : 4cm(T.L.)

Source : A state fish hatchery in Louisiana

Culture water : Dechlorinated tap water

**Study design****Test type**

static

**Water media type**

freshwater

**Limit test**

no

**Total exposure duration**

96 h Remarks

**Test conditions****Test temperature**

23 ± 2°C

**pH**

7.5, 5.0, 4.5, 4.0, 3.5, 3.25 and 3.0

**Details on test conditions**

Experiment Design : Eight fish were exposed in aquaria.

pH : Lethal concentrations were initially maintained at pH7.5.

Stabilization period : 1 week

**Results and discussions****Effect concentrations**

Duration	24 h
Endpoint	LC50
Effect conc.	3 — 3.25 pH

**Nominal/Measured**Conc.  
based  
on

Basis for effect	mortality
------------------	-----------

Remarks  
(e.g.  
95%  
CL)

Duration	48 h
Endpoint	LC50
Effect conc.	3 — 3.25 pH

**Nominal/Measured**Conc.  
based  
on

Basis for effect	mortality
------------------	-----------

Remarks  
(e.g.  
95%  
CL)

Duration	96 h
Endpoint	LC50
Effect conc.	3 — 3.25 pH

**Nominal/Measured**Conc.  
based  
on

Basis for effect	mortality
------------------	-----------

Remarks  
(e.g.  
95%  
CL)**Details on results**

The mortality of bluegill, *L. macrochirus*, exposed to various concentrations of the phosphoric acid is presented in Table 1. The 96h-LC50 was between pH 3.25 and 3.0. No acute mortality was observed in phosphoric acid until the pH reached 3.5. When, however, the pH reached 3.0 the mortality was 100%.

Any other information on results incl. tables

Table 1. Mortality of *L. macrochirus* exposed to phosphoric acid. No fish died in control aquaria maintained at pH 7.5

Hours of exposure	Percentage mortality at pH				
	5.0	4.5	4.0	3.25	3.0
-	0	0	0	13	100
24	0	0	0	13	100
48	0	0	0	13	100
96	0	0	0	13	100

### Overall remarks, attachments

Overall remarks

### Applicant's summary and conclusion

#### Conclusions

The concentration of hydrogen ions which caused 50% lethality in 96h (96h LC50) in the bluegill, *L. macrochirus*, was between pH 3.25 and 3.0 for phosphoric acid.

**Short-term toxicity to fish.003**

UUID IUC5-f70f5bce-7844-44e2-a2c7-6d49125eac23

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 09:48:56 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 3 (not reliable)

Rationale for reliability 3a-Documentation insufficient for assessment

**Data source****Reference**

Reference type publication

Author Alkahem, H.F. Year 1989

Title Effect of different acids on the freshwater fish. Aphanus dispar

Bibliographic source J. Biol. Sci. Res. 20(3): 537-545

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Materials and methods****Test guideline**

Qualifier no guideline followed

Guideline

Deviations

**GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Test organisms****Test organisms (species)**

other: Aphanus dispar

**Details on test organisms**

Name : Freshwater fish, Aphanus dispar

Weight :  $1.92 \pm 0.01$  g

Length :  $45.4 \pm 2.1$  mm

Source : From Irrigation canal (Al-Kharj) by hand nets

Acclimation : Two weeks

Culture water : Dechlorinated tap water

**Study design****Test type**

static

**Water media type**

freshwater

**Limit test**

no

**Total exposure duration**

96 h Remarks

**Test conditions****Test temperature**

22.1 ± 0.5°C

**pH**

4.5, 4.0, 3.75, 3.5, 3.25 and 3.0

**Details on test conditions**

Experiment Design : 15 fish were exposed

The pH of water was measured by Metrohm-632 pH meter.

**Any other information on materials and methods incl. tables****Results and discussions****Effect concentrations**

Duration	24 h
Endpoint	LC50
Effect conc.	3 — 3.25 pH

**Nominal/Measured**Conc.  
based  
on

Basis for effect	mortality
------------------	-----------

Remarks  
(e.g.  
95%  
CL)

Duration	48 h
Endpoint	LC50
Effect conc.	3 — 3.25 pH

**Nominal/Measured**Conc.  
based  
on

Basis for effect	mortality
------------------	-----------

Remarks  
(e.g.  
95%  
CL)

Duration	72 h
Endpoint	LC50
Effect conc.	3.25 — 3.5 pH

**Nominal/Measured**Conc.  
based  
on

Basis for effect	mortality
------------------	-----------

Remarks  
(e.g.  
95%  
CL)

Duration	96 h
Endpoint	LC50
Effect	3.25 — 3.5 pH

conc.

Nominal/Measured

Conc.  
based  
onBasis  
for  
effect mortalityRemarks  
(e.g.  
95%  
CL)**Details on results**

Exposure of *Aphanius dispar* to the lethal pH resulted in hyperactivity and the test animals show restlessness erratic swimming with occasional convulsion in the initial stage. On prolongation of time the fish settled at bottom motionless at high pH (4.5 and 4.0) but at low pH (3.25 and 3.0) they show restlessness throughout the experimental periods. The data embodied in table 1 were subjected to prohibit analysis (Finney, D. J., 1952)

**Any other information on results incl. tables****Table 1. Percentage mortality of *Aphanius dispar* at different time intervals after exposure of various levels of activity.**

Exposure (Time) h	Percentage mortality at pH					
	4.5	4.0	3.75	3.5	3.25	3.0
<b>H<sub>3</sub>PO<sub>4</sub></b>						
6	-	-	-	-	-	-
24	-	6.66	-	13.33	13.33	100
48	-	6.66	6.66	26.66	26.66	100
72	-	6.66	13.33	33.33	53.33	100
96	-	6.66	20.00	40.00	80.00	100

**Applicant's summary and conclusion****Conclusions**

The hydrogen ion concentration of the phosphoric acid which cause 50% mortality of *Aphanius dispar* in 96h are between 3.5 pH and 3.25 pH.



**Short-term toxicity to fish.004**

UUID IUC5-697de085-74a7-4652-9774-9e9242e9624e

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 09:50:01 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type no data

Reliability 4 (not assignable)

Rationale for reliability 4c- Original reference not available

**Data source****Reference**

Reference type publication

Author R. von Burg Year 1992

Title Phosphoric acid/Phosphates a Review

Bibliographic source Journal of Applied Toxicology, 12(4). 301-303.

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Materials and methods****GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Analytical monitoring**

no data

**Vehicle**

no data

**Test organisms****Test organisms (species)**

other: Mosquito fish

**Study design****Test type**

no data

**Water media type**

no data

**Total exposure duration**

96 h Remarks

**Test conditions****Any other information on materials and methods incl. tables**

HSDB(2005). Hazardous Substance Data Bank (HSDB/1187).

Ecotoxicity Values

TLm mosquito fish 138mg/L/24-96hr in turbid water at 22-24 deg C. (Conditions of bioassay not specified.)

[Environment Canada; Tech Info for Problem Spills: Phosphoric Acid (Draft) p.61 (1981)]

**Results and discussions****Effect concentrations**

Duration	96 h
Endpoint	other: TLm
Effect conc.	138 mg/L

**Nominal/Measured**

Conc.  
based  
on

Basis  
for  
effect

Remarks  
(e.g.  
95%  
CL)

**Overall remarks, attachments**

Overall remarks

**Applicant's summary and conclusion**

Executive summary

**6.1.3 Short-term toxicity to aquatic invertebrates*****Short-term toxicity to aquatic invertebrates.001***

UUID IUC5-7c699f08-0429-44d1-a611-581c848e77ee

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 10:06:08 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result Study period September 22, 2005-October 8, 2005

Reliability 1 (reliable without restriction)

Rationale for reliability 1a-GLP guideline study **Data**

**source****Reference**

Reference type study report

Author National Institute of Environmental Research (NIER)

Year 2005

Title Acute toxicity test of Phosphoric acid to Daphnia magna.

Bibliographic source

Testing laboratory Korea Institute of Toxicology, Korea Research Institute of Chemical Technology (KRICT) Report no. EG05041

Owner company

Company study no.

Report date

**Data access**

data submitter is data owner

**Data protection claimed**

yes, but willing to share

**Materials and methods****Test guideline**

Qualifier according to

Guideline OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test)

Deviations no

**GLP compliance**

yes (incl. certificate)

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Details on test material**

Purity: 99.999%, 85wt. % in H<sub>2</sub>O

Description: Colorless liquid

Source: Sigma-Aldrich Co., Lot No. 09604TR

**Analytical monitoring**

yes

**Details on sampling**

The concentrations of the test substance were analyzed in control and test solutions at 0 and 48 hrs. 10mL of samples was taken from test solution and filtered using 0.45µm syringe filter.

**Details on analytical methods**

Test solutions were analyzed with ICP-AES.

**Details on test solutions**

1. Culturing and dilution water : M4 medium
2. Test solution preparation
  - 1) Range-finding test concentration : Each 1 mL of stock solutions was added to 99 mL of test medium to give exposure level of 0.1, 1, 10 and 100mg/L (without pH adjustment). The pH of 100 mg/L test solution was 3.65. Therefore, pH of 10 and 100 mg/L test solution were adjusted to pH 8.0 (equivalent to the pH level of 0.1 mg/L test solution) by adding 1N-NaOH. Precipitation of the test substance was observed in the pH adjusted 100mg/L test solution.
  - 2) Definitive test : Each 1 mL of stock solutions (2,500, 5,000, 10,000, 20,000 and 40,000 mg/L) was added to 99 mL of test medium to give exposure level of 29, 61, 81, 157 and 376 mg/L and then pH were adjusted to  $8.0 \pm 0.2$ . Only the dilution water was used for the control. Precipitation of the test substance was observed in the test solution 81, 157 and 376 mg/L.

**Test organisms****Test organisms (species)**

Daphnia magna

**Details on test organisms**

Name : Daphnia magna Straus

Source : The ecotoxicology Research Team, Korea Institute of Toxicology (KIT), KRICT, Deajeon, Korea (origin: the Institute of Ecological Chemistry, GSF, Germany)

Test organism : First-instar Daphnia magna neonates (< 24 hours old)

Photoperiod : 16 hours of continuous artificial light and 8 hours of continuous darkness with 30 minutes dawn and dusk transition periods.

Temperature : 18~22°C during the culture period.

**Study design****Test type**

static

**Water media type**

freshwater

**Limit test**

no

**Total exposure duration**

48 h

**Remarks****Test conditions****Hardness**

265 mg/L (as CaCO<sub>3</sub>)

**Test temperature**

20.4± 0.3°C

**pH**

7.50 to 8.14

**Dissolved oxygen**

8.4 ~ 8.9 mg/L (% saturation: 92~98 %)

**Nominal and measured concentrations**

Nominal test concentrations: 0, 25, 50, 100, 200 and 400 mg/L

Mean measured test concentrations: 0, 29, 61, 81, 157 and 376 mg/L

**Details on test conditions**

Light intensity : Between 650 and 660 Lux.

Feeding and aeration : Without feeding and aeration during 48 hours of exposure period.

Experimental design : Thirty daphnids (three replicates)

Criteria of effect : The symptoms of intoxication and immobilisation were examined daily. The criterion of immobilisation employed in this study was an inability to swim for approximately 15 seconds after gentle agitation.

**Any other information on materials and methods incl. tables****Evaluation of data**

EC<sub>50</sub> and 95% confidence limits were not calculated, therefore EC<sub>50</sub> value was expressed as above the highest test concentration in this test.

**Deviations from the protocols and guidelines**

The statistical analysis was not conducted because 376 mg/L (mean measured concentration) of test substance showed immobilization less than 50%. 24hr- and 48hr-EC<sub>50</sub> values were expressed as above the highest test concentration in this test.

#### Definitive test concentration

In 48 -hour pre-test without pH adjustment, there was 100% immobilisation at 100mg/L, but none at 10 mg/L. In 48 -hour pre-test with pH adjustment, there was 50% immobilisation at 100mg/L, but none at 10 mg/L. To estimate 48hr-EC<sub>50</sub> with pH adjustment, the test concentration for the definitive test were determined as follows:

-Nominal test concentrations: Control, 25, 50, 100, 200, 400 mg/L

-Mean measured test concentrations: Control, 29, 61, 81, 157, 376 mg/L

## Results and discussions

### Effect concentrations

Duration 24 h  
Endpoint EC50  
Effect conc. > 376 mg/L  
Nominal/Measured meas. (geom. mean)

Conc. based on Basis for effect

Remarks (e.g. 95% CL)

Duration 48 h  
Endpoint EC50  
Effect conc. > 376 mg/L

Nominal/Measured meas. (geom. mean)

Conc. based on Basis for effect

Remarks (e.g. 95% CL)

### Details on results

No immobilisation and adverse effects was observed in control. The number of immobilised daphid at 157 and 376 mg/L was one each at 24 hours. At 48 hours, one daphnid at 157 mg/L and 3 daphnids at 376 mg/L were immobilized (Table 1). Any abnormal behaviors of the daphnids were not observed in each treatment group during the test period (Table 2). All results were expressed in terms of measured concentration. The EC50 values and other parameters were shown in Table 3.

### Remarks on results including tables and figures

Table 1. Cumulative immobilisation data for *Daphnia magna*

Measured Concentration (mg/L)	Number of organisms tested	Cumulative number of organisms immobilized	
		24 hrs	48 hrs
Control	30	0	0
29	30	0	0
61	30	0	0
81	30	0	0
157	30	1	1
376	30	1	3

Table 2. Symptoms of intoxication of the test substance to *Daphnia magna*

Measured Concentration (mg/L)	Symptoms of Intoxication	
	24 hrs	48 hrs
Control	NOR(30)	NOR(30)
29	NOR(30)	NOR(30)
61	NOR(30)	NOR(30)
81	NOR(30)	NOR(30)
157	NOR(29)	NOR(29)
376	NOR(29)	NOR(27)

(( ) : No. of *Daphnia magna*, NOR : Normal)

**Table 3. Summary of test results**

Parameter	24 hours	48 hours
EC <sub>50</sub> values	> 376 mg/L	> 376 mg/L

**Applicant's summary and conclusion****Conclusions**

The 48hr-EC50 values of Phosphoric acid to *Daphnia magna* was determined as > 376 mg/L (with adjustment of pH ).

**Executive summary**

The study was conducted to assess the acute toxicity of phosphoric acid (CAS No. 7664 -38 -2) to *Daphnia magna*. The study was conducted in accordance with the OECD Guidelines for the Testing of Chemical No. 202. " *Daphnia* sp., Acute Immobilisation Test (Adopted: 13th April 2004)".

Thirty daphnids (less than 24 hours old) per treatment level, in three replicates of 10 each, were exposed to measured concentration of 29, 61, 81, 157 and 376 mg/L of test substance and control for 48 hours under static conditions. The incidence of immobilization was recorded for each treatment level at 24 and 48 hours. The following values, expressed in terms of measured concentrations, were derived from the test.

Exposure period	24 hours	48 hours
EC <sub>50</sub>	> 376 mg/L	> 376 mg/L

The concentrations were expressed as geometric means of measured concentration obtained at the beginning (0hr) and end (48 hrs) of the test.

**6.1.5 Toxicity to aquatic algae and cyanobacteria*****Toxicity to aquatic algae and cyanobacteria-1 [1] (NIER, 2007)***

UUID IUC5-26b6bbad-9b94-4489-8e21-a6edecc17dd7

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 10:20:38 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result Study period August 1, 2007-August 31, 2007

Reliability 1 (reliable without restriction)

Rationale for reliability 1a-GLP guideline study **Data**

**source****Reference**

Reference type study report

Author National Institute of Environmental Research (NIER)

Year 2007

Title Growth inhibition test of Phosphoric acid to the alga, Pseudokirchneriella subcapitata.

Bibliographic source

Testing laboratory Korea Institute of Toxicology, Korea Research Institute of Chemical Technology (KRICT) Report no. EG07063

Owner company

Company study no.

Report date

**Data access**

data submitter is data owner

**Data protection claimed**

yes, but willing to share

**Materials and methods****Test guideline**

Qualifier according to

Guideline OECD Guideline 201 (Alga, Growth Inhibition Test)

Deviations no

**GLP compliance**

yes (incl. certificate)

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Details on test material**

Purity: 99.999%, 85 wt. % in H<sub>2</sub>O

Description: Colorless liquid

Supplier: Sigma-Aldrich, Lot No. 09405LE

**Analytical monitoring**

yes

**Details on sampling**

The concentration of test substance in the test solution was analyzed at the beginning (0hr) and at the end (72hrs) of the study. Samples at 72hours were centrifuged slightly (5000rpm, 10min) to remove grown algae.

**Details on analytical methods**

ICP-AES was used for determination of phosphorus in test substance.

**Details on test solutions**

Dilution water: OECD nutrient medium

Preparation of the test solutions: After 116mg of the test substance was added in a 1000ml beaker, and the dilution water was added up the mark of the beaker. This solution was then stirred for about 30 minutes. Serial dilution water prepared with dilution water to give the desired of exposure levels which were nominally 60.3, 12.5, 25, and 50 mg/L. For the control group, only the OECD culture medium was used.

**Test organisms****Test organisms (species)**

*Pseudokirchnerella subcapitata*

**Details on test organisms**

Name: *Pseudokirchnerella subcapitata* (Strain No. UTEX 1648)

Source: Division of Non-clinical studies, Korea Institute of Toxicology (KIT), Korea Research Institute of Chemical Technology (KRICT), Daejeon, Korea (origin: purchased from UTEX (The Culture Collection of Algae, The University of Texas at Austin, USA) on August, 2006.)

Medium: OECD nutrient medium, prepared according to the OECD test guideline (2006).

Pre-culture: Two to four days before the test, sterile OECD nutrient medium (OECD, 2006) was inoculated about 5000 cells/ml from a stock culture and incubated in a shaking incubator under continuous illumination (shaking rate: about 100 times/min, and light intensity: 60-120  $\mu\text{E}/\text{m}^2/\text{s}$ ) at 21-24 °C to give an algal suspension in log phase growth.

**Study design****Test type**

static

**Water media type**

freshwater

**Limit test**

no

**Total exposure duration**

72 h

Remarks

**Test conditions****Test temperature**

24.0±0.2°C

**pH**

3.4-8.48

**Nominal and measured concentrations**

Nominal test concentrations: 0, 6.3, 12.5, 25.0, 50.0 and 100.0 mg/L

Mean measured test concentrations: 0, 7.5, 14.5, 29.8, 56.7 and 109.6 mg/L

**Details on test conditions**

Light intensity: 86-87  $\mu\text{E}/\text{m}^2/\text{s}$

Inoculation: The test was started (0hr) by inoculating 5100 cells/mL in 250mL conical flasks each containing 100mL of test solution under sterile conditions.

Culture condition: The cultures were incubated, without media renewal, for 72 hours under continuous illumination. The gaseous exchange and suspension of the algal cells were ensured by the action of the orbital shaker oscillating at cycles per minute.

Observation and Measurement: Samples were taken at 0, 24, 48 and 72 hours and the cells densities were determined by direct counts using a BECKMEN COUNTER Multisizer 3 particle analyzer.

**Any other information on materials and methods incl. tables****Statistical analysis method**

The result was analyzed using a TOXCALC version 5.0.12 (Tidepool Scientific Software, USA). Assumption of homogeneity of variance was using Shapiro-Wilk test, Maximum Likelihood-Logit methods were applied to obtain the effective concentrations,  $\text{EC}_{10}$  (and/or  $\text{EC}_{20}$ ) and  $\text{EC}_{50}$  for each approach. NOEC (No observed effect concentration) and LOEC (Lowest observed effect concentration) were analyzed by Dunnett test ( $P < 0.05$ ).

**Experimental design**

The growth inhibition of above 50% was observed at the nominal concentration of 100 mg/L in both average growth rate and yield. Therefore, the definitive test was conducted at the below test concentrations with triplicates. The results of the range-finding test were as follows:

Nominal concentration (mg/L)	% Inhibition of growth rate	
	Average Growth Rate	Yield
0.1	-0.5	-3.0
1	2.9	15.7
10	2.6	14.2



100	58.7	97.2
-----	------	------

## Results and discussions

### Effect concentrations

Duration	72 h
Endpoint	EC50
Effect conc.	77.9 mg/L
Nominal/Measured	meas. (geom. mean)
Conc. based on	
Basis for effect	growth rate
Remarks (e.g. 95% CL)	66.2-92.8
Duration	72 h
Endpoint	EC50
Effect conc.	32 mg/L
Nominal/Measured	meas. (geom. mean)
Conc. based on	
Basis for effect	other: yield
Remarks (e.g. 95% CL)	21.3-48.6
Duration	72 h
Endpoint	NOEC
Effect conc.	< 7.5 mg/L
Nominal/Measured	meas. (geom. mean)
Conc. based on	
Basis for effect	growth rate
Remarks (e.g. 95% CL)	
Duration	72 h
Endpoint	NOEC
Effect conc.	< 7.5 mg/L
Nominal/Measured	meas. (geom. mean)
Conc. based on	
Basis for effect	other: yield
Remarks (e.g. 95% CL)	
Duration	72 h
Endpoint	LOEC
Effect conc.	7.5 mg/L
Nominal/Measured	meas. (geom. mean)
Conc. based on	
Basis for effect	growth rate

Remarks  
(e.g.  
95%  
CL)

Duration 72 h

Endpoint LOEC

Effect conc. 7.5 mg/L

Nominal/Measured meas. (geom. mean)

Conc.  
based  
on

Basis  
for  
effect other: yield

Remarks  
(e.g.  
95%  
CL)

#### Details on results

No abnormalities were detected in any of the cultures and there was no sign of contamination by foreign algal cells or protozoa. The growth inhibition rates, calculated by an average growth rate and a yield, were given in Table 1, and the toxicity values of the test substance expressed in terms of the mean measured concentration were shown in Table 4.

#### Remarks on results including tables and figures

**Table 1. Growth inhibition rates based on mean value during the test period**

##### (1) Average growth rate

Nominal concentration (mg/L)	Mean measured concentration (mg/L)	Average growth rate	Relative inhibition (%)	Mean relative inhibition (%)
Control	ND	1.7758 <sup>1)</sup>	-	-
6.3	7.5	1.6187 1.4735 1.6915	8.8 17.0 4.7	10.2
12.5	14.5	1.6151 1.7057 1.7032	9.0 3.9 4.1	5.7
25.0	29.8	1.7319 1.6460 1.7524	2.5 7.3 1.3	3.7
50.0	56.7	1.2409 1.3340 1.2739	30.1 24.9 28.3	27.8
100	109.6	0.5736 0.4295 0.3914	67.7 75.8 78.0	73.8

##### (2) Yield

Nominal concentration (mg/L)	Mean measured concentration (mg/L)	Average growth rate	Relative inhibition (%)	Mean relative inhibition (%)
Control	ND	1051733 <sup>1)</sup>	-	-
6.3	7.5	650400 418900 810400	38.2 60.2 22.9	40.4
12.5	14.5	643400 854900 839400	38.8 19.6 20.2	26.2
25.0	29.8	915400 706400 973900	13.0 32.8 7.4	17.7
50.0	56.7	205900 273900 227900	80.4 74.0 78.3	77.6
100	109.6	23400 13400 11400	97.8 98.7 98.9	98.5

<sup>1)</sup> Mean value of average growth rate or yield in the control group  
ND : Not detected

**Table 2. pH**

Nominal conc. (mg/L)	Mean measured conc. (mg/L)	0hr	72hr	Change of pH during the test period
Control	ND	8.12	8.48	0.36
6.3	7.5	7.63	8.00	0.37
12.5	14.5	7.60	7.87	0.24

25.0	29.8	7.24	7.48	0.24
50.0	56.7	6.00	5.61	-0.39
100.0	109.6	3.42	3.40	-0.02

Table 3. Cell densities of *Pseudokirchneriella subcapitata* (UTEX 1648) during the test period

Nominal conc. (mg/L)	Mean cell densities (Triplicates)			
	0hr	24hr	48hr	72hr
Control	5.1x10 <sup>3</sup>	3.0x10 <sup>4</sup>	1.3x10 <sup>5</sup>	1.0x10 <sup>6</sup>
6.3	5.1x10 <sup>3</sup>	2.2x10 <sup>4</sup>	8.8x10 <sup>4</sup>	6.3x10 <sup>5</sup>
12.5	5.1x10 <sup>3</sup>	2.4x10 <sup>4</sup>	1.2x10 <sup>5</sup>	7.8x10 <sup>5</sup>
25.0	5.1x10 <sup>3</sup>	2.7x10 <sup>4</sup>	1.2x10 <sup>5</sup>	8.7x10 <sup>5</sup>
50.0	5.1x10 <sup>3</sup>	2.1x10 <sup>4</sup>	5.1x10 <sup>4</sup>	2.4x10 <sup>5</sup>
100.0	5.1x10 <sup>3</sup>	1.4x10 <sup>4</sup>	1.3x10 <sup>4</sup>	2.2x10 <sup>4</sup>

Table 4. Summary of test results (Unit: mg/L, mean measured test concentration)

Estimates of Toxicity	Calculation Method	
	Average Growth Rate	Yield
72-hr EC <sub>10</sub> (95% confidence limits)	37.7 (21.9-48.1)	5.8 (1.1-10.9)
72-hr EC <sub>20</sub> (95% confidence limits)	49.2 (34.1-59.2)	10.9 (3.5-17.3)
72-hr EC <sub>50</sub> (95% confidence limits)	77.9 (66.2-92.8)	32.0 (21.3-48.6)
No Observed Effect Concentration(NOEC)	<7.5	<7.5
Lowest Observed Effect Concentration(LOEC)	7.5	7.5

## Applicant's summary and conclusion

### Validity criteria fulfilled

yes

### Conclusions

The 72hr-EC50 values expressed in terms of the mean measured concentration of phosphoric acid to *Pseudokirchneriella subcapitata* (Strain No. UTEX 1648) were determined as 77.9 mg/L (between pH 5.61 and 3.4) for average growth rate, and 32.0 mg/L (between pH 7.48 and 5.61) for yield, respectively.

### Executive summary

The study was performed to assess the inhibition effect of phosphoric acid (CAS No. 7664 -38 -2) on the growth of the unicellular green alga, *Pseudokirchneriella subcapitata* (Strain No. UTEX 1648).

The study was conducted in accordance with the OECD Guidelines for the Testing of Chemicals No. 201 Freshwater Alga and Cyanobacteria, Growth Inhibition Test (Adopted: March 23, 2006).

The Toxicity test was performed with control and nominal concentrations of 6.3, 12.5, 25.0, 50.0 and 100.0 mg/L each in triplicates, with mean measured concentrations of 7.5, 14.5, 29.8, 56.7 and 109.6 mg/L, respectively. Cultures were incubated on a shaking incubator under continuous illumination at 24.0 +/- 0.2 °C for 72 hours. Growth was monitored daily by determining the cell density of each culture by direct counts using a BECKMAN COULTER™ Multisizer 3 particle analyzer (table 3).

The following values, expressed in terms of the mean measured concentrations, were obtained from the test.

(Unit: mg/L, mean measured test concentration)

Estimates of Toxicity	Calculation Method	
	Average Growth Rate	Yield
72-hr EC <sub>10</sub> (95% confidence limits)	37.7 (21.9-48.1)	5.8 (1.1-10.9)
72-hr EC <sub>20</sub> (95% confidence limits)	49.2 (34.1-59.2)	10.9 (3.5-17.3)
72-hr EC <sub>50</sub> (95% confidence limits)	77.9 (66.2-92.8)	32.0 (21.3-48.6)
No Observed Effect Concentration(NOEC)	7.5	7.5
Lowest Observed Effect Concentration(LOEC)	7.5	7.5

All results were expressed in terms of the mean measured concentration (geometric mean). At 0 -hour (the start of the test), the mean measured concentrations were 7.5, 14.6, 29.9, 57.4 and 110.6 mg/L (110.6 -119.6% of the nominal concentration). The mean concentrations measured at 72 -hour (the end of the test) were 7.6, 14.5, 29.8, 56.0 and 108.7 mg/L (108.7 -120.6 % of the nominal concentration).

## **6.3 Terrestrial toxicity**

### ***Terrestrial toxicity***

UUID IUC5-742d01d0-a6ad-40ec-88b3-213a51bf1c06

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 10:21:16 KST

Remarks

### **Administrative Data**

[IP] OECD: HPVC

### **Discussion**

#### **1. Terrestrial toxicity**

##### **1). Soil macroorganisms except arthropods & terrestrial arthropods**

No data are available for phosphoric acid.

##### **2). Terrestrial plant**

Lettuce fruit: 72-hour EC<sub>50</sub> : 16,366 mg/L (germination, observed pH 1.3 )

**6.3.3 Toxicity to terrestrial plants*****Toxicity to terrestrial plants.001***

UUID IUC5-d46c375e-29cc-4d3f-a3d2-b4d6bf7e3788

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 10:23:13 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 3 (not reliable)

Rationale for reliability 3a-Documentation insufficient for assessment

**Data source****Reference**

Reference type publication

Author Reynolds, T. Year 1974

Title pH Restraints on Lettuce Fruit Germination

Bibliographic source Annals of Botany 39: 797-805

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Materials and methods****GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Test organisms****Test organisms**

Species Lactuca sativa

Plant group Cryptogamae, vascular (ferns and allies)

Details on test organisms Lettuce Fruit

**Study design****Study type**

laboratory study

**Test duration type**

short-term toxicity

**Test type**

seed germination/root elongation toxicity test

**Substrate type**

other: 0.5 percent agar

**Limit test**

no

**Total exposure duration**

72 h

**Remarks****Test conditions****Test temperature**

29°C

**pH**

1.30

**Nominal and measured concentrations**

167±25mM

**Any other information on materials and methods incl. tables**

Reynolds, T. 1975. Characterization of Osmotic Restraints on Lettuce Fruit Germination. Annals of Botany. 39; 791 -796.

Materials and Methods : Germination at single temperatures was determined by means of thermostatically controlled water baths. Twenty lettuce fruits were sown on 0.5 percent agar (10ml) in polystyrene pots (2.8 X 3.5 cm) closed by lids floating in the water baths. Each set contained five replicates and germination was counted after 72h.

**Results and discussions****Effect concentrations**

Species Lactuca sativa  
Duration 72 h  
Endpoint EC50  
Effect conc. 16366 mg/L  
Nominal/Measured meas. (not specified)  
Conc. based on Basis for effect germination  
Remarks (e.g. 95% CL)

**Remarks on results including tables and figures**

Table 1. Concentration of acids at which percentage germination of lettuce fruits (cv. Arctic King) at 29°C is 50 percent.

Inorganic acid	Molecular weight	pK <sub>25</sub>	Conc. (mM) for 50 % germination (confidence limits for p=0.05)	Observed pH of effective conc.
Hydrochloric acid	36.5	-	68+/-8	1.50
Sulphuric acid	98	1.92	50+/-4	1.60
Nitric acid	63	-	15+/-2	2.00
<b>Orthophosphoric acid</b>	<b>98</b>	2.15, 7.20, 12.38	<b>167+/-25</b>	<b>1.30</b>

**Overall remarks, attachments****Overall remarks****Applicant's summary and conclusion****Conclusions**

The 72hr-EC50 of orthophosphoric acid to Lettuce Fruit was determined as 167mM (16,366mg/L, pH 1.3).

**Executive summary**

## 6.6 Additional ecotoxicological information

### Additional ecotoxicological information.001

**UUID** IUC5-3e0f0f81-1323-498c-8f4a-b536a11ade19  
**Dossier UUID** 0  
**Author** nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
**Date** 2011-04-11 14:33:13 KST  
**Remarks**

### Administrative Data

**OECD: HPVC**

**Purpose flag** supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS  
**Study result type** experimental result  
**Reliability** 3 (not reliable)  
**Rationale for reliability** 3c-Unsuitable test system

### Data source

#### Reference

**Reference type** study report  
**Author** Schindler, D. W., Hesslein, R. H., and Turner, M. A. **Year** 1987  
**Title** Exchange of nutrients between sediments and water after 15 years of experimental eutrophication

**Bibliographic source** Can. J. Fish. Aquat. Sci. 44: 26-33

<b>Testing laboratory</b>	<b>Report no.</b>
<b>Owner company</b>	
<b>Company study no.</b>	<b>Report date</b>

#### Data access

data published

### Materials and methods

#### Test guideline

**Qualifier** no guideline available  
**Guideline**  
**Deviations**

#### Test materials

##### Test material equivalent to submission substance identity

yes

##### Test material identity

**Identifier** CAS number  
**Identity** 7664-38-2  
**Identifier** IUPAC name  
**Identity** Phosphoric Acid

##### Any other information on materials and methods incl. tables

##### Description of the lake

Lake 227 has a surface area of 5.00 ha, a mean depth of 4.4 m and a maximum depth of 10.0 m. Its terrestrial drainage is 29.4 ha and contains bedrock ridges and thin tills (usually less than 0.5 m thick). The basin is covered by mature forests of *Pinus banksiana* and *Picea mariana*. There are no inflowing lakes or streams. The outlet is a discrete channel at the northwestern corner of the lake, draining over a v-notch weir. The lake stratifies in summer, with a thermocline at 2-4 m. Since fertilization began, the depth of the thermocline has decreased by 1-2 m, and the duration of anoxia has increased. Spring turnover is usually incomplete below 7 m, and fall turnover is seldom complete below 9 m. Anoxic conditions prevail in the hypolimnion for much of the year. The average water renewal time for 1970-74 was 2.3 years. For the much drier period 1975-82, it average 4.1 years. Upper sediment layers have 95% water content and contain > 50% organic matter. They are dark in colour and high flocculent. Visible laminar structure appears in sediments deposited since 1974.

##### Method

Beginning in June, 1969, the lake was fertilized with  $\text{NaNO}_3$  and either  $\text{Na}_2\text{HPO}_4$  (1969) or  $\text{H}_3\text{PO}_4$  (1970 and thereafter). Fertilizer

was added in 20 or 21 weekly increments, from mid-May until early October from 1970 onward. The mass ratio of N:P was 14:1 in 1969 -74, and 5:1 from 1975 onward.

Samples were taken from 4 to 11 depths between 1 and 10m, at intervals of 1 -4 wk during the ice-free season and 4 -6 wk during the ice-covered season. Samples were filtered through Whatman GF/C filters and analyzed the same day for total dissolved phosphorus (TDP),  $\text{NO}_3^-$ ,  $\text{NH}_4^+$ , and total dissolved nitrogen (TDN). The filters were frozen for later analysis of suspended phosphorus and nitrogen (SP and SN) at the Freshwater Institute in Winnipeg. An aliquot of unfiltered sample was acidified and analyzed for sodium at the Freshwater Institute by atomic absorption analyses. The methods of Stainton et al (1977) were used for all analyses. Total phosphorus (TP) was calculated as the sum of TDP and SP; totals nitrogen (TN) as TDN + SN.

Water samples for algal identifications and counts were taken at 1 -2 wk intervals.

Annual inputs of all elements to the lake (I) were calculated as the sum of runoff, precipitation, and fertilizer additions.

Losses of elements via the outflow (O) were calculated from continuous flow records and chemical analyses of weekly epilimnion or outflow samples. Annual changes in the mass of an element in the lake (M) were calculated as the difference between volume-weighted concentrations on January 1 of successive years.

Annual sedimentation (S) was calculated as I-O- M.

## Results and discussions

### Remarks on results including tables and figures

#### Results

##### 1. Elemental Mass Balances

Annual budgets revealed high net fluxes of phosphorus into sediments throughout the study period, despite the hypolimnetic anoxia (Table 1). The average sedimentation rate was 89% of phosphorus input in 1970 -74, and 91% in 1975 -82. Total retention by the lake was only slightly higher, 90 and 93% of input. The average annual increase in phosphorus in the water column, M, was only 1 -2% of input.

Table 1. The annual phosphorus budget for lake 227 since fertilization began. M is the change of mass of phosphorus in the water column from January 1 until December 31. Values marked est prior to fertilization are estimates derived from long-term averages for unfertilized lakes of the area. The horizontal line between 1974 and 1975 indicates when the N:P ratio in fertilizer was decreased. All values are in kg, except where indicated.

Year	Input (I)	Outflow (O)	O/I, %	Retention (R)	R/I, %	M	Average mass lake in	Sedimentation (S)	S/I, %
Pre-fert	1.0(est.)	0.2(est.)	-	0.8(est.)	-	0.0	3.0(est.)	0.8(est.)	80
1969	22.0	-	-	-	-	1.3	4.2	-	-
1970	31.3	3.0	10	28.3	90	2.4	6.0	25.9	83
1971	32.6	3.4	10	29.2	90	-3.1	8.3	32.4	99
1972	29.9	3.3	11	26.6	89	2.8	7.8	23.8	80
1973	30.4	3.8	13	26.6	88	-0.6	9.0	27.1	89
1974	30.5	1.9	6	28.6	94	0.3	8.4	28.3	93
1975	28.4	1.7	6	26.7	94	-1.5	6.4	28.2	99
1976	27.9	0.8	3	27.1	97	5.5	7.0	21.6	77
1977	28.5	2.0	7	26.5	93	2.3	10.6	24.2	85
1978	28.7	3.0	10	25.7	90	0.4	13.9	25.3	88
1979	28.8	2.2	8	26.6	92	-4.0	14.6	30.5	106
1980	28.0	0.8	3	27.2	97	8.5	17.0	18.7	67
1981	28.2	2.8	10	25.4	90	-8.2	15.3	33.6	119
1982	28.6	3.0	10	25.6	90	2.5	12.0	23.1	81

##### 2. Pore Water Profiles

Concentrations of phosphorus in pore waters did not increase between 1975 and 1982. There is, therefore, no reason to modify the conclusions of Schindler et al. (1977), that return of phosphorus from sediments is of minor consequence in the lake.

#### Discussion

The mass-balance model indicates that increased concentrations of phosphorus observed in the lake are caused by slower water renewal rates, and not by return from sediments. This is confirmed by pore water results.

They found that the maximum rate of phosphorus return from sediments was less than 4% of input. These results confirm that there has been no loss in efficiency of phosphorus sedimentation over 15yr of eutrophication, even though the lake has been anoxic below 7m for 10-12 months of the year.

In summary, after 15 years of fertilization, both sodium and phosphorus concentrations appear to be in equilibrium with inputs of these elements, and there have been no major changes in the cycle of either element. Due to the lack of mixing after 1974, surface sediments now appear to be rapidly approaching equilibrium with phosphorus inputs. Nevertheless, concentrations of phosphorus in the water are still governed by input, water renewal, and sedimentation of plankton. In contrast, even after such a long period of stable inputs, neither nitrogen fixation nor nitrogen concentrations in pore waters have stabilized.

### Overall remarks, attachments



**Overall remarks****Applicant's summary and conclusion****Executive summary**

Increases in the concentrations of nitrogen and phosphorus occurred in the water column of Lake 227 during 15 years of fertilization with phosphoric acid and sodium nitrate. The sources of the increases were deduced by comparing the budgets of N and P to the budget for sodium, using a simple model, and from the chemistry of sediment pore water.

Total inventories for sodium since fertilization began confirmed that the element was almost perfectly conservative, as expected. When model results for phosphorus and sodium were calculated, the apparent increase in phosphorus was found to be due entirely to lower water renewal rates during recent years. This agrees with the observation that phosphorus concentrations in sediment pore water did not change between 1975 and 1982. Both phosphorus and sodium in the lake have been in equilibrium with external loading for the past several years.

In contrast, the observed increase in nitrogen could not be accounted for by the decreased water renewal rate, implying that the element was either becoming more efficiently recycled or that there was an increasing, unmeasured external source of the element. An increase in pore water ammonium between 1975 and 1982 was balanced by an increase in the concentration in overlying waters, so that diffusive fluxes did not change. Increasing blooms of nitrogen-fixing bluegreen algae after 1975 indicate that  $N_2$  fixation is the increasing source of nitrogen budget has still not reached a new steady state.

**Additional ecotoxicological information.002**

**UUID** IUC5-9672c9d4-d58f-4885-9d57-65074a8989b0  
**Dossier UUID** 0  
**Author** nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
**Date** 2011-04-11 14:33:41 KST  
**Remarks**

**Administrative Data****OECD: HPVC**

**Purpose flag** supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS  
**Study result type** experimental result  
**Reliability** 3 (not reliable)  
**Rationale for reliability** 3c- Unsuitable test system

**Data source****Reference**

<b>Reference type</b>	publication		
<b>Author</b>	Shindler, D. W.	<b>Year</b>	1974
<b>Title</b>	Eutrophication and recovery in experimental lakes: Implications for lake management		
<b>Bibliographic source</b>	Science 184: 897-899.		
<b>Testing laboratory</b>		<b>Report no.</b>	
<b>Owner company</b>			
<b>Company study no.</b>		<b>Report date</b>	

**Data access**

data published

**Materials and methods****Test guideline**

**Qualifier** no guideline available  
**Guideline**  
**Deviations**

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

**Identifier** CAS number  
**Identity** 7664-38-2  
**Identifier** IUPAC name  
**Identity** Phosphoric Acid

**Any other information on materials and methods incl. tables**

In an early experiment, phosphate and nitrate were added to lake 227, which has an extremely low content of dissolved inorganic carbon, to see whether shortage of carbon would prevent the eutrophication of such a lake [Additions equivalent to 0.5g of PO<sub>4</sub>-P and 6.9 g of NO<sub>3</sub>-N per square meter of lake surface per year were made over a 21-week period. This is five to ten times the input expected from natural sources and simulates the degree of nutrient enrichment in the Great Lakes (R. A. Vollenweider, Technical report DAS/CSI/68.27 (Organisation for economic cooperation and development, Paris, 1968)). Before fertilization, the concentration of dissolved inorganic carbon in equilibrium of lake 227 was about 50 umole/liter in midsummer. This is only about 2 to 3 percent of that found in the lower Great Lakes].

Experiments conducted in smaller enclosures (2 to 3 m<sup>3</sup>) in the same lake revealed that if phosphorus was not supplied, algal blooms did not occur [D. W. Schindler (unpublished data) has found that if phosphorus is not supplied, no algal increases do occur, the magnitude being determined by available nitrogen, which in some cases may be fixed from the atmosphere. When both phosphorus and nitrogen are supplied in excess, algae increase until light become limiting].

In order to test the validity of this conclusion on a whole lake, and experiment was begun in 1973 in another small lake, 226. This lake, which has two similar basins separated by a shallow neck, was divided into two equal areas by using a sea curtain (60 by 6 m) of vinyl reinforced with nylon (Kepner Plastics, Torrance, California), which was sealed into the sediments and fastened to the bedrock in the narrow section of the lake. Beginning in late May 1973, additions of nitrogen and carbon were made equally to both basins, but phosphorus was added only to the northeast basin of the lake [Additions equivalent to 3.16 g of NO<sub>3</sub>-N and 6.05 g of sucrose

C per square meter per year were made to both basins, in 20 equal weekly increments. The northeast basin also received  $0.59 \text{ g m}^{-2} \text{ year}^{-1}$  of  $\text{PO}_4\text{-P}$ . The N/P and C/P ratios are greater than in sewage, while the quantity of P added is not exceptionally high for a culturally affected lake].

## Results and discussions

### Remarks on results including tables and figures

A bloom of the blue-green alga *Anabaena spiroides* covered that basin receiving phosphorus. Throughout the year, phytoplankton species and standing crops in the basin that received only nitrogen and carbon remained similar to those before fertilization was begun, consisting chiefly of *Tabellaria fenestrata*, *Synedra acus*, and other diatoms. The results indicate the efficacy to be expected from controlling phosphorus content of the influents to such waters as a means of preventing eutrophication.

A Whole-lake experiment was designed to test the speed of lake recovery and the efficiency of the sediments at removing and retaining phosphorus.

As in lakes 227 and 226, an algal bloom occurred in response to this application of fertilizer. In 1973, we continued to add nitrogen and carbon, but discontinued phosphorus additions, simulating conditions that might exist in a culturally eutrophied lake after phosphorus control measures were taken. The recovery of the lake was nearly complete, as the chlorophyll a concentrations indicate. These results can be explained by our experiments in lake 227, which have shown that phosphate in the hypolimnion is taken up rapidly by microplankton, and then sedimented to the lake bottom, where it remains, regardless of oxygen concentration.

## Overall remarks, attachments

### Overall remarks

## Applicant's summary and conclusion

### Conclusions

An important eutrophication potential for inorganic phosphate was elegantly demonstrated by the fertilization performed on a lake of northwestern. A basin of the lake receiving additions of phosphate, nitrate and carbon was covered by a dense algal bloom within two months. No increases in algae abundance was observed in another basin of the lake which received similar quantities of nitrogen and carbon but no phosphorus.

### Executive summary

Combinations of phosphorus, nitrogen, and carbon were added to several small lakes in northwestern Ontario, Canada, at rates similar to those in many culturally eutrophied lakes. Phosphate and nitrate caused rapid eutrophication. A similar result was obtained with phosphate, ammonia, and sucrose, but recovery was almost immediate when phosphate additions only were discontinued. When two basins of one lake were fertilized with equal amounts of nitrate and sucrose, and phosphorus was also added to one of the basins, the phosphate enriched basin quickly became highly eutrophic, while the basin receiving only nitrogen and carbon remained at prefertilization conditions. These results, and the high affinity of sediments for phosphorus indicate that rapid abatement of eutrophication may be expected to follow phosphorus control measures.

**7 Toxicological information****7.1 Toxicokinetics, metabolism and distribution*****Toxicokinetics, metabolism and distribution***

UUID IUC5-18860a84-3712-4623-b9f5-b3a114ae24d1

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 14:34:31 KST

Remarks

**Administrative Data****[IP] OECD: HPVC****Discussion**

Phosphoric acid can be absorbed by ingestion, inhalation and dermal contact. Absorbed Hardman is distributed widely in the body. Phosphate is present in plasma and extracellular fluid in cell membranes and intracellular fluid, and in collagen and bone tissue. More than 90% of plasma phosphate is filterable, of which 80% is actively reabsorbed. Phosphate excreted in the urine represents the difference between the amount filtered and that reabsorbed.

**7.1.1 Basic toxicokinetics*****Basic toxicokinetics-1 [2] (Hardman et al., 1996)***

UUID IUC5-7f893fd5-6d69-49a8-9f61-1b85b31d5d93

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-26 20:55:19 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type other:

Reliability 2 (reliable with restrictions)

Rationale for reliability 2g - Data from handbook or collection of data

**Data source****Reference**

Reference type review article or handbook

Author Hardman JG, Limbird LE, Molinoff PB, Ruddon RW and Goodman AG

Year 1996

Title Goodman and Gilman's The Pharmacological Basis of Therapeutics.

Bibliographic source Goodman and Gilman's The Pharmacological Basis of Therapeutics. 9th ed. New York, NY: McGraw-Hill, p. 1524-1525

Testing laboratory

Report no.

Owner company

Company study no.

Report date

**Data access**

data published

**Materials and methods****Objective of study**

absorption

distribution

excretion

**Test guideline**

Qualifier no guideline followed

Guideline

Deviations

**Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity Phosphoric Acid

**Test materials****Details on test material**

Phosphate - Absorbed Phosphoric acid is distributed sidely in the body as phosphate.

**Results and discussions****Pharmacokinetic studies****Absorption**

Phosphoric acid can be absorbed by ingestion, inhalation and dermal contact. Absorbed phosphate is distributed widely in the body. Transport of phosphate from the gut lumen is an active, energy-dependent process that is modified by several factors. Presence of large quantities of Ca<sup>2+</sup> or Al<sup>3+</sup> may lead to formation of large amounts of insoluble phosphate and diminish net

phosphate absorption. Vitamin D stimulates phosphate absorption, an effect reported to precede its action on  $\text{Ca}^{2+}$  transport.

**Distribution in tissues**

Phosphate is present in plasma and extracellular fluid in cell membranes and intracellular fluid, and in collagen and bone tissue. In extracellular fluid, the bulk of phosphate exists in inorganic form as the two constituents,  $\text{NaH}_2\text{PO}_4$  and  $\text{Na}_2\text{HPO}_4$ ; the ratio of disodium to monosodium phosphate is 4:1 at pH 7.40. This ratio varies with pH; however, due to its relatively low concentration, phosphate contributes little to the buffering capacity of extracellular fluid.

**Excretion**

Renal phosphate excretion has been extensively studied. More than 90% of plasma phosphate is filterable, of which 80% is actively reabsorbed. Most reabsorption occurs in the initial segment of the proximal tubule, with a lesser component in the pars recta. The extent of phosphate reabsorption at more distal sites remains controversial. There is little evidence for tubular phosphate secretion in the mammalian kidney. Phosphate excreted in the urine represents the difference between the amount filtered and that reabsorbed. Expansion of plasma volume increases urinary phosphate excretion.

**Metabolite characterisation studies****Remarks on results including tables and figures**

**7.2 Acute Toxicity****Acute Toxicity**

UUID IUC5-80c3baf1-a280-4c18-af68-0d0d92a26924

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2008-12-23 15:54:37 KST

Remarks

**Administrative Data****[IP] OECD: HPVC****Key parameter (optional)****Acute toxicity: oral**

Effect level	LD50	in	2000
		mg/kg	
		bw	

**Acute toxicity: dermal**

Effect level	LD50	in	1260
		mg/kg	
		bw	

**Acute toxicity: inhalation**

Effect level	LD50	in	3846
		mg/m <sup>3</sup>	
		air	

**7.2.1 Acute toxicity: oral****Acute toxicity: oral.001**

UUID IUC5-231d172c-fed6-4fb3-bebd-a8f1e3d3a2a8

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 10:25:02 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result Study period Jun 27, 2008 - Aug 25, 2008

Reliability 1 (reliable without restriction)

Rationale for reliability 1a - GLP guideline study

**Data source****Reference**

Reference type study report

Author National Institute of Environmental Research (NIER), Korea

Year 2008

Title A single-dose oral toxicity study of phosphoric acid in Sprague-Dawley rats (Acute toxic class method)

Bibliographic source

Testing laboratory ChemOn

Report no. 08-RA-252

Owner company

Company study no.

Report date

**Data access**

data submitter is data owner

**Data protection claimed**

yes, but willing to share

**Materials and methods****Test type**

acute toxic class method

**Limit test**

no

**Test guideline**

Qualifier according to

Guideline OECD Guideline 423 (Acute Oral toxicity - Acute Toxic Class Method)

Deviations

**GLP compliance**

yes (incl. certificate)

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Details on test material**

purity: 99.999 + % based on trace metal analysis

Lot No.: 06723J

appearance: White crystals

provider: Sigma-Aldrich Co.



**Test animals****Species**

rat

**Strain**

Sprague-Dawley

**Sex**

female

**Details on test animals and environmental conditions**

Test animals (at administration)

- age: 8-9 weeks of age
- number of animals: 12
- weight ranges: 168.61 g - 196.27 g

Environmental conditions

The animals were housed in a room that was maintained at temperature of  $23.7 \pm 0.2$  °C and relative humidity of  $54.9 \pm 0.77$  %, with artificial lighting from 08:00 to 20:00, 150-300 Lux of luminous intensity and 10-20 air change per hour. All the researchers wore autoclaved working clothes and special protective equipments during the testing.

**Administration / exposure****Route of administration**

oral: gavage

**Vehicle**

other: sterile distilled water (water for injection)

**Details on oral exposure**

(1) Method of administration

The prepared article was directly injected into stomach using sonde and syringe tube. Before the administration, animals were fasted overnight. Food was offered 3-4 hours after administration.

The time interval between treatment groups was determined by the onset, duration, and severity of toxic signs. Treatment of animals at the next dose was delayed until the survival or death of the previously dosed animals was confirmed.

The dose of 2,000 mg/kg was given in the step 1 and 2, and 300 mg/kg was administered in the following two steps. Three rats were dosed for each step and 4 times of dosing was done.

(2) Volume of administration

Volume was fixed at 10 ml/kg, and individual volume for each rat was calculated based on the fasted body weight measured on the day of dosing.

(3) Frequency and period of administration

The test article was given once and the administration was finished before 12:00. The day of administration was designated as day 0.

**Doses**

300 and 1200 mg/kg (10ml/kg)

**No. of animals per sex per dose**

3

**Control animals**

no

**Details on study design**

(1) Selection of dose levels

According to existing information the LD50 of the test article was 1,530 mg/kg. The starting dose was set at 2,000 mg/kg, at which mortality was anticipated, according to the OECD Test guideline 423. Since one out of three rats died at the starting 2,000 mg/kg dose and two out of three rats died at the following same dose, the 300 mg/kg dose was the next lower dose.

(2) Items of observation and examination

- Clinical signs and mortality

Clinical signs and mortalities were checked continuously for the first one hour after administration (on day 0), and then every hour until 4 hrs thereafter. Then during the remaining observation period, every animal was daily observed for any clinical signs.

- Body weights

All survivors were weighed on day 0 (just before administration), day 3, day 7 and day 14. Dead animals were also weighed.

- Necropsy

Rats were anesthetized with ether, and then terminated by exsanguination from the posterior vena cava and abdominal aorta. Complete post-mortem examinations were performed on all vital organs.

**Statistics**

Statistical analysis was not done.

**Any other information on materials and methods incl. tables****Group identification**

Steps	Genders	No. of animals	Animal ID	Dose volume (ml/kg)	Dose (mg/kg)
1	F	3	1-3	10	2,000
2	F	3	4-6	10	2,000
3	F	3	7-9	10	300
4	F	3	10-12	10	300

## Results and discussions

### Effect levels

Sex female

Endpoint LD50

Effect level <= 2000 mg/kg bw

95%

CL

Remarks The approximate LD50 was 2,000 mg/kg.

### Mortality

At dose of 2,000 mg/kg, one out of three rats in step 1 and two out of three rats died on day 1, the next day of administration.

### Clinical signs

Among the 6 rats at dose of 2,000 mg/kg, 4 cases of salivation, 3 cases of staining around mouth and 2 cases of lacrimation were observed on day 0. On day 1 each one case of staining around mouth and vaginal discharge were observed.

No signs were observed in rats treated with 300 mg/kg of the test article.

### Body weight

There were no notable test article-related changes in body weights.

### Gross pathology

In 3 dead rats received 2,000 mg/kg, yellow brown or dark fluid in the stomach and adsorption of dark contents in the glandular stomach were observed.

No abnormal signs were observed in the survivors.

### Remarks on results including tables and figures

## Applicant's summary and conclusion

### Interpretation of results

Toxicity Category IV GHS category 4

### Criteria used for interpretation of results

OECD GHS

### Conclusions

The deaths of the three rats received 2,000 mg/kg could be attributed to the acute toxicity of the test article in view of the clinical signs such as salivation, staining around mouth and lacrimation; and necropsy findings, yellow brown or dark fluid in the stomach and adsorption of dark contents in the glandular stomach.

Based on the results, three out of six rats died by a single oral administration of 2,000 mg/kg phosphoric acid, and the article was classified as GHS category 4. The approximate LD50 was 2,000 mg/kg.

### Executive summary

**Acute toxicity: oral.002**

**UUID** IUC5-db2f81c2-d2a5-40b7-a246-cbacd7c8f4e2  
**Dossier UUID** 0  
**Author** nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
**Date** 2011-04-11 10:28:09 KST  
**Remarks**

**Administrative Data****[IP] OECD: HPVC**

**Purpose flag** supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS  
**Study result type** experimental result **Study period** 1975-1976  
**Reliability** 2 (reliable with restrictions)  
**Rationale for reliability** 2e - Study well documented, meets generally accepted scientific principles, acceptable for assessment

**Data source****Reference**

**Reference type** publication  
**Author** Randall DJ and Robinson EC **Year** 1990  
**Title** Acute toxicologic evaluation of various concentrations of phosphoric acid

**Bibliographic source** Journal of the American College of Toxicology B, 1(1): 69-70

**Testing laboratory** Monsato Company **Report no.**  
**Owner company**  
**Company study no.** **Report date**

**Reference type** study report  
**Author** Monsanto Co. **Year** 1975  
**Title** Toxicological investigation of phosphoric acid 85% NF

**Bibliographic source**

**Testing laboratory** Younger Labs **Report no.**  
**Owner company** Monsanto Company, St. Louis, Missouri  
**Company study no.** YO-75-027 **Report date** 1975-03-06

**Data access**

data published

**Cross-reference to same study**

Acute toxicity: dermal. 001  
 Eye irritation. 002

**Materials and methods****Limit test**

no

**Test guideline**

**Qualifier** no guideline followed

**Guideline****Deviations****GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

**Identifier** CAS number

**Identity** 7664-38-2

**Identifier** IUPAC name **Identity**

phosphoric acid **Identifier**

Common name **Identity**

orthophosphoric acid

#### **Details on test material**

Dose Preparation: Neat, liquid (Monsanto Preparations of 75 %, 80 % and 85 % phosphoric acid(PA) - aqueous solutions)

Commercial aqueous solutions of phosphoric acid produced by Monsanto.

#### **Test animals**

##### **Species**

rat

##### **Strain**

Sprague-Dawley

##### **Sex**

male/female

##### **Details on test animals and environmental conditions**

mix of male and female Sprague-Dawley albino rats

#### **Administration / exposure**

##### **Route of administration**

oral: gavage

##### **Vehicle**

unchanged (no vehicle)

##### **Doses**

2,510, 3,160, 3,980, 5,010 and 6,310 mg/kg (5,010 mg/kg was the highest test dose for PA 85 %)

##### **No. of animals per sex per dose**

5

##### **Control animals**

no data

##### **Details on study design**

A 14-d observation period followed administration.

Calculation of LD50s was done according to the method of E.J. de Beer (1945; Journal of Pharmacology and Experimental Therapeutics, 85:1)

#### **Results and discussions**

##### **Effect levels**

**Sex** male/female

**Endpoint** LD50

**Effect level** 3500 mg/kg bw

**95% CL**  $\geq 3150$  —  $\leq 3890$

**Remarks** PA 85 %

**Sex** male/female

**Endpoint** LD50

**Effect level** 4200 mg/kg bw

**95% CL**  $\geq 3780$  —  $\leq 4660$

**Remarks** PA 80 %

**Sex** male/female

**Endpoint** LD50

**Effect level** 4400 mg/kg bw

**95% CL**  $\geq 3870$  —  $\leq 4970$

**Remarks** PA 75 %

**Sex** male/female

**Endpoint** LDLo

Effect level 2510 mg/kg bw

95%  
CL

Remarks PA 85 %

Sex male/female

Endpoint LDLo

Effect level 3160 mg/kg bw

95%  
CL

Remarks PA 80 %

Sex male/female

Endpoint LDLo

Effect level 3160 mg/kg bw

95%  
CL

Remarks PA 75 %

#### **Mortality**

One male of 2510 mg/kg treated group, 1 female of 3160 mg/kg treated group, 1 male and 3 female of 3980 mg/kg treated group and 3 male and 2 female of 5010 mg/kg treated group rats were died after one to two days administration.

#### **Clinical signs**

Reduced appetite and activity (one to three days in survivors), increasing weakness, collapse and death.

#### **Gross pathology**

Hemorrhagic areas of the lungs, liver hyperemia, and hemorrhaging and necrosis of gastrointestinal tract.

#### **Other findings**

Survivors (14 days): Viscera appeared normal.

#### **Remarks on results including tables and figures**

**Table. Average initial weight and mortality (85% phosphoric acid, undiluted)**

Dosage (mg/kg)	Ave. Initial Weight		Mortalities/Dosed			Time of Mortality
	Male	Female	Male	Female	Combined	
2510	225	225	1/2	0/3	1/5	one to two days
3160	225	240	0/3	1/2	1/5	
3980	225	230	1/2	3/3	4/5	
5010	220	215	3/3	2/2	5/5	

#### **Overall remarks, attachments**

##### **Overall remarks**

#### **Applicant's summary and conclusion**

##### **Conclusions**

The calculated oral LD50s for PA 85 %, PA 80 % and PA 75 % were 3,500, 4,200 and 4,400 mg test material/kg, respectively (95 % confidence limits 3,150-3,890, 3,780-4,660 and 3,870-4,970 mg/kg); LDLo were 2,510, 3,160 and 3,160 mg/kg, respectively.

**Acute toxicity: oral.003**

**UUID** IUC5-ca57c235-ab1b-409d-a19a-bfff9c7766c9  
**Dossier UUID** 0  
**Author** nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
**Date** 2008-12-30 16:50:52 KST  
**Remarks**

**Administrative Data****[IP] OECD: HPVC**

**Purpose flag** supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS  
**Study result type** other:  
**Reliability** 4 (secondary literature)  
**Rationale for reliability** 2g - Data from handbook or collection of data

**Data source****Reference**

**Reference type** review article or handbook  
**Author** ITII, The International Technical Information Institute **Year** 1988  
**Title** Toxic and hazardous industrial chemicals safety manual.  
**Bibliographic source** Toxic and hazardous industrial chemicals safety manual. Tokyo, Japan. p. 414  
**Testing laboratory** **Report no.**  
**Owner company**  
**Company study no.** **Report date**

**Data access**

data published

**Cross-reference to same study**

Acute toxicity: dermal.002

**Materials and methods****Test guideline****Qualifier** no guideline followed**Guideline****Deviations****GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

**Identifier** CAS number  
**Identity** 7664-38-2  
**Identifier** IUPAC name  
**Identity** phosphoric acid  
**Identifier** Common name  
**Identity** o-Phosphoric acid

**Test animals****Species**

rat

**Administration / exposure****Route of administration**

oral: unspecified

**Results and discussions**

**Effect levels**

Sex no data

Endpoint LD50

Effect level 1530 mg/kg bw

95%

CL

Remarks

**Applicant's summary and conclusion**

Criteria used for interpretation of results

Japan

**Conclusions**

Acute oral LD50 of phosphoric acid is 1530 mg/kg in rat.

**7.2.2 Acute toxicity: inhalation*****Acute toxicity: inhalation.001***

UUID IUC5-928e1b98-d579-46cd-a4e8-5018a95f7698

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 10:27:50 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 2 (reliable with restrictions)

Rationale for reliability 2e - Study well documented, meets generally accepted scientific principles, acceptable for assessment

**Data source****Reference**

Reference type publication

Author Ballantyne B Year 1998

Title Acute inhalation toxicity of red phosphorus smoke.

Bibliographic source Toxic Substance Mechanisms, 17(4): 251-266.

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Cross-reference to same study**

Acute toxicity: inhalation.002, 003, 004

**Materials and methods****Limit test**

no

**Test guideline**

Qualifier no guideline followed

Guideline

Deviations

**GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

no

**Test material identity**

Identifier other:

Identity Solid red phosphorus

**Details on test material**

Smoke generated from pure unformulated red phosphorus ignited in an air stream

**Test animals****Species**

rat

**Strain**

other: Porton-strain



**Sex**

male

**Administration / exposure****Route of administration**

inhalation

**Type of inhalation exposure**

whole body

**Vehicle**

unchanged (no vehicle)

**Analytical verification of test atmosphere concentrations**

yes spectrophotometric method

**Duration of exposure**1 h **Remarks** in a 10 m<sup>3</sup> chamber**Concentrations**

Concentration of smoke : 450, 870, 1600, 2130 mg/m<sup>3</sup>  
 (as orthophosphoric acid equivalents: 1422, 2749, 5056, 6731 mg/m<sup>3</sup>)

**No. of animals per sex per dose**12(450 mg/m<sup>3</sup>), 10(870), 9(1600), 12(2130)**Details on study design**

Study design

Animals were exposed, whole body, for 1 h to various concentrations of red phosphorus smoke in a 10 m<sup>3</sup> chamber. Based on pilot exposures, to assess the differential susceptibility of the species studied, the target concentrations of smoke ranged from 35 to 2000 mg/m<sup>3</sup> (expressed as phosphorus; 111-6320 mg/m<sup>3</sup> as ortho-phosphoric acid equivalents). They were allowed free access to food and water, except during the exposures. Survivors were sacrificed 14 days after the exposure.

Animals that died and sacrificed survivors were subject to necropsy and the larynx, trachea, lungs, liver, and kidney removed for fixation in phosphate-buffered neutral formalin. Microtome sections, 5 µm thick, were stained with hematoxylin and eosin, and by Schmorl's technique for incipient fibrosis.

**Atmosphere Analysis**

The atmosphere was sampled at 5-min intervals, by drawing air at 5 liters/min through Whatman No. 1 filter papers. Phosphorus in the papers was measured based on its conversion to ammonium phosphomolybdate, then reduced in the presence of acid to give a blue coloration that was measured spectrophotometrically. Filters were immersed in 20 ml 1.25 N sulfuric acid. Aliquots, 4 ml volume, were added to 5 ml 0.25 % ammonium molybdate and 1 ml hydrogen sulfate. This solution was heated to 80 °C for 20 min, cooled, and made up to 10 ml with 1.25 N sulfuric acid. Optional density was measured at 630 nm against a blank.

**Any other information on materials and methods incl. tables****Table 1. Numbers of animals exposed for 1 h to various concentrations of red phosphorus smoke.**

Concentration of smoke (mg/m <sup>3</sup> ) <sup>a</sup>		Number Exposed
as P <sup>a</sup>	as OPA <sup>b</sup>	Rats
2,130	6,731	12
1,600	5,056	9
870	2,749	10
450	1,422	12

<sup>a</sup> As phosphorus<sup>b</sup> As ortho-phosphoric acid equivalents**Results and discussions****Effect levels****Sex** male**Endpoint** LC50**Effect level** 3846 mg/m<sup>3</sup> air**95% CL** 3065 — 4705**Exp. duration** 1 h**Remarks** as OPA

**Mortality**

Rabbits and rats did not differ significantly in respect to lethal toxicity and were the least sensitive species. Red phosphorus smoke was significantly more toxic to the mouse, and even more toxic to the guinea pig, which appeared highly susceptible to this smoke. There was a 28-fold difference in the 1 h-LC<sub>50</sub> values between the guinea pig and rabbit. Most animals that died did so during exposure, although a small proportion survived a few hours or days postexposure.

**Gross pathology**

see the table 4 below.

**Remarks on results including tables and figures**

**Table 2. Exposure concentration-mortality data for the species having a 1-h exposure to red phosphorus smoke.**

Species	Concentration (mg/m <sup>3</sup> ) <sup>a</sup>	Inhalation exposure dose(CT) (mg min/m <sup>3</sup> ) <sup>a</sup>	Mortality <sup>b</sup>	Time to Death
Rat	2,130	128,000	12/12	DE(9) 3h(2) 1d(1)
	1600	97,100	6/9	DE(3) 4h(1) 2d(1) 12d(1)
	870	52,100	2/10	DE(1) 4h(1)
	450	27,300	0/12	----

<sup>a</sup> As phosphorus

<sup>b</sup> As (number dying)/(number exposed)

<sup>c</sup> DE = during exposure; expressed at time (number)

**Table 3. LC<sub>50</sub> and L(CT)<sub>50</sub> value calculated from mortality data for several species exposed for 1 h to red phosphorus smoke.**

Species	LC <sub>50</sub> (95% confidence limits) (mg/m <sup>3</sup> ) <sup>a</sup>		L(CT) <sub>50</sub> (95% confidence limits) (mg min/m <sup>3</sup> ) <sup>a</sup>	
	as P <sup>a</sup>	as OPA <sup>b</sup>	as P <sup>a</sup>	as OPA <sup>b</sup>
Rat	1,217 (970-1,489)	3,846 (3,065-4,705)	73,237 (56,483-89,740)	231,429 (178,486-283,578)

<sup>a</sup> As phosphorus

<sup>b</sup> As ortho-phosphoric acid equivalents

**Table 4. Histopathology in rats exposed for 1 h to various concentrations of red phosphorus smoke.**

Organ and histology		Exposure group (mg/m <sup>3</sup> ) <sup>a,b,c</sup>			
		2130	1600	870	450
<b>ANIMALS DYING</b>					
Group size		12	6	2	0
Larynx	Necrosis	G++(1) E++(1);E+(9) -(1);	G++ (2) E++(1);E+(2) -(1)	E+++ (1);E++ (1)	.
	Inflammation	+++ (1);++(2);+ (4) -(5)	++(2);+1(4)	+++ (1);+(1)	.
Trachea	Necrosis	G+(1) E+(8) -(3)	E++(3);E+(2) -(1)	-(2)	.
	Inflammation	++(1);+(1) -(5)	++(1);+(4) -(1)	+(1) -(1)	.
Lung	Congestion	++(9);+(2) -(1)	++(3);+(2) -(1)	+++ (2)	.
	Hemorrhage	++(3);+(7) -(2)	++(1) -(5)	++(2)	.
	Edema	++(1);+(4) -(7)	++(1);+(1) -(4)	-(2)	.
	Pneumonitis	++(3);+(8) -(1)	++(1) -(5)	+++ (1) -(1)	.
Liver	Congestion	+++ (7);++(4) -(1)	+++ (2);++(3) -(1)	+(1) -(1)	.
		+ (2)			

Kidney	Congestion	-(10)	-(6)	-(2)	.
	Cortical neurosis	-(12)	+(1) -(5)	-(2)	.
<b>SURVIVORS</b> <sup>d</sup>					
Group size		0	3	8	12
Larynx	Inflammation	.	+(1) -(2)	-(8)	+(1) -(11)
Trachea	Necrosis	.	E+(1) -(2)	E++(1) -(7)	-(12)
	Inflammation	.	+(2) -(1)	++(1) -(7)	+(1) -(11)
Lung	Congestion	.	-(3)	+(3) -(5)	+(5) -(7)
	Hemorrhage	.	-(3)	-(8)	-(12)
	Edema	.	-(3)	+(1) -(7)	-(12)
	Pneumonitis	.	+++ (2) -(1)	-(8)	-(12)

<sup>a</sup> Concentration as phosphorus

<sup>b</sup> Expressed as severity (number showing)

<sup>c</sup> Severity: - not seen; + mild; ++ moderate; +++ severe. G = generalized; E = epithelial localized

<sup>d</sup> No hepatorenal pathology in survivors

## Applicant's summary and conclusion

### Conclusions

The acute inhalation LC50 for phosphoric acid was 3846 mg orthophosphoric acid/kg (95 % confidence limits 3065-4705 mg/kg).

### Executive summary

**Acute toxicity: inhalation.002**

UUID IUC5-6e95100c-b1af-4216-8a2a-ac58ccc1607c

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 10:29:00 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 4 (secondary literature)

Rationale for reliability 2e - Study well documented, meets generally accepted scientific principles, acceptable for assessment

**Data source****Reference**

Reference type publication

Author Ballantyne B Year 1998

Title Acute inhalation toxicity of red phosphorus smoke.

Bibliographic source Toxic Substance Mechanisms, 17(4): 251-266.

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Cross-reference to same study**

Acute toxicity: inhalation.001, 003, 004

**Materials and methods****Limit test**

no

**Test guideline**

Qualifier no guideline followed

Guideline

Deviations

**GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

no

**Test material identity**

Identifier other:

Identity Solid red phosphorus

**Details on test material**

Smoke generated from pure unformulated red phosphorus ignited in an air stream

**Test animals****Species**

rabbit

**Strain**

New Zealand White

**Sex**

male

**Administration / exposure****Route of administration**

inhalation

**Type of inhalation exposure**

whole body

**Vehicle**

unchanged (no vehicle)

**Analytical verification of test atmosphere concentrations**

yes spectrophotometric method

**Duration of exposure**1 h **Remarks** in a 10 m<sup>3</sup> chamber**Concentrations**

Concentration of smoke: 450, 870, 1600, 2130 mg/m<sup>3</sup>  
 (as orthophosphoric acid equivalents: 1422, 2749, 5056, 6731 mg/m<sup>3</sup>)

**No. of animals per sex per dose**

10

**Details on study design**

Study design

Animals were exposed, whole body, for 1 h to various concentrations of red phosphorus smoke in a 10 m<sup>3</sup> chamber. Based on pilot exposures, to assess the differential susceptibility of the species studied, the target concentrations of smoke ranged from 35 to 2000 mg/m<sup>3</sup> (expressed as phosphorus; 111-6320 mg/m<sup>3</sup> as ortho-phosphoric acid equivalents). They were allowed free access to food and water, except during the exposures. Survivors were sacrificed 14 days after the exposure.

Animals that died and sacrificed survivors were subject to necropsy and the larynx, trachea, lungs, liver, and kidney removed for fixation in phosphate-buffered neutral formalin. Microtome sections, 5 µm thick, were stained with hematoxylin and eosin, and by Schmorl's technique for incipient fibrosis.

**Atmosphere Analysis**

The atmosphere was sampled at 5-min intervals, by drawing air at 5 liters/min through Whatman No. 1 filter papers. Phosphorus in the papers was measured based on its conversion to ammonium phosphomolybdate, then reduced in the presence of acid to give a blue coloration that was measured spectrophotometrically. Filters were immersed in 20 ml 1.25 N sulfuric acid. Aliquots, 4 ml volume, were added to 5 ml 0.25 % ammonium molybdate and 1 ml hydrogen sulfate. This solution was heated to 80 °C for 20 min, cooled, and made up to 10 ml with 1.25 N sulfuric acid. Optional density was measured at 630 nm against a blank.

**Any other information on materials and methods incl. tables****Table 1. Numbers of animals exposed for 1 h to various concentrations of red phosphorus smoke.**

Concentration of smoke (mg/m <sup>3</sup> ) <sup>a</sup>		Number Exposed
as P <sup>a</sup>	as OPA <sup>b</sup>	Rabbits
2,130	6,731	10
1,600	5,056	10
870	2,749	10
450	1,422	10

<sup>a</sup> As phosphorus<sup>b</sup> As ortho-phosphoric acid equivalents**Results and discussions****Effect levels**

**Sex** male  
**Endpoint** LC50  
**Effect level** 5337 mg/m<sup>3</sup> air  
**95% CL** 3792 — 11332  
**Exp. duration** 1 h  
**Remarks** Rabbit; as OPA

**Mortality**

Rabbits and rats did not differ significantly in respect to lethal toxicity and were the least sensitive species. Red phosphorus smoke

was significantly more toxic to the mouse, and even more toxic to the guinea pig, which appeared highly susceptible to this smoke. There was a 28-fold difference in the 1 h-LC<sub>50</sub> values between the guinea pig and rabbit. Most animals that died did so during exposure, although a small proportion survived a few hours or days postexposure.

#### Gross pathology

see the table 4 below.

#### Remarks on results including tables and figures

**Table 2. Exposure concentration-mortality data for the species having a 1-h exposure to red phosphorus smoke.**

Species	Concentration (mg/m <sup>3</sup> ) <sup>a</sup>	Inhalation exposure dose(CT) (mg min/m <sup>3</sup> ) <sup>a</sup>	Mortality <sup>b</sup>	Time to Death
Rabbit	2,130	128,000	8/10	DE <sup>c</sup> (5) 12h(2) 3d(1)
	1,600	97,100	3/10	24h(1) 29h(1) 38h(1)
	870	52,100	1/10	18h
	450	27,300	1/10	5d

<sup>a</sup> As phosphorus

<sup>b</sup> As (number dying)/(number exposed)

<sup>c</sup> DE = during exposure; expressed at time (number)

**Table 3. LC<sub>50</sub> and L(CT)<sub>50</sub> value calculated from mortality data for several species exposed for 1 h to red phosphorus smoke.**

Species	LC <sub>50</sub> (95% confidence limits) (mg/m <sup>3</sup> ) <sup>a</sup>		L(CT) <sub>50</sub> (95% confidence limits) (mg min/m <sup>3</sup> ) <sup>a</sup>	
	as P <sup>a</sup>	as OPA <sup>b</sup>	as P <sup>a</sup>	as OPA <sup>b</sup>
Rabbit	1,689 (1,200-3,586)	5,337 (3,792-11,332)	101,869 (73,338-215,584)	321,906 (231,748-681,245)

<sup>a</sup> As phosphorus

<sup>b</sup> As ortho-phosphoric acid equivalents

**Table 4. Histopathology in rabbits exposed for 1 h to various concentrations of red phosphorus smoke.**

Organ and histology		Exposure group (mg/m <sup>3</sup> ) <sup>a,b,c</sup>			
		2130	1600	870	450
<b>ANIMALS DYING</b>					
Group size		8	3	1	1
Larynx	Necrosis	G+++ (1); G+++ (4) E++ (1); E+ (1) - (1);	G+++ (2); G++ (1)	- (1)	- (1)
	Inflammation	+++ (6); ++ (1); + (1)	+++ (3)	- (1)	++ (1)
Trachea	Necrosis	G++ (3); G+ (1) E++ (2); E+ (1) - (1)	G+++ (3)	E++ (1)	- (1)
	Inflammation	+++ (5); + (2) - (1)	+++ (3)	++ (1)	++ (1)
Lung	Congestion	+++ (1); ++ (6); + (1)	++ (1); + (1) - (1)	+++ (1)	- (1)
	Hemorrhage	++ (3); + (4) - (1)	- (3)	+++ (1)	- (1)
	Edema	+++ (1); ++ (4); + (1) - (2)	+++ (1); ++ (1) - (1)	- (1)	- (1)
	Pneumonitis	++ (4); + (1) - (3)	+++ (2) - (1)	- (1)	++ (1)
Liver	Congestion	+ (8)	++ (1) - (2)	- (1)	- (1)
Kidney	Congestion	+ (8)	- (3)	- (1)	- (1)
	Cortical neurosis	+ (1) - (7)	- (3)	- (1)	- (1)
<b>SURVIVORS <sup>d</sup></b>					
Group size		2	7	9	9

Larynx	Necrosis	-(2)	-(7)	-(9)	-(9)
	Inflammation	+(2)	+(7)	-(9)	-(9)
Trachea	Necrosis	-(2)	E+(2) -(5)	E+(1) -(8)	-(9)
	Inflammation	+(2)	+(6) -(1)	-(9)	-(9)
Lung	Congestion	++(1);+(1)	+++ (2);++(3) -(2)	++(1);+ (1) -(7)	+(2) -(7)
	Hemorrhage	-(2)	++(2) -(6)	++(1) -(8)	-(9)
	Edema	+(1) -(1)	+(2) -(6)	+(1) -(8)	-(9)
	Pneumonitis	++(1);+(1)	-(7)	-(9)	++(1) -(8)

<sup>a</sup> Concentration as phosphorus

<sup>b</sup> Expressed as severity (number showing)

<sup>c</sup> Severity: - not seen; + mild; ++ moderate; +++ severe. G = generalized; E = epithelial localized

<sup>d</sup> No hepatorenal pathology in survivors

## Applicant's summary and conclusion

### Conclusions

The acute inhalation LC50 for phosphoric acid was 5,337 mg orthophosphoric acid/kg (95 % confidence limits 3,792-11,332 mg/kg).

### Executive summary

**Acute toxicity: inhalation.003**

UUID IUC5-f2a47a2d-e2fa-41e1-953f-a0e194344325

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 13:06:26 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 2 (reliable with restrictions)

Rationale for reliability 2e - Study well documented, meets generally accepted scientific principles, acceptable for assessment

**Data source****Reference**

Reference type publication

Author Ballantyne B Year 1998

Title Acute inhalation toxicity of red phosphorus smoke.

Bibliographic source Toxic Substance Mechanisms, 17(4): 251-266.

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Cross-reference to same study**

Acute toxicity: inhalation.001, 002, 004

**Materials and methods****Limit test**

no

**Test guideline**

Qualifier no guideline followed

Guideline

Deviations

**GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

no

**Test material identity**

Identifier other:

Identity Solid red phosphorus

**Details on test material**

Smoke generated from pure unformulated red phosphorus ignited in an air stream

**Test animals****Species**

mouse

**Strain**

other: Porton-strain

**Sex**



male

**Administration / exposure****Route of administration**

inhalation

**Type of inhalation exposure**

whole body

**Vehicle**

unchanged (no vehicle)

**Analytical verification of test atmosphere concentrations**

yes spectrophotometric method

**Duration of exposure**1 h **Remarks** in a 10 m<sup>3</sup> chamber**Concentrations**

Concentration of smoke: 111, 136, 220, 450, 870 mg/m<sup>3</sup>  
 (as orthophosphoric acid equivalents: 351, 430, 695, 1422, 2749 mg/m<sup>3</sup>)

**No. of animals per sex per dose**20(111 mg/m<sup>3</sup>), 50(136 mg/m<sup>3</sup>), 50(220 mg/m<sup>3</sup>), 20(450 mg/m<sup>3</sup>), 20(870 mg/m<sup>3</sup>)**Details on study design**

Study design

Animals were exposed, whole body, for 1 h to various concentrations of red phosphorus smoke in a 10 m<sup>3</sup> chamber. Based on pilot exposures, to assess the differential susceptibility of the species studied, the target concentrations of smoke ranged from 35 to 2000 mg/m<sup>3</sup> (expressed as phosphorus; 111-6320 mg/m<sup>3</sup> as ortho-phosphoric acid equivalents). They were allowed free access to food and water, except during the exposures. Survivors were sacrificed 14 days after the exposure.

Animals that died and sacrificed survivors were subject to necropsy and the larynx, trachea, lungs, liver, and kidney removed for fixation in phosphate-buffered neutral formalin. Microtome sections, 5 µm thick, were stained with hematoxylin and eosin, and by Schmorl's technique for incipient fibrosis.

**Atmosphere Analysis**

The atmosphere was sampled at 5-min intervals, by drawing air at 5 liters/min through Whatman No. 1 filter papers. Phosphorus in the papers was measured based on its conversion to ammonium phosphomolybdate, then reduced in the presence of acid to give a blue coloration that was measured spectrophotometrically. Filters were immersed in 20 ml 1.25 N sulfuric acid. Aliquots, 4 ml volume, were added to 5 ml 0.25 % ammonium molybdate and 1 ml hydrogen sulfate. This solution was heated to 80 °C for 20 min, cooled, and made up to 10 ml with 1.25 N sulfuric acid. Optional density was measured at 630 nm against a blank.

**Any other information on materials and methods incl. tables****Table 1. Numbers of animals exposed for 1 h to various concentrations of red phosphorus smoke.**

Concentration of smoke (mg/m <sup>3</sup> ) <sup>a</sup>		Number Exposed
as P <sup>a</sup>	as OPA <sup>b</sup>	Mice
870	2,749	20
450	1,422	20
220	695	50
136	430	50
111	351	20

<sup>a</sup> As phosphorus<sup>b</sup> As ortho-phosphoric acid equivalents**Results and discussions****Effect levels****Sex** male**Endpoint** LC50**Effect level** 856 mg/m<sup>3</sup> air**95% CL** 691 — 2117**Exp. duration** 1 h**Remarks** Mouse; as OPA**Mortality**

Rabbits and rats did not differ significantly in respect to lethal toxicity and were the least sensitive species. Red phosphorus smoke was significantly more toxic to the mouse, and even more toxic to the guinea pig, which appeared highly susceptible to this smoke. There was a 28-fold difference in the 1 h-LC<sub>50</sub> values between the guinea pig and rabbit. Most animals that died did so during exposure, although a small proportion survived a few hours or days postexposure.

#### Gross pathology

see the table 4 below.

#### Remarks on results including tables and figures

**Table 2. Exposure concentration-mortality data for the species having a 1-h exposure to red phosphorus smoke.**

Species	Concentration (mg/m <sup>3</sup> ) <sup>a</sup>	Inhalation exposure dose(CT) (mg min/m <sup>3</sup> ) <sup>a</sup>	Mortality <sup>b</sup>	Time to Death
Mice	870	52,000	20/20	DE(20)
	450	27,300	15/20	DE(5) 12h(10)
	220	13,400	22/50	DE(1) 12h(19) 36h(2)
	136	8,170	1/50	12h
	111	6,650	0/20	----

<sup>a</sup> As phosphorus

<sup>b</sup> As (number dying)/(number exposed)

<sup>c</sup> DE = during exposure; expressed at time (number)

**Table 3. LC<sub>50</sub> and L(CT)<sub>50</sub> value calculated from mortality data for several species exposed for 1 h to red phosphorus smoke.**

Species	LC <sub>50</sub> (95% confidence limits) (mg/m <sup>3</sup> ) <sup>a</sup>		L(CT) <sub>50</sub> (95% confidence limits) (mg min/m <sup>3</sup> ) <sup>a</sup>	
	as P <sup>a</sup>	as OPA <sup>b</sup>	as P <sup>a</sup>	as OPA <sup>b</sup>
Mice	271 (196-670)	856 (691-2,117)	16,438 (14,523-19,338)	51,944 (45,893-61,108)

<sup>a</sup> As phosphorus

<sup>b</sup> As ortho-phosphoric acid equivalents

**Table 4. Histopathology in mice exposed for 1 h to various concentrations of red phosphorus smoke.**

Organ and histology		Exposure group (mg/m <sup>3</sup> ) <sup>a,b,c</sup>				
		870	450	220	136	111
<b>ANIMALS DYING</b>						
Group size		20	15	22	1	0
Larynx	Necrosis	G++(11) E++(4); E+(5) -(1)	G++(4) E++(2); E+(7) -(7)	G+++ (16); G++(4) E+(1) -(1)	E++(1)	.
	Inflammation	+++ (8); ++ (4); + (5) -(3)	+++ (3); ++ (2); + (2) -(8)	++ (16); + (6)	++ (1)	.
Trachea	Necrosis	E++ (10); E+ (4) -(6)	E++ (2); E+ (2) -(11)	G++ (4) E++ (3); E+ (14) -(1)	E++ (1)	.
	Inflammation	++ (6); + (8) -(6)	+(6) -(7)	++ (16); + (6)	+(1)	.
Lung	Congestion	++ (12); + (8) -(3)	++ (6); + (9)	+++ (16); ++ (6)	+++ (1)	.
	Hemorrhage	+(3) -(17)	-(15)	+++ (4); ++ (16) -(2)	+(1)	.
	Edema	+(4) -(16)	-(15)	+(4) -(18)	-(1)	.
	Pneumonitis	+(2) -(18)	-(15)	-(22)	-(1)	.
Liver	Congestion	++ (8) -(12)	-(15)	++ (12); + (2) -(8)	+(1)	.
Kidney	Congestion	+(8) -(12)	-(15)	+(6) -(16)	-(1)	.
	Cortical neurosis	-(20)	-(15)	++ (5); + (2) -(15)	-(1)	.
<b>SURVIVORS<sup>d</sup></b>						
Group size		0	5	28	49	20
Larynx	Necrosis	.	-(5)	-(28)	E+(3) -(46)	-(20)
	Inflammation	.	+(1) -(4)	+(6) -(22)	+(4) -(45)	-(20)
Trachea	Necrosis	.	E+(1) -(4)	E+(3) -(25)	E+(5) -(44)	-(20)
			+(1)	++ (2); + (4)	++ (1); + (4)	

	Inflammation	.	-(4)	-(22)	-(44)	-(20)
	Congestion	.	+(2) -(3)	+(28)	++(29);+(20)	+(6) -(14)
Lung	Hemorrhage	.	-(5)	-(28)	-(49)	-(20)
	Edema	.	-(5)	-(28)	-(49)	-(20)
	Pneumonitis	.	-(5)	+(1) -(27)	-(49)	-(20)

<sup>a</sup> Concentration as phosphorus

<sup>b</sup> Expressed as severity(number showing)

<sup>c</sup> Severity: - not seen; + mild; ++ moderate; +++ severe. G = generalized; E = epithelial localized

<sup>d</sup> No hepatorenal pathology in survivors

## Applicant's summary and conclusion

### Conclusions

The acute inhalation LC50 for phosphoric acid was 856 mg orthophosphoric acid/kg (95 % confidence limits 691-2,117 mg/kg).

### Executive summary

**Acute toxicity: inhalation.004**

UUID IUC5-1b656397-f4e2-4e79-b997-d1431225aef5

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2008-12-30 17:31:39 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 2 (reliable with restrictions)

Rationale for reliability 2e - Study well documented, meets generally accepted scientific principles, acceptable for assessment

**Data source****Reference**

Reference type publication

Author Ballantyne B Year 1998

Title Acute inhalation toxicity of red phosphorus smoke.

Bibliographic source Toxic Substance Mechanisms, 17(4): 251-266.

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Cross-reference to same study**

Acute toxicity: inhalation.001, 002, 003

**Materials and methods****Limit test**

no

**Test guideline**

Qualifier no guideline followed

Guideline

Deviations

**GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

no

**Test material identity**

Identifier other:

Identity Solid red phosphorus

**Details on test material**

Smoke generated from pure unformulated red phosphorus ignited in an air stream

**Test animals****Species**

guinea pig

**Strain**

Dunkin-Hartley

**Sex**

male

**Administration / exposure****Route of administration**

inhalation

**Type of inhalation exposure**

whole body

**Vehicle**

unchanged (no vehicle)

**Analytical verification of test atmosphere concentrations**

yes spectrophotometric method

**Duration of exposure**1 h **Remarks** in a 10 m<sup>3</sup> chamber**Concentrations**

Concentration of smoke: 36, 52, 111, 450 mg/m<sup>3</sup>  
 (as orthophosphoric acid equivalents: 114, 164, 351, 1,422 mg/m<sup>3</sup>)

**No. of animals per sex per dose**20(36 mg/m<sup>3</sup>), 20(52 mg/m<sup>3</sup>), 10(111 mg/m<sup>3</sup>), 10(450 mg/m<sup>3</sup>)**Details on study design**

Study design

Animals were exposed, whole body, for 1 h to various concentrations of red phosphorus smoke in a 10 m<sup>3</sup> chamber. Based on pilot exposures, to assess the differential susceptibility of the species studied, the target concentrations of smoke ranged from 35 to 2000 mg/m<sup>3</sup> (expressed as phosphorus; 111-6731 mg/m<sup>3</sup> as ortho-phosphoric acid equivalents). They were allowed free access to food and water, except during the exposures. Survivors were sacrificed 14 days after the exposure. Animals that died and sacrificed survivors were subject to necropsy and the larynx, trachea, lungs, liver, and kidney removed for fixation in phosphate-buffered neutral formalin. Microtome sections, 5 µm thick, were stained with hematoxylin and eosin, and by Schmorl's technique for incipient fibrosis.

**Atmosphere Analysis**

The atmosphere was sampled at 5-min intervals, by drawing air at 5 liters/min through Whatman No. 1 filter papers. Phosphorus in the papers was measured based on its conversion to ammonium phosphomolybdate, then reduced in the presence of acid to give a blue coloration that was measured spectrophotometrically. Filters were immersed in 20 ml 1.25 N sulfuric acid. Aliquots, 4 ml volume, were added to 5 ml 0.25 % ammonium molybdate and 1 ml hydrogen sulfate. This solution was heated to 80 °C for 20 min, cooled, and made up to 10 ml with 1.25 N sulfuric acid. Optional density was measured at 630 nm against a blank.

**Any other information on materials and methods incl. tables****Table 1. Numbers of animals exposed for 1 h to various concentrations of red phosphorus smoke.**

Concentration of smoke (mg/m <sup>3</sup> ) <sup>a</sup>		Number Exposed
as P <sup>a</sup>	as OPA <sup>b</sup>	Guinea Pigs
450	1,422	10
111	351	10
52	164	20
36	114	20

<sup>a</sup> As phosphorus<sup>b</sup> As ortho-phosphoric acid equivalents**Results and discussions****Effect levels****Sex** male**Endpoint** LC50**Effect level** 193 mg/m<sup>3</sup> air**95% CL** 164 — 253**Exp. duration** 1 h**Remarks** Guinea Pig; as OPA

**Mortality**

Rabbits and rats did not differ significantly in respect to lethal toxicity and were the least sensitive species. Red phosphorus smoke was significantly more toxic to the mouse, and even more toxic to the guinea pig, which appeared highly susceptible to this smoke. There was a 28-fold difference in the 1 h-LC<sub>50</sub> values between the guinea pig and rabbit. Most animals that died did so during exposure, although a small proportion survived a few hours or days postexposure.

**Gross pathology**

see the table 4 below.

**Remarks on results including tables and figures**

**Table 2. Exposure concentration-mortality data for the species having a 1-h exposure to red phosphorus smoke.**

Species	Concentration (mg/m <sup>3</sup> ) <sup>a</sup>	Inhalation exposure dose(CT) (mg min/m <sup>3</sup> ) <sup>a</sup>	Mortality <sup>b</sup>	Time to Death
Guinea Pigs	870	27,300	10/10	DE(10)
	111	6,650	9/10	DE(7) 30min(1) 18h(1)
	52	3,130	9/20	DE(4) 3h(3) 5h(1) 18h(1)
	36	2,130	0/20	----

<sup>a</sup> As phosphorus

<sup>b</sup> As (number dying)/(number exposed)

<sup>c</sup> DE = during exposure; expressed at time (number)

**Table 3. LC<sub>50</sub> and L(CT)<sub>50</sub> value calculated from mortality data for several species exposed for 1 h to red phosphorus smoke.**

Species	LC <sub>50</sub> (95% confidence limits) (mg/m <sup>3</sup> ) <sup>a</sup>		L(CT) <sub>50</sub> (95% confidence limits) (mg min/m <sup>3</sup> ) <sup>a</sup>	
	as P <sup>a</sup>	as OPA <sup>b</sup>	as P <sup>a</sup>	as OPA <sup>b</sup>
Guinea Pigs	61 (52-80)	193 (164-253)	3,641 (3,113-4,783)	11,506 (9,837-15,114)

<sup>a</sup> As phosphorus

<sup>b</sup> As ortho-phosphoric acid equivalents

**Table 4. Histopathology in guinea pigs exposed for 1 h to various concentrations of red phosphorus smoke.**

Organ and histology		Exposure group (mg/m <sup>3</sup> ) <sup>a,b,c</sup>			
		870	111	52	36
<b>ANIMALS DYING</b>					
Group size		10	9	9	0
Larynx	Necrosis	-(10)	-(9)	E+(2) -(7)	.
	Inflammation	-(10)	-(9)	+(4) -(5)	.
Trachea	Necrosis	-(10)	-(9)	E+(3) -(6)	.
	Inflammation	-(10)	-(9)	+(2) -(7)	.
Lung	Congestion	+(3) -(7)	+(9)	++(3);+(6)	.
	Hemorrhage	-(10)	-(9)	-(9)	.
	Edema	-(10)	-(9)	-(9)	.
	Pneumonitis	-(10)	-(9)	-(9)	.
Liver	Congestion	+(1) -(9)	++(1) -(8)	+(3) -(1)	.
Kidney	Congestion	+(2) -(9)	++(1);+(1) -(7)	++(1) -(8)	.
<b>SURVIVORS <sup>d</sup></b>					
Group size		0	1	11	20
Larynx	Necrosis	.	-(1)	E+(3) -(8)	E+(4) -(16)

	Inflammation	.	-(1)	++(2);+(1) -(8)	+(4) -(16)
Trachea	Necrosis	.	-(1)	E+(4) -(5)	E+(8) -(18)
	Inflammation	.	-(1)	+(6) -(5)	+(18) -(2)
Lung	Congestion	.	+(1)	++(4) -(7)	++(5);+ (15)
	Hemorrhage	.	-(1)	+(1) -(10)	+(2) -(18)
	Edema	.	-(1)	-(11)	+(4) -(16)
	Pneumonitis	.	-(1)	+(2) -(9)	-(20)

<sup>a</sup> Concentration as phosphorus

<sup>b</sup> Expressed as severity (number showing)

<sup>c</sup> Severity: - not seen; + mild; ++ moderate; +++ severe. G = generalized; E = epithelial localized

<sup>d</sup> No hepatorenal pathology in survivors

**RED:** Sum of the observed animal number was not the same as the group size (refer to reference)

## Applicant's summary and conclusion

### Conclusions

The acute inhalation LC50 for phosphoric acid was 3846 mg orthophosphoric acid/kg (95 % confidence limits 3065-4705 mg/kg).

### Executive summary

**Acute toxicity: inhalation.005**

**UUID** IUC5-3bbdd399-24eb-4ff5-ad83-b4878263716f  
**Dossier UUID** 0  
**Author** nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
**Date** 2009-01-06 12:48:52 KST  
**Remarks**

**Administrative Data****[IP] OECD: HPVC**

**Purpose flag** supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS  
**Study result type** experimental result  
**Reliability** 3 (not reliable)  
**Rationale for reliability** 3b - Significant methodological deficiencies.

**Data source****Reference**

<b>Reference type</b>	publication		
<b>Author</b>	Marrs T	<b>Year</b>	1984
<b>Title</b>	Histological changes produced by exposure of rabbits and rats to smokes produced from red phosphorus.		
<b>Bibliographic source</b>	Toxicol. Lett. 21(2): 141-146		
<b>Testing laboratory</b>		<b>Report no.</b>	
<b>Owner company</b>			
<b>Company study no.</b>		<b>Report date</b>	

**Data access**

data published

**Cross-reference to same study**

Acute toxicity: inhalation.006

**Materials and methods****Limit test**

no

**Test guideline****Qualifier** no guideline followed**Guideline****Deviations****GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

no

**Test material identity****Identifier** other:**Identity** Pyrotechnic mixtures**Details on test material**

Pyrotechnic mixtures  
 Composition I: 95% red phosphorus+5% butyl rubber  
 Composition II: 97% red phosphorus+3% butadiene styrene

**Test animals****Species**

rat

**Strain**

other: Porton Wistar-derived rats



**Sex**

female

**Details on test animals and environmental conditions**

Porton Wistar-derived rats(170-190 g)  
 Supplier: Animal Breeding Unit, CDE, Porton Down.

**Administration / exposure****Route of administration**

inhalation

**Type of inhalation exposure**

whole body

**Vehicle**

unchanged (no vehicle)

**Analytical verification of test atmosphere concentrations**

yes spectrophotometric method

**Duration of exposure**30 min **Remarks****Concentrations**

Composition I: Mass of solid material (3.2 g/m<sup>3</sup>), Phosphorus content (0.68 g/m<sup>3</sup> as phosphorus)  
 Composition II: Mass of solid material (3.1 g/m<sup>3</sup>), Phosphorus content (0.67 g/m<sup>3</sup> as phosphorus)

**No. of animals per sex per dose**

5

**Control animals**

yes

**Details on study design**

30 female rats were used.

After a 30-min exposure the animals were removed from the chamber and placed in an accommodation. The survivors were observed for up to 14 days. Decedents were subjected to autopsy as were survivors after killing at 24 h or 14 days. Larynx, trachea, lung, liver, kidney, adrenal, spleen and pancreas were fixed in phosphate-buffered formain pH 7. 5-µm sections were stained with haematoxylin and eosin.

**Any other information on materials and methods incl. tables****Results and discussions****Mortality**

Exposed to composition I: 1(during exposure), 4(within 24 h of exposure)  
 Exposed to composition II: 2(within 15 min of exposure), 2(4 and 5 h after exposure)

**Gross pathology**

The lungs and other organs of the control animals were normal.

During exposure to composition I, one of the rats died: this animal showed mild laryngotracheal inflammation, blood being present in the tracheal lumen. In this animal severe congestion of the lungs was present together with pulmonary oedema. The 4 rats killed 24 h after exposure showed laryngotracheal inflammatory changes. In 3 of these rats the lung were congested, while the fourth showed additionally polymorphonuclear infiltration in the alveolar walls. The 5 animals killed at 14 days showed mild to moderate inflammation of the larynx predominantly polymorphonuclear in type accompanied by severe pulmonary congestion. Of the other organs examined in the rats, only those of the decedent animal showed any abnormality, namely severe hepatic congestion. 4 of the rats exposed to composition II died within 24 h of exposure. 2 dying within 15 min of exposure showed mild laryngeal inflammation accompanied by severe pulmonary congestion and focal haemorrhage. Mild alveolar oedema was found in one of these animals. 2 animals dying 4 and 5 h after exposure, respectively, showed very similar histological changes but no oedema. One animal killed at a 24 h showed mild laryngotracheal inflammation accompanied by a luminal polymorphonuclear exudates and alveolitis. Of the 5 animals killed at 14 days, 4 had laryngeal inflammation. Apart from mild alveolitis in one of these animals the only other finding was a degree of pulmonary congestion. Of the other organs examined in rats all were normal except for the livers of 2 rats that died 15 min after exposure: both were congested.

**Remarks on results including tables and figures**

Table 1. Animals exposed to the two smokes

Test item	Test animal	Killed		Decedent animals	
		at 24 h	at 14 days	During exposure	Within 24 h of exposure
Composition I	Rats	4	5	1	-
Composition II	Rats	1	5	-	4

**Applicant's summary and conclusion****Conclusions**

Composition II appeared to be somewhat more toxic than composition I in the rats.

**Acute toxicity: inhalation.006**

UUID IUC5-b1d6d337-fbc1-474d-992a-016c39518bff

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2009-01-06 12:49:05 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 3 (not reliable)

Rationale for reliability 3b - Significant methodological deficiencies.

**Data source****Reference**

Reference type publication

Author Marrs T Year 1984

Title Histological changes produced by exposure of rabbits and rats to smokes produced from red phosphorus.

Bibliographic source Toxicol. Lett. 21(2): 141-146

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Cross-reference to same study**

Acute toxicity: inhalation.005

**Materials and methods****Limit test**

no

**Test guideline**

Qualifier no guideline followed

Guideline

Deviations

**GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

no

**Test material identity**

Identifier other:

Identity Pyrotechnic mixtures

**Details on test material**

Pyrotechnic mixtures

Composition I: 95% red phosphorus+5% butyl rubber

Composition II: 97% red phosphorus+3% butadiene styrene

**Test animals****Species**

rabbit

**Strain**

New Zealand White

**Sex**

female

**Details on test animals and environmental conditions**

New Zealand white rabbits(230-240 g)

Supplier: Animal Breeding Unit, CDE, Porton Down.

**Administration / exposure****Route of administration**

inhalation

**Type of inhalation exposure**

whole body

**Vehicle**

unchanged (no vehicle)

**Analytical verification of test atmosphere concentrations**

yes spectrophotometric method

**Duration of exposure**30 min **Remarks****Concentrations**Composition I: Mass of solid material (3.2 g/m<sup>3</sup>), Phosphorus content (0.68 g/m<sup>3</sup> as phosphorus)Composition II: Mass of solid material (3.1 g/m<sup>3</sup>), Phosphorus content (0.67 g/m<sup>3</sup> as phosphorus)**No. of animals per sex per dose**

5

**Control animals**

yes

**Details on study design**

30 female rabbits were used.

After a 30-min exposure the animals were removed from the chamber and placed in an accommodation. Decedents were subjected to autopsy as were survivors after killing at 24 h or 14 days. Larynx, trachea, lung, liver, kidney, adrenal, spleen and pancreas were fixed in phosphate-buffered formain pH 7. 5-µm sections were stained with haematoxylin and eosin.

**Any other information on materials and methods incl. tables****Results and discussions****Gross pathology**

The control animals were normal in all cases except for a mild degree of alveolitis in two of the rabbits.

All the rabbits survived exposure to the smoke from composition I. 4 of the animals of this species, which were killed at 24 h, showed inflammation of the larynx progressing in two cases to epithelial necrosis. Similar findings obtained in the trachea, while 3 out of 5 of the animals also showed alveolitis. Of the remaining two animals killed at 24 h, one had bronchopneumonia. 2 out of 5 rabbits killed at 14 days had laryngeal inflammation and 3 showed tracheal inflammation. All 5 animals had some degree of alveolitis. No oedema was seen in any of the rabbit lung and other organs examined were normal in all but one case. The exception was that one of the animals killed at 24 h had congestion of the liver.

The response of the rabbits to composition II was qualitatively similar to the response of that species to composition I. Two of those killed at 24 h showed severe inflammation of the larynx, with in one case exudate in the lumen. 4 out of 5 of these animals showed mild to severe tracheal inflammation. All of the animals showed parenchymal abnormalities, congestion and alveolitis being present in 4 cases and bronchopneumonia in the fifth. Of the rabbits retained for 14 days, all 5 had laryngeal inflammation and the majority had tracheal inflammation with exudates in the lumen. 2 of the animals had alveolitis and 2 others had bronchopneumonia. In addition to the alveolitis one of the animals had focal lung haemorrhages, accompanied by the presence of macrophages and a degree of oedema.

**Remarks on results including tables and figures**

Table 1. Animals exposed to the two smokes

Test item	Test animal	Killed		Decedent animals	
		at 24 h	at 14 days	During exposure	Within 24 h of exposure
Composition I	Rabbits	5	5	-	-
Composition II	Rabbits	5	5	-	-

**7.2.3 Acute toxicity: dermal****Acute toxicity: dermal.001**

**UUID** IUC5-c4d65520-4c61-4361-8d42-54d2b60d946f  
**Dossier UUID** 0  
**Author** nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
**Date** 2011-04-11 13:37:44 KST  
**Remarks**

**Administrative Data****[IP] OECD: HPVC**

**Purpose flag** key study ( ) robust study summary ( ) used for classification ( ) used for MSDS  
**Study result type** experimental result **Study period** 1975-1976  
**Reliability** 2 (reliable with restrictions)  
**Rationale for reliability** 2e - Study well documented, meets generally accepted scientific principles, acceptable for assessment

**Data source****Reference**

**Reference type** publication  
**Author** Randall DJ and Robinson EC **Year** 1990  
**Title** Acute toxicologic evaluation of various concentrations of phosphoric acid

**Bibliographic source** Journal of the American College of Toxicology B, (1): 69-70

**Testing laboratory** Monsanto Company **Report no.**

**Owner company**

**Company study no.** **Report date**

**Reference type** study report  
**Author** Monsato Co. **Year** 1975  
**Title** Toxicological investigation of phosphoric acid 85% NF

**Bibliographic source**

**Testing laboratory** Younger Labs **Report no.**

**Owner company** Monsanto Company St. Louis, Missouri

**Company study no.** YO-75-027 **Report date** 1975-03-06

**Data access**

data published

**Cross-reference to same study**

Acute toxicity: oral.002  
 Eye irritation.002

**Materials and methods****Test type**

standard acute method

**Limit test**

no

**Test guideline**

**Qualifier** no guideline followed

**Guideline**

**Deviations**

**GLP compliance**

no data

**Test materials**

**Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name Identity

phosphoric acid Identifier

Common name Identity

orthophosphoric acid

**Details on test material**

Dose Preparation: Neat, liquid (Monsanto Preparations of 75 %, 80 % and 85 % phosphoric acid(PA) - aqueous solutions, undiluted)

Commercial aqueous solutions of phosphoric acid produced by Monsanto.

**Test animals****Species**

rabbit

**Strain**

New Zealand White

**Sex**

male/female

**Administration / exposure****Type of coverage**

semioclusive

**Vehicle**

unchanged (no vehicle)

**Details on dermal exposure**

Commercial preparations of phosphoric acid of varying concentration were applied for 24-hr directly to the clipped, intact skin using semi-occlusive dressings.

**Duration of exposure**

24-hr

**Doses**

Dose range: from 631, 1000, 160, 2000, 3160, and 5010 mg/kg

**No. of animals per sex per dose**

1 or 2

**Control animals**

no data

**Details on study design**

A 14-d observation period followed application.

**Results and discussions****Effect levels**

Sex male/female

Endpoint LD50

Effect level > 1260 mg/kg bw

95%  
CL

Remarks PA 85 %

Sex male/female

Endpoint LD50

Effect level > 3160 mg/kg bw

95%  
CL

Remarks PA 80 %

Sex male/female

Endpoint LD50

Effect > 3160 mg/kg bw

level  
95%  
CL  
Remarks PA 75 %  
Sex male/female  
Endpoint LDLo  
Effect level 2000 mg/kg bw  
95%  
CL  
Remarks PA 85 %  
Sex male/female  
Endpoint LDLo  
Effect level 5010 mg/kg bw  
95%  
CL  
Remarks PA 80 %  
Sex male/female  
Endpoint LDLo  
Effect level 5010 mg/kg bw  
95%  
CL  
Remarks PA 75 %

**Mortality**

In the 2000 mg/kg treated group, one female rabbit was died after three days administration. In the 3160 and 5010 mg/kg treated group, one male and one female rabbit was died after one day administration.

**Clinical signs**

Reduced appetite and activity (two to four days in survivors), increasing weakness, collapse and death.

**Gross pathology**

Viscera of surviving animals appeared normal at autopsy.

**Other findings**

Survivors (14 days): Viscera appeared normal.

**Remarks on results including tables and figures**

**Table. Mortality (85% phosphoric acid, undiluted)**

Dosage (mg/kg)	Initial weight		Mortalities/Dosed			Time of Mortality
	Male	Female	Male	Female	Combined	
631	-	2.4	-	0/1	0/1	-
1000	2.4	-	0/1	-	0/1	-
1260	1.9	2.5	0/1	0/1	0/2	-
2000	2.0	1.9	0/1	1/1	1/2	3 days
3160	2.2	-	1/1	-	1/1	1 day
5010	-	2.0	-	1/1	1/1	1 day

**Applicant's summary and conclusion****Interpretation of results**

moderately toxic

**Conclusions**

The dermal LD50s for PA 85 %, PA 80 % and PA75 % were >1,260, >3,160 and >3,160 mg test material/kg, respectively; LDLoS were 2,000, 5,010 and 5,010 mg/kg, respectively.

**Acute toxicity: dermal.002**

**UUID** IUC5-82941f63-4353-4139-8e44-3af4a92fd925  
**Dossier UUID** 0  
**Author** nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
**Date** 2011-04-11 13:38:49 KST  
**Remarks**

**Administrative Data****[IP] OECD: HPVC**

**Purpose flag** supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS  
**Study result type** other:  
**Reliability** 4 (secondary literature)  
**Rationale for reliability** 2g - Data from handbook or collection of data

**Data source****Reference**

**Reference type** review article or handbook  
**Author** ITII, The International Technical Information Institute **Year** 1988  
**Title** Toxic and hazardous industrial chemicals safety manual  
**Bibliographic source** Toxic and hazardous industrial chemicals safety manual. Tokyo, Japan. p. 414  
**Testing laboratory** **Report no.**  
**Owner company**  
**Company study no.** **Report date**

**Data access**

data published

**Cross-reference to same study**

Acute toxicity: oral.003

**Materials and methods****Test guideline****Qualifier** no guideline followed**Guideline****Deviations****GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

**Identifier** CAS number  
**Identity** 7664-38-2  
**Identifier** IUPAC name  
**Identity** phosphoric acid  
**Identifier** Common name  
**Identity** o-Phosphoric acid

**Test animals****Species**

rabbit

**Results and discussions****Effect levels**

**Sex** no data  
**Endpoint** LD50



Effect level 2740 mg/kg bw

95%  
CL

Remarks

### **Applicant's summary and conclusion**

Criteria used for interpretation of results

Japan

### **Conclusions**

Acute dermal LD50 of phosphoric acid is 2,740 mg/kg in rabbit.

**7.3 Irritation / corrosion*****Irritation / corrosion***

UUID IUC5-f92e8dba-cf88-4520-b4ca-7270dc87ed61

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2009-01-06 12:17:34 KST

Remarks

**Administrative Data****[IP] OECD: HPVC****Short description of key information**

A 75 % phosphoric acid is not as irritating to intact skin. Phosphoric acid solutions (10 % and 17 % in water) were not an eye irritant in rabbits. However, solutions from 75 % to 85 % phosphoric acid were corrosive to rabbit eyes. There is acute inhalation toxicity animal study available, which has also monitored the irritation potential of phosphoric acid to the respiratory tract, indicating that phosphoric acid is irritating to the respiratory system.

**7.3.1 Skin irritation / corrosion*****Skin irritation / corrosion.001***

UUID IUC5-85cdc54c-ba10-4e99-b710-d02122bde251

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2009-01-06 12:46:53 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 2 (reliable with restrictions)

Rationale for reliability 2e - Study well documented, meets generally accepted scientific principles, acceptable for assessment

**Data source****Reference**

Reference type study report

Author Weiner M, Freeman C, McCarty JD, Kotkoskie LA and Fletcher MJ Year 1990

Title Modified skin irritation study on 75% phosphoric acid in a single rabbit.

Bibliographic source Acute Toxic Data, 1(2): 98-99

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Materials and methods****Type of method**

in vivo

**GLP compliance**

no data

**Test material equivalent to submission substance identity**

yes

**Test materials****Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name Identity

phosphoric acid Identifier

Common name Identity

orthophosphoric acid Identifier

Common name Identity

monophosphoric acid

**Details on test material**

75 % phosphoric acid, 25 % water

**Test animals****Species**

rabbit

**Strain**

New Zealand White

**Test system**

**Type of coverage**

semioclusive

**Preparation of test site**

shaved

**Vehicle**

water

**Duration of treatment / exposure**

4 hours

**Observation period**

4.5, 24 and 48 hours

**Number of animals**

1

**Control animals**

no data

**Details on study design**

A modified skin irritation study was performed using 75 % phosphoric acid. Since the test material was a concentrated acid, only one animal was used in the study for humane reasons. One New Zealand White rabbit was anesthetized with Surital (0.73 ml/kg, i.v.). The test material (0.5 ml) was in contact with shaved, intact skin for 4 hours under a semi-occlusive wrap. Since no corrosion was immediately evident, the animal was allowed to recover from anesthesia. Skin irritation was scored by the method of Draize\* at 4.5, 24 and 48 hours after dosing.

\* Draize J.H., G. Woodard and H.O. Galvery. J. Pharmacol. Exp. Ther. 83: 384, 1944

**Any other information on materials and methods incl. tables****Results and discussions****Irritation / corrosion results**

<b>Irritation parameter</b>	erythema score
-----------------------------	----------------

<b>Basis</b>	animal #1
--------------	-----------

<b>Time point</b>	4.5
-------------------	-----

<b>Score</b>	0
--------------	---

<b>Max. score</b>	
-------------------	--

<b>Reversibility</b>	
----------------------	--

<b>Remarks</b>	
----------------	--

<b>Irritation parameter</b>	erythema score
-----------------------------	----------------

<b>Basis</b>	animal #1
--------------	-----------

<b>Time point</b>	24
-------------------	----

<b>Score</b>	0
--------------	---

<b>Max. score</b>	
-------------------	--

<b>Reversibility</b>	
----------------------	--

<b>Remarks</b>	
----------------	--

<b>Irritation parameter</b>	erythema score
-----------------------------	----------------

<b>Basis</b>	animal #1
--------------	-----------

<b>Time point</b>	48
-------------------	----

<b>Score</b>	0
--------------	---

<b>Max. score</b>	
-------------------	--

<b>Reversibility</b>	
----------------------	--

<b>Remarks</b>	
----------------	--

<b>Irritation parameter</b>	edema score
-----------------------------	-------------

<b>Basis</b>	animal #1
--------------	-----------

<b>Time point</b>	4.5
-------------------	-----

<b>Score</b>	0
--------------	---

<b>Max.</b>	
-------------	--

score

Reversibility

Remarks

Irritation parameter    edema score

Basis                    animal #1

Time point            24

Score                  0

Max.  
score

Reversibility

Remarks

Irritation parameter    edema score

Basis                    animal #1

Time point            48

Score                  0

Max.  
score

Reversibility

Remarks

***Irritant/corrosive response data***

No irritation or corrosion was noted on the test site during the study.

**Other effects**

none

**Remarks on results including tables and figures**

**Applicant's summary and conclusion**

**Interpretation of results**

not irritating

**Conclusions**

Since a single animal was employed, a definitive conclusion on skin irritancy is not possible; however, the data indicate that 75 % phosphoric acid is not as irritating as expected from its chemical properties. In fact, under the conditions of the study, phosphoric acid was considered to be non-irritating to intact skin.

**Skin irritation / corrosion.002**

UUID IUC5-46c8861d-c0f8-4fe1-ba55-88ed82031e45

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 14:04:57 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type estimated by calculation

Reliability 4 (not assignable)

Rationale for reliability 4e - Documentation insufficient for assessment.

**Data source****Reference**

Reference type publication

Author Bucher K, Bucher KE, and Walz D. Year 1981

Title The topically irritant substance: Essentials – biotests – predictions.

Bibliographic source Agents and Actions, 11:515-519

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Materials and methods****Type of method**

in vivo

**Test guideline**

Qualifier no guideline followed

Guideline

Deviations

**GLP compliance**

no data

**Test material equivalent to submission substance identity**

yes

**Test materials****Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Test animals****Species**

mouse

**Details on test animals and environmental conditions**

Juvenile white mice

**Test system****Preparation of test site**

other: intracutaneously into the soft and tender abdominal skin

**Amount/concentration applied**

5 % and 30 % phosphoric acid solution (w/v)

**Observation period**

6 hours

**Any other information on materials and methods incl. tables****Table 1. Scoring of irritative activity of solutions according to their pH and their osmolality**

Acidic	Score	Basic	Score	Osmolalic	Score
pH 7-4	0 pts	pH 7-9	0 pts	0.4-1 osm/kg	0 pts
pH 4-3	1 pt	pH 9-10	1 pt	1-3 osm/kg	1 pt
pH 3-2	2 pts	pH 10-11	2 pts	3-10 osm/kg	2 pts
pH 2	3 pts	pH 11-12	3 pts	>10 osm/kg	3 pts
-	-	pH 12-13	4 pts	-	-
-	-	pH > 13	5 pts	-	-

**Table 2. Prediction for man on acute noxious risks from contact with mucous membranes**

Sum of points	Class <sup>a</sup>
0	a: practically not irritating
1 or 2	b: weakly irritating
3 or 4	c: moderately irritating
5 or 6	d: strongly irritating
7 or 8	e: very strongly irritating

a: Five classes are chosen to adapt the system to the legislative possibilities in

**Results and discussions****Irritation / corrosion results**

Irritation parameter other: Scoring system and predictions

**Basis**

Time point 6 hours

Score 3

Max. score 8

**Reversibility**

Remarks 5 % Phosphoric acid - c: moderately irritating

Irritation parameter other: Scoring system and predictions

**Basis**

Time point 6 hours

Score 5

Max. score 8

**Reversibility**

Remarks 30 % Phosphoric acid - d: strongly irritating

**Remarks on results including tables and figures****Table 3. Predictions of acute noxious risks from contact with mucous membranes**

Solution of	Concentration (w/v) (%)	pH (measured)	Osmolality (osm/kg) (estimated)	Sum	Class	Prediction
Phosphoric acid	5	1.3	0.5-1	3	c	moderately irritating
	30	0.5	4-5	5	d	strongly irritating

**Overall remarks, attachments****Overall remarks**

This study gives a summary of the animal test, with a detailed description of the principle with which the irritative reaction was

quantified, and propose a scoring system to estimate the risks for men.

### **Applicant's summary and conclusion**

#### **Conclusions**

Based on the results from animal test, 5% and 30% of phosphoric acid were estimated moderately and strongly irritating to human skin.

#### **Executive summary**



***Skin irritation / corrosion.003***

UUID IUC5-156cc139-0104-424d-87cc-4fbb0aeb8426

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2009-03-30 17:09:44 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 3 (not reliable)

Rationale for reliability 3a - Documentation insufficient for assessment

**Data source****Reference**

Reference type study report

Author Monsanto Co. Year 1975

Title Toxicological investigation of phosphoric acid 85% NT

**Bibliographic source**

Testing laboratory Younger Labs Report no.

Owner company Monsanto Company, St. Louis, Missouri

Company study no. YO-75-027 Report date 1975-03-06

**Materials and methods****Type of method**

in vivo

**Test guideline**

Qualifier no guideline followed

Guideline

Deviations

**GLP compliance**

no data

**Test material equivalent to submission substance identity**

yes

**Test materials****Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity Phosphoric Acid

**Details on test material**

phosphoric acid 85% NF

**Test animals****Species**

rabbit

**Strain**

New Zealand White

**Test system*****Amount/concentration applied***

0.5 ml applied undiluted

**Duration of treatment / exposure**

4, 24 hours

**Results and discussions****Irritation / corrosion results**

<b>Irritation parameter</b>	overall irritation score
-----------------------------	--------------------------

<b>Basis</b>	mean
--------------	------

<b>Time point</b>	4, 24 hours
-------------------	-------------

<b>Score</b>	
--------------	--

<b>Max. score</b>	
-------------------	--

<b>Reversibility</b>	
----------------------	--

<b>Remarks</b>	Corrosive
----------------	-----------

***Irritant/corrosive response data***

Loosening about edges of scab in seventeen to twenty-one days. There was injury in depth.  
Corrosive within 4 hours.

**Applicant's summary and conclusion****Interpretation of results**

corrosive

**7.3.2 Eye irritation*****Eye irritation.001***

UUID IUC5-02fece07-29aa-4532-8154-e6656e1d6db6

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 14:07:56 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS  
 Study result type experimental result Study period 1988  
 Reliability 2 (reliable with restrictions)  
 Rationale for reliability 2a - guideline study without detailed documentation. The reversibility data was not provided.

**Data source****Reference**

Reference type publication  
 Author Guido JA. Year 1992  
 Title Two Dilutions of Phosphoric Acid tested on Eye  
 Bibliographic source Journal of American College of Toxicology, 11(6): 724  
 Testing laboratory Institute of Hygiene and Epidemiology, Div. Toxicology Report no.  
 Owner company  
 Company study no. Report date

**Data access**

data published

**Materials and methods****Type of method**

in vivo

**Test guideline**

Qualifier according to  
 Guideline OECD Guideline 405 (Acute Eye Irritation / Corrosion)  
 Deviations

**GLP compliance**

yes

**Test material equivalent to submission substance identity**

yes

**Test materials****Test material identity**

Identifier CAS number  
 Identity 7664-38-2  
 Identifier IUPAC name Identity  
 phosphoric acid Identifier  
 Common name Identity  
 orthophosphoric acid

**Details on test material**

compound preparation: 10 % and 17 % in water

**Test animals****Species**

rabbit

**Strain**

New Zealand White

### Test system

#### Vehicle

water

#### Amount/concentration applied

10 % and 17 % in water

#### Observation period

4, 24, 48, 72 and 96-hr

#### Number of animals

6

#### Control animals

no data

#### Details on study design

Six New Zealand White albino rabbits, application 100 µl into the Sodiumfluorescein before visual scoring of percentage corneal damage.

#### Any other information on materials and methods incl. tables

## Results and discussions

### Overall irritation / corrosion results

**Irritation parameter** conjunctivae score

**Basis** mean

**Time point** from 4-hr to 96-hr

$\geq 1.5$  —  $\leq 2.3$

**Max. score** 3

**Reversibility** no data

**Remarks** 17 % in water

**Irritation parameter** chemosis score

**Basis** mean

**Time point** from 4-hr to 96-hr

$\geq 0$  —  $\leq 2.5$

**Max. score** 4

**Reversibility** no data

**Remarks** 17 % in water

**Irritation parameter** iris score

**Basis** mean

**Time point** from 4-hr to 96-hr

$\geq 0$  —  $\leq 1$

**Max. score** 2

**Reversibility** no data

**Remarks** 17 % in water

**Irritation parameter** cornea score Opacity

**Basis** mean

**Time point** from 4-hr to 96-hr

$\geq 0$  —  $\leq 0.7$

**Max. score** 4

**Reversibility** no data

**Remarks** 17 % in water

**Irritation parameter** other: Surface of Corneal Damage

**Basis** mean

Time point from 4-hr to 96-hr

$\geq 0$  —  $\leq 12$

Max. score 100

Reversibility no data

Remarks 17 % in water

Irritation parameter conjunctivae score

Basis mean

Time point from 4-hr to 96hr

$\geq 1.1$  —  $\leq 2.1$

Max. score 3

Reversibility no data

Remarks 10 % in water

Irritation parameter chemosis score

Basis mean

Time point from 4-hr to 96hr

$\geq 0$  —  $\leq 2.2$

Max. score 4

Reversibility no data

Remarks 10 % in water

Irritation parameter iris score

Basis mean

Time point from 4-hr to 96hr

$\geq 0$  —  $\leq 0.8$

Max. score 2

Reversibility no data

Remarks 10 % in water

Irritation parameter cornea score Opacity

Basis mean

Time point from 4-hr to 96hr

$\geq 0$  —  $\leq 0.2$

Max. score 4

Reversibility no data

Remarks 10 % in water

Irritation parameter other: Surface of Corneal Damage

Basis mean

Time point from 4-hr to 96hr

$\geq 0$  —  $\leq 4$

Max. score 100

Reversibility no data

Remarks 10 % in water

Remarks on results including tables and figures

Time after end of application	4-hr	24-hr	48-hr	72-hr	96-hr
<b>Compound preparation: 17 % in water</b>					
Mean Score of Conjunctivitis (3 maximum)	1.5	2.1	2.3	1.8	1.5
Mean Score of Chemosis (4 maximum)	2.5	1.0	0.8	0.0	0.0
Mean Score of Iritis (2 maximum)	0.7	1.0	0.5	0.0	0.0
Mean Score of Corneal Opacity (4 maximum)	0.0	0.3	0.7	0.3	0.2

Mean surface of Corneal Damage (100% maximum)	0	12	7	2	0.8
<b>Compound preparation: 10 % in water</b>					
Mean Score of Conjunctivitis (3 maximum)	1.8	2.0	2.1	1.4	1.1
Mean Score of Chemosis (4 maximum)	2.2	1.0	0.2	0.0	0.0
Mean Score of Iritis (2 maximum)	0.8	0.3	0.5	0.2	0.0
Mean Score of Corneal Opacity (4 maximum)	0.0	0.0	0.2	0.0	0.0
Mean surface of Corneal Damage (100% maximum)	1	4	1	0	0

### Applicant's summary and conclusion

#### Interpretation of results

not irritating

#### Criteria used for interpretation of results

other: EC criteria - EEC (1983). Annex VI, part IID of the Council Directive 79/831/EEC (19 September 1983). Concerning the guide to the classification and labeling of dangerous substances and preparations; criteria for the choice of phrases indicating special r

#### Conclusions

Not irritating to eyes.

**Eye irritation.002**

**UUID** IUC5-60251ca5-d93f-426c-bcad-1b6e404214c9  
**Dossier UUID** 0  
**Author** nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
**Date** 2011-04-11 14:09:09 KST  
**Remarks**

**Administrative Data****[IP] OECD: HPVC**

**Purpose flag** supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS  
**Study result type** experimental result **Study period** 1975-1976  
**Reliability** 2 (reliable with restrictions)  
**Rationale for reliability** 2e - Study well documented, meets generally accepted scientific principles, acceptable for assessment

**Data source****Reference**

**Reference type** publication  
**Author** Randall DJ and Robinson EC **Year** 1990  
**Title** Acute toxicologic evaluation of various concentrations of phosphoric acid

**Bibliographic source** Journal of the American College of Toxicology B, 1(1): 69-70.

**Testing laboratory** Monsanto Company **Report no.**  
**Owner company**  
**Company study no.** **Report date**

**Reference type** study report  
**Author** Montanto Co. **Year** 1975  
**Title** Toxicological investigation of phosphoric acid 85% NF

**Bibliographic source**

**Testing laboratory** Younger Labs **Report no.**  
**Owner company** Montanto Co.  
**Company study no.** YO-75-027 **Report date** 1975-03-06

**Data access**

data published

**Cross-reference to same study**

Acute toxicity: oral.002  
 Acute toxicity: dermal.002

**Materials and methods****Type of method**

in vivo

**Test guideline**

**Qualifier** no guideline followed

**Guideline****Deviations****GLP compliance**

no data

**Test material equivalent to submission substance identity**

yes

**Test materials****Test material identity**

**Identifier** CAS number

**Identity** 7664-38-2

**Identifier** IUPAC name **Identity**

phosphoric acid **Identifier**

Common name **Identity**

orthophosphoric acid

#### Details on test material

Dose Preparation: Neat, liquid (Monsanto Preparations of 75 %, 80 % and 85 % phosphoric acid(PA) - aqueous solutions)

Commercial aqueous solutions of phosphoric acid produced by Monsanto.

#### Test animals

##### Species

rabbit

##### Strain

New Zealand White

#### Test system

##### Vehicle

unchanged (no vehicle)

##### Amount/concentration applied

0.1 ml of commercial preparations ( undiluted) of phosphoric acid of varying concentration were used.

##### Duration of treatment / exposure

24 hours and 1 minute

##### Observation period

14 days

##### Number of animals

3

##### Control animals

no data

##### Details on study design

0.1 ml of commercial preparations of phosphoric acid of varying concentration were placed into the conjunctival sac of New Zealand albino rabbits.

Eye responses were scored in accordance with the Federal Hazardous Substances Act, 21 CFR, 191.12 (1964).

##### Any other information on materials and methods incl. tables

## Results and discussions

### Overall irritation / corrosion results

**Irritation parameter** overall irritation score

**Basis** mean (x/110.0)

**Time point** 24, 48, 72 hours

**Max. score** 40.1

**Reversibility** fully reversible (14 days: All scored zero)

**Remarks**

#### Irritant/corrosive response data

Immediate: Discomfort was severe with thrashing about the stocks and eyes tightly closed.

10 minutes: Areas of barely perceptible to slight corneal cloudiness, iris reaction to light was sluggish, severe erythema, very slight to slight edema, and copious discharge.

1 hour: Areas of slight corneal cloudiness, iris showed sluggish reaction to light, severe erythema (necrosis), slight edema, and copious discharge.

24-168 hours: Gradual improvement.

14 days: all scored zero.

#### Remarks on results including tables and figures

Hours	Structure	Animal number			Mean Score (x /110.0)
		1	2	3	
1	Cornea	45	30	30	56.0
	Iris	5	5	5	
	Conjunctivae	16	16	16	
24	Cornea	30	30	30	52.3
	Iris	5	5	5	



	Conjunctivae	18	18	16	
	Cornea	30	20	15	
48	Iris	5	5	5	42.6
	Conjunctivae	16	16	16	
	Cornea	20	10	10	
72	Iris	5	0	0	25.6
	Conjunctivae	12	12	8	
	Cornea	10	10	10	
120	Iris	0	0	0	20.0
	Conjunctivae	12	10	8	
	Cornea	10	0	5	
168	Iris	0	0	0	13.6
	Conjunctivae	10	8	8	

### Applicant's summary and conclusion

#### Interpretation of results

corrosive

#### Conclusions

Solutions from 75 % to 85 % phosphoric acid were corrosive to rabbit eyes.

## **7.4 Sensitisation**

### ***Sensitisation***

UUID IUC5-b48d9971-158f-4b9d-8365-9987ff03ed6b

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2008-12-30 15:43:44 KST

Remarks

### **Administrative Data**

[IP] OECD: HPV C

### **Skin sensitisation**

#### **Short description of key information**

There were no reliable sensitization studies available

**7.5 Repeated dose toxicity*****Repeated dose toxicity***

UUID IUC5-e74f8d22-24cf-4ae6-b116-853e64643c45

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2009-03-27 16:54:20 KST

Remarks

**Administrative Data****[IP] OECD: HPVC****Key parameter (optional)****Repeated dose toxicity: oral**

Effect level	NOAEL	in	250
		mg/kg	
		bw/day	

**Repeated dose toxicity: inhalation**

Effect level	BMC05	in	64
		mg/m <sup>3</sup>	
		air	

**7.5.1 Repeated dose toxicity: oral*****Repeated dose toxicity: oral.001***

**UUID** IUC5-23cf5765-6634-4edb-8a82-06f616c547f6  
**Dossier UUID** 0  
**Author** nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
**Date** 2010-08-17 17:11:24 KST  
**Remarks**

**Administrative Data****OECD: HPVC**

**Purpose flag** key study ( ) robust study summary ( ) used for classification ( ) used for MSDS  
**Study result type** experimental result **Study period** Apr. 10, 2008 - Oct. 29, 2008  
**Reliability** 1 (reliable without restriction)  
**Rationale for reliability** 1b-comparable to guideline study

**Data source****Reference**

<b>Reference type</b>	study report		
<b>Author</b>	National Institute of Environmental Research (NIER)	<b>Year</b>	2008
<b>Title</b>	Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Phosphoric acid in rats.		
<b>Bibliographic source</b>			
<b>Testing laboratory</b>	Biotoxtech Co., Ltd.	<b>Report no.</b>	B08008
<b>Owner company</b>			
<b>Company study no.</b>		<b>Report date</b>	

**Data access**

data submitter is data owner

**Data protection claimed**

yes, but not willing to share

**Cross-reference to same study**

7.8.1 Toxicity to reproduction.001 and 7.8.2 Developmental toxicity/teratogenicity.001

**Materials and methods****Test type**

combined repeated dose and reproduction / developmental screening

**Limit test**

no

**Test guideline****Qualifier** according to**Guideline** OECD Guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test)**Deviations****GLP compliance**

yes (incl. certificate)

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity****Identifier** CAS number**Identity** 7664-38-2**Identifier** IUPAC name**Identity** phosphoric acid

**Details on test material**

- Name of test material (as cited in study report): Phosphoric acid
- Molecular formula (if other than submission substance):  $\text{H}_3\text{PO}_4$
- Molecular weight (if other than submission substance): 98.00
- Physical state: VISCOUS COLORLESS LIQUID
- Analytical purity: 99.999 % (metals basis), 85wt. % in  $\text{H}_2\text{O}$
- Lot/batch No.: 09405LE, 09411TH
- Storage condition of test material: Stored under refrigeration

**Test animals****Species**

rat

**Strain**

Sprague-Dawley

**Sex**

male/female

**Details on test animals and environmental conditions****TEST ANIMALS**

- Source: Rat, Sprague-Dawley (CrI:CD(SD)), SPF (Supplier: ORIENTBIO INC., Korea)
- Age at study initiation: Male - 9 weeks old, Female - 8 weeks old
- Weight at study initiation: Male - 288.6–336.7 g, Female - 163.5–188.9 g
- Housing: Stainless wire cage, 260W×350D×210H (mm), Polycarbonate cage 260W×420L×180H (mm), 1 animal per cage (During the mating period: 1 male and 1 female, During the lactation period: 1 female and neonate)
- Diet (e.g. ad libitum): ad libitum
- Water (e.g. ad libitum): ad libitum
- Acclimation period: 1 week

**ENVIRONMENTAL CONDITIONS**

- Temperature ( $^{\circ}\text{C}$ ): 19.2–23.4  $^{\circ}\text{C}$
- Humidity (%): 27.6–64.3 %
- Air changes (per hr): 10–15 times/hour
- Photoperiod (hrs dark / hrs light): 12-hour light/dark cycle (lights on at 7 a.m., lights off at 7 p.m.)

**Administration / exposure****Route of administration**

oral: gavage

**Vehicle**

other: Water for injection

**Details on oral exposure****PREPARATION OF DOSING SOLUTIONS:**

At use, the test substance was diluted to necessary concentration using the Water for injection and prepared.

**VEHICLE**

- Amount of vehicle (if gavage): 5 mL/kg
- Lot/batch no. (if required): GBA8002, GBA8003

**Duration of treatment / exposure**

The males were administrated once daily during 2 weeks prior to mating, the 2 weeks of mating period, and 2 weeks after mating (total 6 weeks).

The females of main group were administrated once daily from 2 weeks before mating to Day 4 post partum (approximately 54 days). The females of recovery group (without mating) were administrated approximately 54 days (applied equally main group females).

Also, coitus was confirmed, but females did not show gestational signs, and were administrated until gestation Day 26.

**Frequency of treatment**

once a day

**Doses/concentrations**

0, 125, 250 and 500 mg/kg bw

Basis actual ingested

**No. of animals per sex per dose**

main group: 13 animals per sex per dose

recovery group: 6 animals (control and high dose group)

**Control animals**

yes, concurrent vehicle

**Details on study design**

- Dose selection rationale: The dose levels were determined based on the previous dose range finding study (Study No.: B08008P). In result, food consumption of males and females was decreased at 500 mg/kg, and females were observed in inhibition of weight gain. In addition, 1000 mg/kg dose level was observed in salivation and soft stool, and moribund in one male. As a result, 500 mg/kg was selected as the high dose level for this study and sequentially divided by a geometric ratio of 2 to produce two additional lower doses. 250 and 150 mg/kg were selected as the middle and low dose levels, respectively. In the control group, Water for injection was administered the same as dosing volume of the high dose.

- Rationale for animal assignment (if not random): lowering the period of quarantine and acclimation, 64 males and 64 females which were shown no clinical signs and satisfied body weight gains, were selected and allocated based on body weights to four groups. The control and high dose groups had 19 males and 19 females, and the low and mid dose groups had 13 males and 13 females, respectively.

## Examinations

### *Observations and examinations performed and frequency*

CAGE SIDE OBSERVATIONS: Yes

- Time schedule: The parent's animals were observed for clinical signs including abortion, dystocia, premature birth, parturition, and lactation condition once daily. The moribund and mortality were observed twice daily. The recovery groups were observed during 2 weeks after the end of administration.
- Cage side observations checked in table [No.1-1 and 1-2] and appendix [No.1-1 and 1-2] were included.

DETAILED CLINICAL OBSERVATIONS: Yes

- Time schedule: once a week
- Detailed clinical signs were performed the day before the first administration and once a week during the treatment and recovery period for general appearance, posture, activity, response to handling, nervous system, function of autonomic nervous system, and abnormal behavior.

BODY WEIGHT: Yes

- Time schedule for examinations: once a week
- Body weights of males were measured just before administration and once a week during the treatment and recovery period. Body weights of females were measured just before administration, on Day 0, 7, 14, and 20 of gestation and on Day 0 and 4 of lactation. During the administration and recovery period, body weights were measured once a week. Only, body weights were not measured during the mating period.

HAEMATOLOGY: Yes

- Time schedule for collection of blood: on the day necropsy
- Anaesthetic used for blood collection: Yes (with isoflurane)
- Animals fasted: Yes (fasted from approximately over 18 hours prior to necropsy)
- How many animals: 6 males and 6 females selected from each group
- Parameters checked in table [No.13-1 and 13-2] and appendix [No.13-1 and 13-2] were examined.

CLINICAL CHEMISTRY: Yes

- Time schedule for collection of blood: on the day necropsy
- Animals fasted: Yes (fasted from approximately over 18 hours prior to necropsy)
- How many animals: 6 males and 6 females selected from each group
- Parameters checked in table [No.14-1 and 14-2] and appendix [No.14-1 and 14-2] were examined.

URINALYSIS: Yes

- Time schedule for collection of urine: Urine samples were collected for approximately 3 hours as fresh urine and approximately 24 hours as cumulative urines
- Metabolism cages used for collection of urine: No data
- Animals fasted: No data
- Parameters checked in table [No.12-1 ~ 6] and appendix [No.12-1 ~ 6] were examined.

NEUROBEHAVIOURAL EXAMINATION: Yes

- Time schedule for examinations: on the day before necropsy
- Dose groups that were examined: Six males and six females selected from each group in the main group and all animals of the recovery group
- Battery of functions tested:
  - Pinna reflex: Checked the reflex at the stimulation of animal's auricle.
  - Auditory reflex: Checked the reflex to sound at the sound generation.
  - Corneal reflex: Checked the reflex at the stimulation of animal's cornea.
  - Papillary reflex: Checked the reflex of pupil by the light.
  - Traction test: Measured the times to grasp the metal horizontal bar by forepaws.
  - Rotarod test: Measured the times to endure on the rotating rod.
  - Open field test: Animals were allocated to the open field test boxes. The frequency for movement of each animal was recorded.

### *Sacrifice and pathology*

NECROPSY FINDINGS: Yes (see table 17-1, 17-2, appendix 17-1 and 17-2)

After completion of observation period of main and recovery groups, all live and dead animals were performed to detailed macroscopic examination about body surface and organ and tissue of the whole body.

HISTOPATHOLOGY: Yes (see table 18-1, 18-2, appendix 18-1 and 18-2)

Histopathological examinations for 6 males and 6 females selected from each group in the main group such as the control group

and the high dose group, and the recovery group, the number of dead animals, and organ of macroscopic lesions were performed.

#### **Other examinations**

##### **ORGAN WEIGHTS:**

The following organs which were selected from six males and six females each group in the main group and all animals of the recovery group were weighed individually at necropsy. Organ-to-body weights (terminal body weights) percentages were calculated. Only, testis and epididymides were weighed from all male animals. Paired organs (\*) were weighed together. [Brain · Heart · Liver · Thymus · Spleen · Kidney\* · Adrenal\* · Testis\* · Epididymis\* · Ovary\* · Uterus ]

#### **Statistics**

Statistical analysis of this study was performed by the SAS program (SAS 9.1.3, SAS Institute Inc., U.S.A.).

For the data including body weights, food consumption, urine, hematology, blood biochemistry parameters, organ weights, sensory reflex, and motor function test, the Bartlett test was conducted to test for variance homogeneity at the 5.0% one-tailed probability level. One-way analysis of variance (ANOVA) test was employed on homogeneity, if significant, followed by Dunnett's t- test for multiple comparisons. Kruskal-wallis was employed on heterogeneity, if significant, followed by Mann-whitney u-test for multiple comparisons. Group comparison was performed at the 5.0 and 1.0% two-tailed probability level.

For the data of recovery, Folded-F test was conducted to test for variance homogeneity at the 5.0% two-tailed probability level. Student t-test was employed on homogeneity, if overrule, Aspin-Welch t-test was performed at the 5.0 and 1.0% two-tailed probability level.

Non pregnancy animals were excluded.

#### **Any other information on materials and methods incl. tables**

## **Results and discussions**

#### **Effect levels**

**Endpoint** NOAEL

**Effect level** 250 mg/kg bw/day (actual dose received)

**Sex** male/female

**Basis for effect level / Remarks** Two dead females in the 500 mg/kg treatment group were occurred, and findings of gaseous distension of gastrointestinal tract were observed. Also, mucous stool, soft stool, and dirty nose were observed in one male of the 500 mg/kg treatment group.

#### **Observations**

##### **Clinical signs and mortality**

yes

##### **Body weight and weight gain**

yes

##### **Food consumption and compound intake (if feeding study)**

yes

##### **Haematology**

yes

##### **Clinical chemistry**

yes

##### **Urinalysis**

yes

##### **Neurobehaviour**

yes

##### **Organ weights**

yes

##### **Histopathology: non-neoplastic**

yes

#### **Details on results**

##### **CLINICAL SIGNS AND MORTALITY (Table 1 & Appendix 1)**

In the main group, death was observed in one female (2403) of the 500 mg/kg treatment group on Day 16 of administration. And in the recovery group, death was observed in one female (2416) of the 500 mg/kg treatment group on Day 52 of administration.

In the main group, no clinical signs were observed in males and females of 125 mg/kg treatment group and in females of the 250 mg/kg treatment group. But, transient salivations which were appeared immediately after administrations were sporadically observed in four males of the 250 mg/kg treatment group during from Day 22 of administration to completion of administration. Also, transient salivations were observed in all males of the 500 mg/kg treatment group from Day 20 of administration to completion of administration and in four females of the 500 mg/kg treatment group from Day 2 of gestation to completion of administration, sporadically or persistently. In addition, mucous stool, soft stool, and dirty nose were observed in one male (1407) of the 500 mg/kg treatment group on Day 22 and 23.

In the recovery group, transient salivations were observed in almost all males of the 500 mg/kg treatment group from Day 16 of administration to completion of administration and in almost all females of the 500 mg/kg treatment group from Day 20 of administration to completion of administration, sporadically or persistently.

Detailed clinical signs (Table 2 & Appendix 2) were performed once a week during the study period, and no clinical signs were observed in all animals of the control and treatment groups.

#### BODY WEIGHT AND WEIGHT GAIN (Figure 1, 2, 3, 4 & Table 3 & Appendix 3)

In the main group, no treatment-related abnormalities in body weight gain were noted in all animals of the control and treatment groups.

In females of the recovery group, body weights on Day 55 of administration were significantly decreased ( $p<0.05$ ) compared with the control group in the 500 mg/kg treatment group. Besides, no treatment-related abnormalities in body weight gain were noted in all males.

#### FOOD CONSUMPTION (Table 4 & Appendix 4)

In the main group, no treatment-related abnormalities in food consumption were noted in all animals of the control and treatment groups.

In females of the recovery group, food consumption was significantly decreased ( $p<0.05$ ) compared with the control group on Day 13 and 34 of administration in the 500 mg/kg treatment group. Besides, no treatment-related abnormalities in food consumption were noted in all males.

#### HAEMATOLOGY (Table 13 & Appendix 13)

In the main group, no treatment-related abnormalities in haematology were noted in all animals of the control and treated groups.

In the recovery group, eosinophils (EOS) of males and prothrombin time (PT) of females were significantly increased ( $p<0.05$ ) compared with the control group in the 500 mg/kg treatment group.

#### CLINICAL CHEMISTRY (Table 14 & Appendix 14)

In blood biochemistry of the main group, phosphorus (P) was significantly decreased ( $P<0.05$ ) compared with the control group in females of the 125 mg/kg treatment group.

In female of the recovery group, triglycerides (TG,  $p<0.05$ ), total proteins (TP,  $p<0.05$ ), and albumin (Alb,  $p<0.01$ ) were significantly decreased compared with the control group in the 500 mg/kg treatment group.

#### URINALYSIS (Table 12 & Appendix 12)

In the main and recovery groups, no treatment-related abnormalities were noted in the urinalysis parameters.

#### NEUROBEHAVIOUR (Table 10, 11 & Appendix 10, 11)

No treatment-related abnormalities in the pinna reflex, auditory reflex, corneal reflex, papillary reflex, traction, rota rod, and open field test were observed in all animals of the control and treatment groups.

#### ORGAN WEIGHTS (Table 15, 16 & Appendix 15, 16)

In the main group, no treatment-related abnormalities in absolute and relative organ weights of the males were noted compared with the control group. However, in females, absolute organ weights of kidney were significantly increased ( $p<0.05$ ,  $p<0.01$ ) compared with the control group in all treatment groups; however, dose-dependent was not observed. Relative organ weights of uterus were significantly decreased ( $p<0.05$ ) compared with the control group in the 500 mg/kg treatment group; however, the difference was slight.

In the recovery group, no treatment-related abnormalities in absolute and relative organ weights of the males were noted.

However, in females, fasted body weights ( $p<0.01$ ) and absolute organ weights of heart ( $p<0.05$ ) were significantly decreased compared with the control group in the 500 mg/kg treatment group.

#### GROSS PATHOLOGY (Table 17 & Appendix 17)

In the necropsy findings of the main group, agenesis of spleen was observed in one male (1302) of the 250 mg/kg treatment group, and yellow spot of epididymis was observed in one male (1408) of the 500 mg/kg treatment group. The other abdominal signs were not observed, and the necropsy finding of recovery group was not noted.

In the necropsy findings for dead animals, gaseous distension was observed in one female (2403) of the 500 mg/kg treatment group in the main group on Day 16 of administration. In the recovery group, gaseous distension, severe hydronephrosis of left kidney and dilation of left uterine horn were observed in one female (2416) of the 500 mg/kg treatment group in the recovery group on Day 52 of administration.

#### HISTOPATHOLOGY: NON-NEOPLASTIC (Table 18 & Appendix 18)

In the main group, cast of kidney was observed in one male (1104) of the control group, and sperm granuloma of epididymis was observed in one male (1408) of the 500 mg/kg treatment group. The other abnormal findings were not observed.

In the recovery group, basophilic tubules of kidney was observed in one female (2119) of the control group. The other abnormal findings were not observed.

In the 500 mg/kg treatment group of the main group female, no histopathological change in one dead animal (2403) was observed. In the 500 mg/kg treatment group of the recovery group female, renal tissue in one dead animal (2416) was not observed by severe hydronephrosis of gross findings, and left uterine horn was dilated; however, no histopathological change was observed.

#### Remarks on results including tables and figures

### Overall remarks, attachments

#### Overall remarks



**Attached full study report**

TG 422\_7664-38-2.pdf / 943.57 KB (application/pdf)

## **Applicant's summary and conclusion**

### **Conclusions**

Based on these results, there were no effects of the test substance in males and females at 250 mg/kg and below. However, two dead females in the 500 mg/kg treatment group were occurred, and findings of gaseous distension of gastrointestinal tract were observed. Mucous stool, soft stool, and dirty nose were observed in one male of the 500 mg/kg treatment group. Therefore, NOAEL for repeated dose toxicity was determined at 250 mg/kg in all males and females.

### **Executive summary**

**7.5.3 Repeated dose toxicity: inhalation*****Repeated dose toxicity: inhalation.001***

UUID IUC5-69496b66-5c65-4273-bd15-6fe351afeb7e

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-18 16:43:44 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 3 (not reliable)

Rationale for reliability 3a - documentation insufficient for assessment

**Data source****Reference**

Reference type publication

Author Aranyi C, Henry MC, Vana SC, Gibbons RD and Iverson WO Year 1988

Title Effects of multiple intermittent inhalation exposures to red phosphorus/butyl rubber obscurant smokes in Sprague-Dawley rats

Bibliographic source Inhalation Toxicology, Premier issue. 65-78.

Testing laboratory Report no.

Owner company

Company study no. Report date

Reference type review article or handbook

Author United States Environmental Protection Agency (US EPA) Year 1995

Title Documentation of the reference concentration for chronic inhalation exposure (RfC) for phosphoric acid.

Bibliographic source Integrated Risk Information System (IRIS on-line: <http://www.epa.gov/iris/subst/0697.htm>). Washington, DC: U.S. EPA.

Testing laboratory Report no.

Owner company

Company study no. Report date

**Data access**

data published

**Materials and methods****Test type**

chronic

**Test guideline**

Qualifier no guideline followed

Guideline

Deviations

**GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

no

**Test material identity**

Identifier CAS number

Identity 7664-38-2

**Identifier** IUPAC name

**Identity** Phosphoric Acid

**Details on test material**

combustion products of 95% red phosphorus and 5% butyl rubber

**Test animals**

**Species**

rat

**Strain**

Sprague-Dawley

**Sex**

male

**Administration / exposure**

**Route of administration**

inhalation: aerosol

**Type of inhalation exposure**

no data

**Vehicle**

no data

**Details on inhalation exposure**

The combustion products were mixed and diluted with filtered air and introduced into 1-cu.m exposure chambers.

**Analytical verification of doses or concentrations**

yes

**Details on analytical verification of doses or concentrations**

The aerosol mass concentration was monitored continuously by optical methods and periodically by gravimetric filter sampling.

**Duration of treatment / exposure**

4 consecutive days/week

**Frequency of treatment**

2.25 hours/day

**Doses/concentrations**

Study 1: 0, 300, 750, or 1200 mg/m<sup>3</sup> combustion products,

**Basis** no data

Study 2: 0, 50, 180, or 300 mg/m<sup>3</sup> combustion products

**Basis** no data

**MMAD / GSD**

Aerosol particle size was determined once a day with MMADs ranging from 0.49-0.65 microns and sigma g's of 1.56-1.83. The percent of the aerosols that were phosphoric acids ranged from 71-79% (apparently based on gravimetric analysis).

**No. of animals per sex per dose**

Study 1: 176, 84, 176, 176 animals/group

Study 2: 40 animals/group

**Control animals**

yes, concurrent no treatment

**Details on study design**

Control animals were exposed to filtered air only.

**Results and discussions**

**Effect levels**

**Endpoint** LOAEL

**Effect level** 180 mg/m<sup>3</sup> air

**Sex** male

**Basis for effect level /** Based on the histologic lesions in the tracheobronchiolar region

**Remarks**

**Endpoint** NOAEL

Effect level 50 mg/m<sup>3</sup> air  
 Sex male  
 Basis for effect level / Remarks Based on the histologic lesions in the tracheobronchiolar region

## Observations

### *Clinical signs and mortality*

yes

### *Body weight and weight gain*

yes

### *Gross pathology*

yes

### *Histopathology: non-neoplastic*

yes

### *Details on results*

One of the 176 animals in the 750 mg/m<sup>3</sup> dose group and 19 of the 176 animals in the 1200 mg/m<sup>3</sup> dose group died of treatment related effects. Decreases in body weight gain also were observed, but only in the two groups exposed to the highest concentrations. No deaths were noted in the second study. In the first study, all major organs and respiratory tract tissues were examined histologically in a portion of the animals (n = 12) from each exposure group. Neurobehavioral studies also were performed in the first study. The focus of the second, lower concentration study was the respiratory tract; tissues examined in this study included the turbinates (two sections), trachea, and five lobes of the lung from 20 animals in each exposure group and controls. Concentration-related decreases in pulmonary bactericidal activity was observed for all exposure groups only in the first study, although no significant effects were noted in the second study. Both studies clearly indicated the target organ to be the respiratory tract, specifically the terminal bronchioles. Pathological examination of a portion of those animals that died revealed extensive involvement of bronchiolar and laryngeal mucosa, the latter probably being contributory to death. Terminal bronchiolar fibrosis (minimal to severe) with no or minimal involvement of pulmonary tissues was the only concentration-dependent lesion noted in the respiratory tract of animals surviving repeated exposures. This lesion was present in all animals examined that had been exposed to 750 or 1200 mg/m<sup>3</sup>, including those necropsied after an 8-week recovery period, and was judged predominately as moderate and severe. In the second study, this lesion was present with minimal severity in 9/20 animals exposed to 300 mg/m<sup>3</sup>, 4/20 animals exposed to 180 mg/m<sup>3</sup>, and 0/20 animals exposed to 50 mg/m<sup>3</sup>.

### *Remarks on results including tables and figures*

## Overall remarks, attachments

### Overall remarks

#### DERIVATION OF A BENCHMARK CONCENTRATION (BMC):

The data for bronchiolar fibrosis were combined from both studies for BMC analyses. Estimates of the 1, 5, and 10% incidence levels [extra risk; P(d)-P(0)/P(0)] were obtained using both Weibull and linear models. The Weibull model (no threshold) gave the better goodness-of-fit to the data. The maximum likelihood estimate (MLE) of the 10% incidence level was 150 mg/cu.m, with the lower 95% confidence level bound of the MLE at **100 mg/cu.m = BMC10**. The corresponding estimates for the 5% incidence level were 112 mg/cu.m for the MLE and **64 mg/cu.m = BMC05**. These estimates were nearly the same with the linear model. As there is some evidence suggesting that a 10% incidence level correlates with a NOAEL for one type of noncancer endpoint and, because both the BMC05 and BMC10 were below the empirical LOAEL of 180 mg/cu.m, the BMC10 of 100 mg/cu.m was chosen for further quantitative analysis. This practice is in general concordance with the RFC methodology in choosing the highest NOAEL with the lowest LOAEL.

## Applicant's summary and conclusion

### Conclusions

Based on the histologic lesions in the tracheobronchiolar region, 180 mg/cu.m is the LOAEL, and 50 mg/cu.m is the NOAEL.

### Executive summary

**7.6 Genetic toxicity*****Genetic toxicity***

UUID IUC5-e5c34d31-01aa-47b3-becf-399928b592b1

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2008-12-30 11:31:44 KST

Remarks

**Administrative Data****[IP] OECD: HPV C****Short description of key information**

Phosphoric acid did not show the chromosome aberrations regardless of application of metabolic activation system in the chromosome aberration assay system using Chinese hamster lung cell(CHL/IU). Phosphoric acid was considered to be non-genotoxic in the bacterial reverse mutation test.  
No in vivo genotoxicity studies were available.

**Key parameter (optional)****Genetic toxicity**

negative

**Discussion**

**7.6.1 Genetic toxicity in vitro*****Genetic toxicity in vitro.001***

UUID IUC5-9022b8f9-226e-4c0f-a319-52b6a9d08702

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-07 18:09:04 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result Study period Jun 1, 2005 - Oct 10, 2005

Reliability 1 (reliable without restriction)

Rationale for reliability 1a - GLP guideline study

**Data source****Reference**

Reference type study report

Author National Institute of Environmental Research (NIER), Korea

Year 2005

Title In vitro chromosome aberration test of Phosphoric acid (CAS No. 7664-38-2) using mammalian cultured cell

Bibliographic source

Testing laboratory Biototech

Report no. R05145

Owner company

Company study no.

Report date

**Data access**

data submitter is data owner

**Data protection claimed**

yes, but willing to share

**Materials and methods****Type of genotoxicity**

chromosome aberration

**Type of study**

in vitro mammalian chromosome aberration test

**Test guideline**

Qualifier according to

Guideline OECD Guideline 473 (In vitro Mammalian Chromosome Aberration Test)

Deviations no

**GLP compliance**

yes (incl. certificate)

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Details on test material**

Purity: 86.3%

Lot No.: 09604TR

Supplier: Sigma-Aldrich Korea Ltd.

**Method**

**Species/strain**

<b>Species/strain</b>	mammalian cell line, other: Chinese Hamster Lung (CHL/IU)
<b>Details on mammalian cell lines (if applicable)</b>	Cell lines were received on Nov. 15, 2002 from the American Type Culture collection (ATCC) (Lot No.: 2184656, USA).
<b>Additional strain characteristics</b>	
<b>Metabolic activation</b>	with and without
<b>Metabolic activation system</b>	Rat liver S9 (Aroclor-1254 induced)

**Test concentrations**

0, 112.5, 225, 450 µg/mL

**Vehicle**

Water for injection (Lot No.: AAW4AU, Choongwae Pharma Corp., Korea)

**Controls**

<b>Negative controls</b>	yes
<b>Solvent / vehicle controls</b>	yes Water for injection (Lot No.: AAW4AU, Choongwae Pharma Corp., Korea)
<b>True negative controls</b>	
<b>Positive controls</b>	yes
<b>Positive control substance</b>	mitomycin C Benzo[a]pyrene (Lot No. : 111K3454, Sigma, USA)
<b>Remarks</b>	

**Details on test system and conditions**

MTT assay and chromosome aberration test were conducted as follows;

**(1) MTT assay**

Cultured cells in 75 cm<sup>2</sup> cell culture flask (Nunc, USA) were cultured in a fresh medium to make final density for 5×10<sup>4</sup> cell/mL using the hemocytometer in 96 well plate (200 µL/well; Nunc, USA). Cells were incubated in the 5% CO<sub>2</sub> incubator containing 95% relative humidity and 37 °C. All plates were divided into three as follows; (a) the continuous treatment, (b) in the absence and (c) the presence of metabolic activation system of short time treatment. Well number and others were recorded in surfaces and sides of the plates. For this experiments, 4 wells per dose were made.

In the short time treatment, both negative control and the test substance were added in the wells regardless of application of the metabolic activation system. In addition, S9 mix and 0.1 mol/L phosphate buffer (pH 7.4) were treated to make 5 % of the final concentration without and with metabolic activation system. In 6 hours cultivation, each well was washed by a culture medium and then mediums were replaced to culture for 18 hours more.

In the continuous treatment system, both negative control and the test substance were added in the wells as the short time treatment and cultured for 24 hours.

Both the short time treatment and continuous treatment systems were incubated in a 5 % CO<sub>2</sub> incubator containing 95 % of relative humidity and 37 °C.

In 24 hours (culture completion time), 50 µL of MTT (5 mg/mL PBS) were treated and cultured for 4 hours. After 4 hours, the wells were washed with PBS and were dried. DMSO (150 µL/well) was added and dissolved in it. The spectrophotometrical absorbance of the sample was measured, using the ELISA reader (VERSA mat<sup>TM</sup>, Molecular Devices, USA) at 540 nm. The results were expressed as a graph for an absorbance and calculated IC<sub>50</sub>.

**(2) In vitro Chromosome aberration test**

The cultured cells in a 75 cm<sup>2</sup> cell culture flask (Nunc, USA) were cultured in fresh mediums to make the final density for 5×10<sup>4</sup> cell/mL using the hemocytometer (5 mL/dish; Nunc, USA) in 60 mm culture dish. All dishes were divided into three as follows; (a) the 24 hour culture system of continuous treatment, (b) in the absence and (c) presence of metabolic activation system of short time treatment. In the surfaces and sides of the dishes, well number and others were recorded. In the experiments, 2 slides per dish were prepared and used as the negative control and positive control in each group.

In the short time treatment, the negative control, the test substance (all dose levels), In addition, S9 mix and 0.1 mol/L phosphate buffer (pH 7.4) were treated to make 5 % of the final concentration without and with metabolic activation system. and 0.05 µg/mL of MMC were treated in the absence of metabolic activation system and it was cultured for 6 hours. In addition, of the negative control, the test substance (all dose levels), 20 µg/mL of B[a]P and 5% (final concentration) of S9 mix were treated in the presence of metabolic activation system. Then culture mediums were removed from dishes and washed. Fresh mediums were newly placed and cultured for 18 hours.

In the continuous treatment, the negative control, the test substance, and 0.05 µg/mL of MMC were treated and cultured for 24 hours.

The short time treatment and continuous treatment system were incubated in a 5 % CO<sub>2</sub> incubator containing 95 % of relative humidity and 37 °C.

About 2 hours before culture completion, 0.25 µg/mL of colcemid (Gibco, USA) was treated. After the culture completion, cells were treated by 0.25 % trypsin-EDTA and were sedimented by the centrifuger at 1000 rpm, 4 °C for 5 minutes. The cells were treated with a hypotonic solution (0.075 mol/L, KCl) for 30 minutes at 37 °C, and then were fixed using 1 mL of freshly prepared fixative (methanol: glacial acetic acid, 3:1). After the centrifugation (at 2000 rpm, 4 °C for 5 minutes), the supernant was removed and 5 mL of cooling fixative was added. This process was repeated twice. Then 1 ~ 2 drops of cell suspensions were dropped on the slides.

The slides were dried at a room temperature overnight and stained with 5 % Giemsa solution (manufactured with 0.1 mol/L Sörenson Phosphate buffer (pH 6.8)) for 30 minutes. The numbers of slides were randomized.

#### Evaluation criteria

##### Observation

In each slide, 100 metaphases (200 metaphases/dose) were examined using the biological microscope of differential interference type (BX-51, Olympus, Japan) of 1000-fold magnification. There are two types of chromosome aberrations namely, structural aberration and numerical aberration and these were counted. Structural aberration was classified as follows; chromatid break (ctb), chromatid exchange (cte), chromosome break (csb), chromosome exchange (cse) and etc(o). These two types aberration such as chromatid and chromosome gap(g) were recorded separately. In the meta phase, if there are several gap or cuttings, it was recorded as a fragment (frg). For a numerical aberration, any cell with 1 or more aberration was counted as 1 aberrant cell. For numerical aberration, any cell with 1 or more polyploidy (pol) aberration was counted as 1 aberrant cell.

##### Results judgment

If the number of chromosome aberration cells were increased clearly as compared with that of negative control or increased significantly dose-dependently or increased significantly at any dose level several times, then we confirmed that it was positive. Evaluation of results did not include gaps while the gaps were recorded in raw data of structural aberration.

The final decision of chromosome aberration in relation to the test substance was carried out in accordance with Toshio Sofuni and etc (4). If an appearance rate was below 5 %; between 5 and 10 %; and over 10 %, it was judged as a negative, equivocal, and positive, respectively.

#### Statistics

Any specific statistical analysis was not performed. The mean value was calculated in relation to the measured value in the main test.

#### Any other information on materials and methods incl. tables

##### Metabolic activation system

S9 (Lot No.: 1789, 1809) originated from hormone-induced liver homogenized solution of Sprague-Dawley rat using Aroclor 1254, in which was purchased from Molecular Toxicology, Inc., was used. it was kept in -80 °C (Deep freezer, DFU-657CL, Operon, Korea) till using.

**Table 1. Composition and preparation of S9 mix**

Component	Formation	Amount
Rat liver S9 (Aroclor-1254 induced)	50%	0.5 mL
MgCl <sub>2</sub>	8.0 µmol*	0.02 mL
KCl	33.0 µmol	
Glucose-6-phosphate	5.0 µmol	0.005 mL
NADP	4.0 µmol	0.04 mL
Sodium phosphate buffer, pH 7.4	50.0 µmol	0.25 mL
Water for injection	-	0.185 mL
Total volume	-	1.0 mL

\* µmol: micro mol

## Results and discussions

### Test results

Species/strain	mammalian cell line, other: Chinese Hamster Lung (CHL/IU)
Metabolic activation	with and without
Test system	strain/cell type:
Genotoxicity	negative
Cytotoxicity	yes
Vehicle controls valid	yes
Negative controls valid	yes
Positive controls valid	yes

#### Additional information on results

The MTT assay was conducted with 0, 4.9, 9.8, 19.6, 39.1, 78.2, 156.3, 312.5, 625, 1250, 2500 and 5000 µg/mL to examine a cytotoxicity of test substance.

According to result of the growth inhibition test (MTT assay), a cytotoxicity was showed regardless of application of metabolic



activation system. The IC<sub>50</sub> (Inhibition concentration 50%) were calculated as 450.0 µg/mL, in the short time treatment and continuous treatment system without and with metabolic activation system. Accordingly the chromosome aberration test was performed with 112.5, 225.0 and 450.0 µg/mL for the short time treatment without and with metabolic activation system and the continuous treatment accompanying with appropriate positive and negative control.

According to the chromosome aberration test, regardless of metabolic activation system, averages of chromosomal aberration cells were 0.5–3.0 %, therefore, there was no increase as compared with the negative control group.

Averages of chromosomal aberration cells in the positive control group were calculated as 16.0, 18.0 and 17.0 % for short time treatment without and with metabolic activation system; and the continuous treatment, respectively. The positive control induced undeniable frequency of chromosomal aberration (Table).

#### Remarks on results including tables and figures

**Table. Results of *in vitro* chromosome aberration test of CHL/IU cells treated with Phosphoric acid (CAS No.: 7664-38-2)**

S9 mix / time	Test substance	Dose (ug/ml)	No. of cell scored	No. of aberration cell							Aberration cell (%)	Chromosome aberration cell / 100 metaphase cell (%) (mean+/-SD)	
				ctb	csb	cte	cse	frg	o	pol			
S9 mix (-) / 6+18hrs	Water for injection	0	100	0	1	0	0	0	0	0	1	1.5+/-0.7	
			100	0	0	1	1	0	0	0	2		
			100	0	1	0	1	0	0	0	2		
	Phosphoric acid (CAS No.:7664-38-2)	112.5	100	0	0	0	1	0	0	0	1	1.5+/-0.7	
			100	0	0	3	0	0	0	0	3		
			100	0	0	1	0	0	0	0	1		
		225.0	100	0	0	1	0	0	0	0	1	2.0+/-1.4	
			100	0	0	1	0	0	0	0	1		
			100	0	0	1	2	0	0	0	3		
		450.0	100	0	0	1	2	0	0	0	3	3.0+/-0.0	
			100	0	0	1	2	0	0	0	3		
			100	5	3	4	5	0	0	0	17		
	MMC	0.05	100	5	4	3	2	1	0	0	15	16.0+/-1.4	
			100	1	1	2	0	0	0	0	4		
			100	0	0	0	0	0	0	0	0		
S9 mix (+) / 6+18hrs	Water for injection	0	100	1	1	0	0	0	0	0	2	2.0+/-2.8	
			100	0	0	0	0	0	0	0	0		
			100	0	0	0	0	0	0	0	0		
	Phosphoric acid (CAS No.:7664-38-2)	112.5	100	1	1	0	0	0	0	0	2	1.5+/-0.7	
			100	0	0	0	1	0	0	0	1		
			100	0	1	1	0	0	0	0	2		
		225.0	100	0	1	1	0	0	0	0	2	2.5+/-0.7	
			100	2	0	0	1	0	0	0	3		
			100	2	0	1	0	0	0	0	3		
		450.0	100	0	0	0	0	2	0	0	2	2.5+/-0.7	
			100	4	5	3	2	3	0	0	17		
			100	7	4	5	2	1	0	0	19		
	B[a]P	20	100	4	5	3	2	3	0	0	17	18.0+/-1.4	
			100	7	4	5	2	1	0	0	19		
			100	7	4	5	2	1	0	0	19		
S9 mix (-) / 24+0hrs	Water for injection	0	100	0	0	1	1	0	0	0	2	2.0+/-0.0	
			100	0	0	1	1	0	0	0	2		
			100	0	0	0	0	0	0	0	0		
	Phosphoric acid (CAS No.:7664-38-2)	112.5	100	1	0	0	0	0	0	0	1	0.5+/-0.7	
			100	2	0	0	1	0	0	0	3		
			100	0	0	1	0	0	0	0	1		
		225.0	100	2	0	0	0	0	0	0	2	2.0+/-1.4	
			100	2	0	0	2	0	0	0	4		
			100	2	0	0	2	0	0	0	4		
		450.0	100	6	5	4	1	0	0	0	16	3.0+/-1.4	
			100	5	5	4	3	1	0	0	18		
			100	5	5	4	3	1	0	0	18		
	MMC	0.05	100	5	5	4	3	1	0	0	18	17.0+/-1.4	
			100	5	5	4	3	1	0	0	18		
			100	5	5	4	3	1	0	0	18		

**MMC:** Mitomycin C, **B[a]** **P:** Benzo[a]pyrene, **ctb:** chromatid break, **csb:** chromosome break, **cte:** chromatid exchange, **cse:** chromosome exchange, **frg:** fragment, **o:** other, **pol:** polyploidy

#### Overall remarks, attachments

##### Overall remarks

#### Applicant's summary and conclusion

##### Interpretation of results

negative

##### Conclusions

Phosphoric acid (CAS No.: 7664-38-2) did not show the chromosome aberrations regardless of application of metabolic activation system in the chromosome aberration assay system using Chinese hamster lung cell(CHL/IU), under the conditions of this study.

##### Executive summary

This study was designed to examine a mutagenic potential of phosphoric acid (CAS No. 7664-38-2) in the chromosome aberration test system using Chinese hamster lung cell (CHL/IU).

The treatment levels were 112.5, 225.0 and 450 ug/mL, regardless of application of metabolic activation system by the result of growth inhibition test and accompanying with appropriate positive and negative control.

As a result, the structural and numerical chromosome aberrations were not observed in both the short time treatment without and with metabolic activation system and the continuous treatment as the negative control.

In the positive control, the structural chromosome aberration was significantly increased.

In conclusion, phosphoric acid did not show the chromosome aberrations regardless of application of metabolic activation system (S9) in the chromosome aberration assay system using Chinese hamster cell (CHL/IU), under the conditions of this study.

**Genetic toxicity in vitro.002**

UUID IUC5-9e04f3df-bd0a-43cf-9c2c-9309ca926900

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 14:13:25 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 1 (reliable without restriction)

Rationale for reliability 1a - GLP guideline study

**Data source****Reference**

Reference type study report

Author National Institute of Environmental Research (NIER), Korea Year 2008

Title Bacterial reverse mutation test of Phosphoric acid using microorganisms

Bibliographic source

Testing laboratory MEDVILL

Report no. G01-08085

Owner company

Company study no.

Report date

**Data access**

data submitter is data owner

**Data protection claimed**

yes, but willing to share

**Materials and methods****Type of genotoxicity**

gene mutation

**Type of study**

bacterial reverse mutation assay (e.g. Ames test)

**Test guideline**

Qualifier according to

Guideline OECD Guideline 471 (Bacterial Reverse Mutation Assay)

Deviations no

**GLP compliance**

yes (incl. certificate)

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Details on test material**

Purity: 99.999+%

Supplier: Sigma-Aldrich, Inc.

Lot No.: 09823ME

**Method**

**Species/strain**

**Species/strain** S. typhimurium TA 1535, TA 1537, TA 98 and TA 100

**Details  
on  
mammalian  
cell  
lines  
(if  
applicable)**

**Additional  
strain  
characteristics**

**Metabolic  
activation** with and without

**Metabolic  
activation  
system** rat liver S9 mix

**Species/strain** E. coli WP2 uvr A

**Details  
on  
mammalian  
cell  
lines  
(if  
applicable)**

**Additional  
strain  
characteristics**

**Metabolic  
activation** with and without

**Metabolic  
activation  
system** rat liver S9 mix

**Test concentrations**

156.3, 312.5, 625, 1,250 and 5,000 µg/plate

**Vehicle**

Sterilized distilled water

Lot No.: 400644

Manufacturer: GIBCO 15230-147

**Controls**

**Negative  
controls** yes

**Solvent /  
vehicle  
controls** yes Sterilized distilled water

**True  
negative  
controls**

**Positive  
controls** yes

**Positive  
control  
substance** sodium azide 2-Nitrofluorene, 9-Aminoacridine, 2-Aminoanthracene, 2-Aminofluorene

**Remarks**

**Details on test system and conditions**

Six concentrations of the test substance were tested in triplicate against each tester strain, using a plate incorporation method.

1) Master plate was prepared from the frozen permanent.

2) A colony was selected from the master plate and inoculated to 10 ml of 1.6 % Oxoid Nutrient Broth (pH 7.0–7.5) for 12–14 hr by shaking at 200 rpm.

3) The test substance (or vehicle, or positive controls) 0.1 ml, 0.1 ml of bacterial cultures, and 0.5 ml of S9 mix (or sodium phosphate buffer, 0.2 M, pH 7.4) were added to a test tube and then, 2 ml of molten top agar containing trace histidine or tryptophan was added to each tube. The mixture was overlaid onto sterile plates of Vogel-Bonner Minimal glucose agar.

4) After approximately 48 hr incubation at 37 °C the frequency of revertant colonies was assessed.

5) In order to assess the sterility of the test substance and S9 mix, 0.1 ml of the test substance at a maximal concentration (or 0.5 ml of S9 mix) and 2 ml of molten top agar were overlaid onto a sterile minimal glucose agar plate.

6) Three plates were used at each dose levels.

7) The plate was selected randomly in order to avoid a confounding effects.

8) The project number, the name of bacteria strain, the treatment dose and absence or presence of S9 mix were recorded on the bottom of plate.

**Evaluation criteria**

Data were presented using tables and figures as individual plate counts, the mean number of revertant colonies per plate and standard deviation.

The following several criteria were used to determine a positive result.

1) The case that under the S9- or S9+ condition, the increase of reverse mutation colony of a strain in a dose-dependent manner, detection of repeated increase at doses more than one concentration, or having a significant linear relation.

Biological relevance of the results was considered.

2) An increase in revertant colonies over two times in bacterial strains TA98, TA100 and WP2uvrA, and over three times in strains TA1535 and TA1537 than those in negative control group.

Besides the above cases, it was judged negative. Statistical significance-analysis was not carried out.

**Any other information on materials and methods incl. tables****Acceptability of test**

Bacterial reverse mutation study was considered acceptable if it met the following criteria.

1) The negative control data should be within the following range for each tester strain.

.	S9 (-)	S9 (+)
TA98	15-60	20-80
TA100	50-180	60-200
TA1535	10-40	10-40
TA1537	5-20	5-60
WP2uvrA	10-60	20-120

2) The positive control data should be within the following range for each tester strain.

.	Strain	Positive control	Treatment concentration (ug/plate)*	Standard range
S9 (-)	TA98	2-NF	1	150-700
	TA100	SA	1	300-1000
	TA1535	SA	1	100-1000
	TA1537	9-AA	80	80-700
	WP2uvrA	AF-2	0.01	100-200
S9 (+)	TA98	2-AA	0.5	150-1000
	TA100	2-AA	1	300-2000
	TA1535	2-AA	2	100-500
	TA1537	2-AA	2	100-500
	WP2uvrA	2-AA	20	250-1500

\* ug/plate: micro g/plate

**Results and discussions****Test results**

**Species/strain** S. typhimurium TA 1535, TA 1537, TA 98 and TA 100

**Metabolic activation** with and without

**Test system** strain/cell type:

**Genotoxicity** negative

**Cytotoxicity** yes at 5,000 µg/plate in TA100 strain with S9 mix

**Vehicle controls** valid

**Negative controls** valid

**Positive controls** valid

**Species/strain** E. coli WP2 uvr A

**Metabolic activation** with and without

**Test system** strain/cell type:

**Genotoxicity** negative

**Cytotoxicity** yes at 5,000 µg/plate in TA100 strain with S9 mix

**Vehicle**

controls  
valid

Negative  
controls  
valid

Positive  
controls  
valid

Remarks on results including tables and figures

Table. Summary of revertant colony numbers obtained per plate with/without S9 mix

S9 mix (5 %)	Dose (ug/plate)*	Number of revertant colonies/plate				
		Base replacement type			Frame shift type	
		TA100	TA1535	WP2uvrA	TA98	TA1537
-	NC	165+/-6	15+/-3	24+/-1	17+/-2	9+/-2
	156.3	173+/-2	20+/-2	25+/-5	19+/-4	6+/-2
	312.5	163+/-10	15+/-2	19+/-6	21+/-5	5+/-3
	625	153+/-6	17+/-6	20+/-5	16+/-3	7+/-1
	1250	158+/-6	17+/-6	14+/-2	16+/-3	5+/-1
	2500	165+/-10	15+/-1	20+/-6	17+/-3	9+/-3
	5000	166+/-2	11+/-4	23+/-7	20+/-7	5+/-4
	PC	479+/-15	520+/-82	122+/-8	174+/-29	771+/-21
+	NC	174+/-5	11+/-2	22+/-3	29+/-6	11+/-0
	156.3	161+/-16	13+/-4	18+/-3	25+/-10	6+/-3
	312.5	156+/-5	15+/-5	19+/-4	25+/-8	8+/-2
	625	160+/-7	18+/-5	16+/-3	25+/-8	10+/-3
	1250	159+/-8	16+/-5	28+/-8	30+/-3	9+/-1
	2500	154+/-26	18+/-2	18+/-7	18+/-4	9+/-2
	5000	1+/-1	1+/-1	23+/-4	0+/-0	1+/-1
	PC	587+/-30	144+/-22	329+/-37	493+/-59	317+/-31

Data are presented as mean+/-SD (N=3)

NC: negative control (Sterilized distilled water, 100 ul/plate\*)

PC: positive control

\*ug/plate, ul/plate: micro g/plate, micro l/plate

## Overall remarks, attachments

### Overall remarks

## Applicant's summary and conclusion

### Interpretation of results

negative

### Conclusions

Phosphoric acid was considered to be non-genotoxic under the present test conditions.

### Executive summary

#### Introduction

This study was conducted to evaluate the mutagenic potential of the test substance, phosphoric acid using a bacterial system. This study was performed in accordance with the procedures described in the following internationally accepted guidelines and recommendations: OECD Guidelines for Testing of Chemicals (Jul. 21, 1997) No. 471[ Bacterial Reverse Mutation Test] and [Genotoxicity Test] described in the TCCA-Good Laboratory Practice Standards and Test Guideline (NIER Public Notice No. 2007-29) issued by Korean National Institute of Environmental Research.

#### Dose range-finding test

Dose range-finding test was performed using the *Salmonella typhimurium* strains TA98, TA100 and the *Escherichia coli* strain WP2uvrA in the presence and absence of a metabolic activation containing S9 fraction (rat liver postmitochondrial fraction). The test substance at 5000 ug/plate\* was used as a maximal concentrations in the absence and presence of S9 mix, in the main mutation test, and diluted to six doses (156.3, 312.5, 625, 1,250 and 5,000 ug/plate) by a factor two.

#### Bacterial reverse mutation test

In the main and the confirmation test, five bacterial strains, *Salmonella typhimurium* TA98, TA100, TA1535, TA1537 and *Escherichia coli* WP2uvrA were treated with the test substance with or without S9 mix using a plate incorporation method and 3 plates at each dose levels were used (triplicates). As a result of the main mutation test, the test substance at any concentrations of 156.3~5,000 ug/plate with or without S9 mix didn't induce the increase in the frequency of revertant colonies in a dose-dependent manner, which representing non-genotoxic.

Regardless of S9 mix and tester strains, the precipitation of the test substance was not observed on the agar plate treated at any

doses. In the confirmation test, the test substance at same concentrations of the main mutation test with or without S9 mix didn't induce the increase in the frequency of revertant colonies dose-related. The precipitation of the test substance was not observed on the agar plate treated at any doses.

The frequency of revertant colonies for the negative control, sterilized distilled water was considered to be acceptable and all of the positive controls induced marked increases in the frequency of revertant colonies confirming the activity of S9 mix and the sensitivity of the bacterial strains.

**Conclusion**

The test substance, phosphoric acid was considered to be non-genotoxic under the present test conditions.

\*ug/plate: micro g/plate

**Genetic toxicity in vitro.003**

**UUID** IUC5-d06a9c83-6dce-4c50-be5c-ce7614424f6e  
**Dossier UUID** 0  
**Author** nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
**Date** 2011-04-11 14:14:53 KST  
**Remarks**

**Administrative Data****[IP] OECD: HPVC**

**Purpose flag** supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS  
**Study result type** experimental result  
**Reliability** 3 (not reliable)  
**Rationale for reliability** 3a - documentation insufficient for assessment

**Data source****Reference**

<b>Reference type</b>	publication		
<b>Author</b>	Al Ani, FY and Al Lami, SK	<b>Year</b>	1988
<b>Title</b>	Absence of mutagenic activity of acidity regulators in the Ames Salmonella/microsome test.		
<b>Bibliographic source</b>	Mutat-Res. 206(4): 467-470		
<b>Testing laboratory</b>		<b>Report no.</b>	
<b>Owner company</b>			
<b>Company study no.</b>		<b>Report date</b>	

**Data access**

data published

**Materials and methods****Type of genotoxicity**

gene mutation

**Type of study**

bacterial reverse mutation assay (e.g. Ames test)

**Test guideline****Qualifier** no guideline followed**Guideline****Deviations****GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity****Identifier** CAS number**Identity** 7664-38-2**Identifier** IUPAC name **Identity**phosphoric acid **Identifier****Common name** **Identity**

orthophosphoric acid

**Details on test material**

Orthophosphoric acid were obtained from BDH.

**Method****Species/strain****Species/strain** S. typhimurium, other: TA97, TA98, TA100, TA104

**Details on mammalian cell lines (if applicable)** Salmonella typhimurium strains were provided by Professor B.N. Ames.

**Additional strain characteristics**

**Metabolic activation** with and without

**Metabolic activation system** liver homogenated S9 fraction (male CD-COBS rats )

#### Test concentrations

0, 0.5, 1 and 2 µl/plate

#### Vehicle

Distilled water

#### Controls

**Negative controls** yes Distilled water

**Solvent / vehicle controls** yes Distilled water

**True negative controls**

**Positive controls** yes

**Positive control substance** other: 2-aminoanthracene (2-AA)

**Remarks**

#### Details on test system and conditions

Several concentrations of phosphoric acid dissolved in distilled water, were tested for mutagenicity in the standard plate incorporation assay (Maron and Ames, 1983).

All tests were done in triplicate, both with and without S9.

## Results and discussions

#### Test results

**Species/strain** S. typhimurium, other: TA97, TA98, TA100, TA104

**Metabolic activation** with and without

**Test system** strain/cell type:

**Genotoxicity** negative

**Cytotoxicity**

**Vehicle controls** valid

**Negative controls** valid

**Positive controls** valid

#### Remarks on results including tables and figures

**Table. His+ revertants/plate induced by various concentrations of Phosphoric acid in the presence and absence of S9**

Phosphoric acid concentration (ul/plate*)	S. typhimurium								D m 3 * m m
	TA97		TA98		TA100		TA104		
	+S9	-S9	+S9	-S9	+S9	-S9	+S9	-S9	
0	47.3 +/-1.52	23.6 +/-2.30	40.0 +/-1.00	34.3 +/-2.08	160.0 +/-4.35	127.3 +/-2.51	448.0 +/-6.92	388.0 +/-4.00	
0.5	43.6 +/-2.30	22.0 +/-3.46	32.6 +/-3.21	26.3 +/-1.52	140.0 +/-1.73	124.3 +/-3.51	522.0 +/-2.00	438.3 +/-3.51	
1.00	45.3 +/-2.68	31.0 +/-1.00	36.0 +/-1.73	31.6 +/-2.08	145.3 +/-6.35	148.3 +/-1.51	536.0 +/-1.73	450.6 +/-5.13	
2.00	4.33 +/-3.05	23.3 +/-2.08	40.3 +/-2.51	34.6 +/-0.57	130.0 +/-3.00	123.3 +/-3.51	489.0 +/-5.29	438.0 +/-3.60	
2-AA (10 ug/plate*)	426.0 +/-4.00	31.0 +/-1.00	440.6 +/-5.68	39.3 +/-0.57	576.0 +/-2.64	150.3 +/-1.52	977.3 +/-2.51	624.3 +/-4.04	



**Overall remarks, attachments****Overall remarks**

2-aminoanthracene is not appropriate as a positive control for incubations in the absence of S9. Therefore, the study lacks a positive control for incubations in the absence of S9 and the results of incubations in the absence of S9 are therefore of questionable validity.

**Applicant's summary and conclusion****Interpretation of results**

negative

**Conclusions**

Although phosphoric acid was non-mutagenic, other genotoxicity tests should be carried out because of the extensive use of this chemical as acidity regulator in foods.

**Executive summary**

**Genetic toxicity in vitro.004**

**UUID** IUC5-b477545f-a064-4bdb-a682-7b09fd0e9906  
**Dossier UUID** 0  
**Author** nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
**Date** 2008-12-30 15:10:01 KST  
**Remarks**

**Administrative Data****[IP] OECD: HPVC**

**Purpose flag** supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

**Study result type** experimental result

**Reliability** 4 (not assignable)

**Data source****Reference**

<b>Reference type</b>	publication		
<b>Author</b>	Cipollaro M, Corsale G, Esposito A, Ragucci E, Staiano N, Giordano GG and Pagano G	<b>Year</b>	1986
<b>Title</b>	Sublethal pH decrease may cause genetic damage to eukaryotic cell: a study on sea urchins and Salmonella typhimurium		
<b>Bibliographic source</b>	Teratogenesis, Carcinogenesis and Mutagenesis, 6, 275-287		
<b>Testing laboratory</b>	Istituto Nazionale Tumori	<b>Report no.</b>	
<b>Owner company</b>			
<b>Company study no.</b>		<b>Report date</b>	

**Data access**

data published

**Materials and methods****Type of genotoxicity**

gene mutation

**Type of study**

bacterial reverse mutation assay (e.g. Ames test)

**Test guideline**

**Qualifier** no guideline followed

**Guideline**

**Deviations**

**Principles of method if other than guideline**

Acidification of the medium was tested for spontaneous reversion to His<sup>+</sup> prototrophy in Salmonella typhimurium (strains TA97, TA98, TA100, TA102 and TA1535) up to toxic levels, by both liquid incubation and agar plate incorporation.

**GLP compliance**

no data

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

**Identifier** CAS number

**Identity** 7664-38-2

**Identifier** IUPAC name

**Identity** phosphoric acid

**Method****Species/strain**

**Species/strain** S. typhimurium, other: TA97, TA98, TA100, TA102 and TA1535

**Details on**

mammalian  
cell  
lines  
(if  
applicable)

Additional  
strain  
characteristics

Metabolic  
activation with and without

Metabolic  
activation  
system S9 microsomal fraction was prepared from liver homogenates of Sprague-Dawley rats induced with Aroclor 1254.

#### Controls

Negative  
controls

Solvent /  
vehicle  
controls

True  
negative  
controls

Positive  
controls yes

Positive  
control  
substance sodium azide daunomycin, methyl methane sulfonate(MMS)

Remarks

#### Details on test system and conditions

The effect of pH changes on bacterial reversion rate was evaluated by adopting two modifications of the standard plate incorporation assay.

First, a preincubation of bacteria with buffers solutions at pH's ranging from 4 to 9 were made by using H<sub>3</sub>PO<sub>4</sub>, H<sub>2</sub>SO<sub>4</sub>, and their sodium salts. Cultures of the tester strains (0.1 ml) were mixed with 0.5 ml of the buffer solutions, incubated at 37 °C for 1 hour, and then added to the top agar, plated on Vogel-Bonner medium plates. These were then incubated at 37 °C for 60 hours. The numbers of revertants per plate were eventually counted. For agar plate incorporation, a modified Vogel-Bonner medium was prepared as described by Popkin and Prival. A 50X salt solution (10 g MgSO<sub>4</sub>•7H<sub>2</sub>O, 100 g citric acid•H<sub>2</sub>O, 500 g K<sub>2</sub>HPO<sub>4</sub> and 175 g NaNH<sub>4</sub>HPO<sub>4</sub>•4H<sub>2</sub>O in 670 ml distilled water) was prepared and 10 ml was added to 220 ml of distilled water. The dilution solution was then adjusted to the final pH's with 10 N NaOH.

After sterilization, 220 ml agar solution (45 g agar per 1,320 ml water) and 50 ml of 5 % dextrose was added to the 230 ml of pH-adjusted salt solution. Plates were then poured with 25 ml of the above media in each. The pH was confirmed for each plate type by using a surface pH electrode (Ingold, Switzerland). The pH of the total plate assay system was assumed to be the same as that of the initial base agar. All the plate types were prepared with enough NaCl added to the medium to result in an ionic strength identical to that of the pH 7.0 controls.

## Results and discussions

#### Test results

Species/strain S. typhimurium, other: TA97, TA98, TA100, TA102 and TA1535

Metabolic  
activation with and without

Test  
system

Genotoxicity negative

Cytotoxicity

Vehicle  
controls  
valid

Negative  
controls  
valid

Positive  
controls  
valid

#### Additional information on results

The reversion properties and specificity of each strain were confirmed by testing MMS, daunomycin, and sodium azide in the standard plate-incorporation assay.

The incubation of S. typhimurium tester strains with different buffer solutions at pH ranging from 5.5 to 9 had no effect on the bacterial reversion rates. The acidification of incubation mixture to pH 5.0 produced toxic effects on bacterial as the appearance of survivors suggested; at lower pH values, complete bacterial death was observed. The same lack of effects was obtained by using the base agar plates at different pH values.

As expected, the ineffectiveness of pH decrease was invariably unchanged by the addition of S9 fraction (data not reported in the reference).

## Overall remarks, attachments

#### Overall remarks

## Applicant's summary and conclusion

**Interpretation of results**

negative

**Conclusions**

No effects were detectable in *S. typhimurium* tester strains following sublethal pH decrease.

**Executive summary**

## 7.7 Carcinogenicity

### Carcinogenicity.001

UUID IUC5-4f38683e-ef3c-48c2-8f85-74d12dd218dd

Dossier UUID 0

Author nier3 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2008-12-11 09:17:27 KST

Remarks

## Administrative Data

OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Reliability 2 (reliable with restrictions)

Rationale for reliability 2g- Data from handbook or collection of data

## Data source

### Reference

Reference type review article or handbook

Author US EPA's IRIS programFile First On-Line Year 1995

Title Phosphoric acid; CASRN 7664-38-2

Bibliographic source

Testing laboratory Report no.

Owner company

Company study no. Report date

## Materials and methods

### Test materials

#### Test material equivalent to submission substance identity

yes

#### Test material identity

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

## Applicant's summary and conclusion

### Conclusions

There is no reliable information on the carcinogenic potential of phosphoric acid in animals or humans.

## 7.8 Toxicity to reproduction

### *Toxicity to reproduction*

UUID IUC5-29808219-54a7-404b-acfb-552b1f147b0c

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-03 14:52:44 KST

Remarks

### Administrative Data

OECD: HPVC

### Effects on fertility

#### Short description of key information

The NOEL value for reproductive toxicity was estimated to be 500 mg/kg bw/day.

#### Key parameter (optional)

Effect level for oral exposure	NOAEL	in mg/kg bw/day	500.000
Effect level for dermal exposure		in mg/kg bw/day	
Effect level for inhalation exposure		in mg/m <sup>3</sup> air	

### Discussion

### Developmental toxicity / teratogenicity

#### Short description of key information

The NOEL value for development toxicity was estimated to be 500 mg/kg bw/day.

#### Key parameter (optional)

Effect level for oral exposure	NOAEL	in mg/kg bw/day	500.000
Effect level for dermal exposure		in mg/kg bw/day	
Effect level for inhalation exposure		in mg/m <sup>3</sup> air	

**7.8.1 Toxicity to reproduction*****Toxicity to reproduction.001***

UUID IUC5-793c685f-0f1e-4b50-ac3b-a0adbe372129

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-13 15:38:35 KST

Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 1 (reliable without restriction)

Rationale for reliability 1a-GLP guideline study (OECD, EC, EPA, FDA, etc)

**Data source****Reference**

Reference type study report

Author National Institute of Environmental Research (NIER)

Year 2008

Title Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Phosphoric acid in rats

Bibliographic source

Testing laboratory Biototech Co., Ltd.

Report no. B08008

Owner company

Company study no.

Report date

**Data access**

data submitter is data owner

**Data protection claimed**

yes, but willing to share

**Materials and methods****Test type**

screening

**Limit test**

no

**Test guideline**

Qualifier according to

Guideline OECD Guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test)

Deviations

**GLP compliance**

yes (incl. certificate)

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Details on test material**

- Name of test material (as cited in study report): Phosphoric acid
- Molecular formula (if other than submission substance): H<sub>3</sub>PO<sub>4</sub>

- Molecular weight (if other than submission substance): 98.00
- Physical state: VISCOUS COLORLESS LIQUID
- Analytical purity: 99.999 % (metals basis), 85wt. % in H<sub>2</sub>O
- Lot/batch No.: 09405LE, 09411TH
- Storage condition of test material: Stored under refrigeration

**Test animals****Species**

rat

**Strain**

Sprague-Dawley

**Sex**

male/female

**Details on test animals and environmental conditions****TEST ANIMALS**

- Source: Rat, Sprague-Dawley (CrI:CD(SD)), SPF (Supplier: ORIENTBIO INC., Korea)
- Age at study initiation: Male - 9 weeks old, Female - 8 weeks old
- Weight at study initiation: Male - 288.6–336.7 g, Female - 163.5–188.9 g
- Housing: Stainless wire cage, 260W×350D×210H (mm), Polycarbonate cage 260W×420L×180H (mm), 1 animal per cage (During the mating period: 1male and 1 female, During the lactation period: 1 female and neonate)
- Diet (e.g. ad libitum): ad libitum
- Water (e.g. ad libitum): ad libitum
- Acclimation period: 1 week

**ENVIRONMENTAL CONDITIONS**

- Temperature (°C): 19.2–23.4 °C
- Humidity (%): 27.6–64.3 %
- Air changes (per hr): 10–15 times/hour
- Photoperiod (hrs dark / hrs light): 12–hour light/dark cycle (lights on at 7 a.m., lights off at 7 p.m.)

**Administration / exposure****Route of administration**

oral: gavage

**Vehicle**

other: Water for injection

**Details on exposure****PREPARATION OF DOSING SOLUTIONS:**

At use, the test substance was diluted to necessary concentration using the Water for injection and prepared.

**VEHICLE**

- Amount of vehicle (if gavage): 5 mL/kg
- Lot/batch no. (if required): GBA8002, GBA8003

**Details on mating procedure**

- M/F ratio per cage: 1:1 (one male to one female)
- Length of cohabitation: 12 days
- Proof of pregnancy: vaginal plug referred to as day 0 of pregnancy

**Duration of treatment / exposure**

The males were administrated once daily during 2 weeks prior to mating, the 2 weeks of mating period, and 2 weeks after mating (total 6 weeks).

The females of main group were administrated once daily from 2 weeks before mating to Day 4 post partum (approximately 54 days). The females of recovery group (without mating) were administrated approximately 54 days (applied equally main group females).

Also, coitus was confirmed, but females did not show gestational signs, and were administrated until gestation Day 26.

**Frequency of treatment**

once a day

**Doses / concentrations**

0, 125, 250 and 500 mg/kg

Basis actual ingested

**No. of animals per sex per dose**

main group: 13 male and 13 female

recovery group: 6 male and 6 female

**Control animals**

yes, concurrent vehicle



**Further details on study design**

- Dose selection rationale: The dose levels were determined based on the previous dose range finding study (Study No.: B08008P). In result, food consumption of males and females was decreased at 500 mg/kg, and females were observed in inhibition of weight gain. In addition, 1000 mg/kg dose level was observed in salivation and soft stool, and moribund in one male. As a result, 500 mg/kg was selected as the high dose level for this study and sequentially divided by a geometric ratio of 2 to produce two additional lower doses. 250 and 150 mg/kg were selected as the middle and low dose levels, respectively. In the control group, Water for injection was administered the same as dosing volume of the high dose.

**Examinations****Parental animals: Observations and examinations**

CAGE SIDE OBSERVATIONS: Yes

- Time schedule: The parent's animals were observed for clinical signs including abortion, dystocia, premature birth, parturition, and lactation condition once daily. The moribund and mortality were observed twice daily. The recovery groups were observed during 2 weeks after the end of administration.
- Cage side observations checked in table [No.1-1 and 1-2] and appendix [No.1-1 and 1-2] were included.

DETAILED CLINICAL OBSERVATIONS: Yes

- Time schedule: once a week
- Detailed clinical signs were performed the day before the first administration and once a week during the treatment and recovery period for general appearance, posture, activity, response to handling, nervous system, function of autonomic nervous system, and abnormal behavior.

BODY WEIGHT: Yes

- Time schedule for examinations: once a week

Body weights of males were measured just before administration and once a week during the treatment and recovery period. Body weights of females were measured just before administration, on Day 0, 7, 14, and 20 of gestation and on Day 0 and 4 of lactation. During the administration and recovery period, body weights were measured once a week. Only, body weights were not measured during the mating period.

**Litter observations**

STANDARDISATION OF LITTERS

- Performed on day 4 postpartum: yes

PARAMETERS EXAMINED

The following parameters were examined in F1 offspring: number and sex of pups, live births, postnatal mortality

**Postmortem examinations (Parental animals)**

SACRIFICE

- Male animals: All surviving animals
- Maternal animals: All surviving animals

After completion of observation period of main and recovery groups, all live and dead animals were performed to detailed macroscopic examination about body surface and organ and tissue of the whole body.

GROSS NECROPSY

- Gross necropsy consisted of external and internal examinations including the cervical, thoracic, and abdominal viscera.
- Brain · Pituitary · Thymus · Lung with bronchi · Trachea · Thyroid · Esophagus · Heart · Liver · Spleen · Kidney · Adrenal · Stomach · Duodenum · Jejunum · Ileum · Cecum · Colon · Rectum · Testis · Epididymis · Prostate · Ovary · Uterus · Submandibular lymph node · Mesenteric lymph node · Femur and sternum · Spinal cord · Sciatic nerve · Eye & etc. · Urinary bladder

HISTOPATHOLOGY / ORGAN WEIGHTS

The tissues indicated in Table 15-1, 15-2, 16-1, 16-2, Appendix 15-1, 15-2, 16-1 and 16-2 were prepared for microscopic examination and Table 18-1, 18-2, Appendix 18-1 and 18-2 were prepared for weighed, respectively.

**Postmortem examinations (Offspring)**

SACRIFICE

- The F1 offspring not selected as parental animals were sacrificed at 4 days of age.

**Statistics**

Statistical analysis of this study was performed by the SAS program (SAS® 9.1.3, SAS Institute Inc., U.S.A.).

For the data including body weights, food consumption, urine, hematology, blood biochemistry parameters, organ weights, mating results, birth and survival rates, sensory reflex, and motor function test, the Bartlett test was conducted to test for variance homogeneity at the 5.0% one-tailed probability level. One-way analysis of variance (ANOVA) test was employed on homogeneity, if significant, followed by Dunnett's t-test for multiple comparisons. Kruskal-wallis was employed on heterogeneity, if significant, followed by Mann-whitney u-test for multiple comparisons. Group comparison was performed at the 5.0 and 1.0% two-tailed probability level. For the data of recovery, Folded-F test was conducted to test for variance homogeneity at the 5.0% two-tailed probability level. Student t-test was employed on homogeneity, if overrule, Aspin-Welch t-test was performed at the 5.0 and 1.0% two-tailed probability level. Non pregnancy animals were excluded.

**Reproductive indices**

- Mating rate (%) = (No. of coitus confirmed females / No. of mated males) × 100
- Mating period = The day observed positive evidence of mating – The day of initial pairing (based on administration day)
- Gestation period = Day 0 of parturition – Day 0 of gestation (based on administration day)

- Male fertility rate (%) = (No. of pregnant females / No. of mated males) × 100
- Female fertility rate (%) = (No. of pregnant females / No. of coitus confirmed females) × 100
- Parturition rate (%) = (No. of dams / No. of coitus confirmed females) × 100
- Pre-implantation loss rate (%) = (1 – (No. of implantations / No. of corpus lutea)) × 100
- Post-implantation loss rate (%) = (1 – (No. of live neonates / No. of implantations)) × 100

#### **Offspring viability indices**

- Mean litter size
- Live birth index = (No. of live neonates at parturition / total No. of neonates at parturition) × 100
- Day 0 post partum survival rate = (No. of live neonates on day 0 post partum / No. of live neonates at parturition) × 100
- Day 4 post partum survival rate = (No. of live neonates on day 4 post partum / No. of live neonates on day 0 post partum) × 100
- Sex ratio = No. of live male neonates / No. of live female neonates

## **Results and discussions**

### **Effect levels**

Endpoint NOAEL

Generation F1

Sex male/female

Effect level 500 mg/kg bw/day

Basis  
for  
effect  
level /  
Remarks

### **Observations: parental animals**

#### **Clinical signs (parental animals)**

no effects

#### **Body weight and food consumption (parental animals)**

no effects

#### **Test substance intake (parental animals)**

no effects

#### **Reproductive performance (parental animals)**

no effects

#### **Organ weights (parental animals)**

no effects

#### **Histopathology (parental animals)**

no effects

#### **Details on results (parental animals)**

##### **CLINICAL SIGNS AND MORTALITY (PARENTAL ANIMALS)**

In the main group, death was observed in one female (2403) of the 500 mg/kg treatment group on Day 16 of administration. And in the recovery group, death was observed in one female (2416) of the 500 mg/kg treatment group on Day 52 of administration. In the main group, no clinical signs were observed in males and females of 125 mg/kg treatment group and in females of the 250 mg/kg treatment group. But, transient salivations which were appeared immediately after administrations were sporadically observed in four males of the 250 mg/kg treatment group during from Day 22 of administration to completion of administration. Also, transient salivations were observed in all males of the 500 mg/kg treatment group from Day 20 of administration to completion of administration and in four females of the 500 mg/kg treatment group from Day 2 of gestation to completion of administration, sporadically or persistently. In addition, mucous stool, soft stool, and dirty nose were observed in one male (1407) of the 500 mg/kg treatment group on Day 22 and 23.

In the recovery group, transient salivations were observed in almost all males of the 500 mg/kg treatment group from Day 16 of administration to completion of administration and in almost all females of the 500 mg/kg treatment group from Day 20 of administration to completion of administration, sporadically or persistently.

Detailed clinical signs (Table 2 & Appendix 2) were performed once a week during the study period, and no clinical signs were observed in all animals of the control and treatment groups.

##### **BODY WEIGHT AND FOOD CONSUMPTION (PARENTAL ANIMALS)**

In the main group, no treatment-related abnormalities in body weight gain were noted in all animals of the control and treatment groups.

In females of the recovery group, body weights on Day 55 of administration were significantly decreased ( $p < 0.05$ ) compared with the control group in the 500 mg/kg treatment group. Besides, no treatment-related abnormalities in body weight gain were noted in all males.

In the main group, no treatment-related abnormalities in food consumption were noted in all animals of the control and treatment groups.

In females of the recovery group, food consumption was significantly decreased ( $p < 0.05$ ) compared with the control group on Day 13 and 34 of administration in the 500 mg/kg treatment group. Besides, no treatment-related abnormalities in food consumption were noted in all males.

**REPRODUCTIVE PERFORMANCE (PARENTAL ANIMALS)**

Mating rate in the control, 125, 250, and 500 mg/kg treatment groups were 100 % in all. Fertility rate in the control, 125, 250, and 500 mg/kg treatment groups were 76.9, 100.0, 92.3; and 100 % in the males; and were 76.9, 100.0, 92.3, and 100 % in the female, respectively. Parturition rate in the control, 125, 250, and 500 mg/kg treatment groups were 76.9, 100.0, 92.3, and 100.0 %, respectively.

Mean mating periods and mean gestation periods in the control, 125, 250, and 500 mg/kg treatment groups were 2.9, 2.5, 3.5, and 3.0 days and 21.7, 21.7, 21.9, and 21.8 days, respectively. No statistically significant difference was observed in all animals.

**ORGAN WEIGHTS (PARENTAL ANIMALS)**

In the main group, no treatment-related abnormalities in absolute and relative organ weights of the males were noted compared with the control group. However, in females, absolute organ weights of kidney were significantly increased ( $p < 0.05$ ,  $p < 0.01$ ) compared with the control group in all treatment groups, and relative organ weights of uterus were significantly decreased ( $p < 0.05$ ) compared with the control group in the 500 mg/kg treatment group.

In the recovery group, no treatment-related abnormalities in absolute and relative organ weights of the males were noted. However, in females, fasted body weights ( $p < 0.01$ ) and absolute organ weights of heart ( $p < 0.05$ ) were significantly decreased compared with the control group in the 500 mg/kg treatment group.

**GROSS PATHOLOGY (PARENTAL ANIMALS)**

In the necropsy findings of the main group, agenesis of spleen was observed in one male (1302) of the 250 mg/kg treatment group, and yellow spot of epididymis was observed in one male (1408) of the 500 mg/kg treatment group. The other abdominal signs were not observed, and the necropsy finding of recovery group was not noted.

In the necropsy findings for dead animals, gaseous distension was observed in one female (2403) of the 500 mg/kg treatment group in the main group on Day 16 of administration. In the recovery group, gaseous distension, severe hydronephrosis of left kidney and dilation of left uterine horn were observed in one female (2416) of the 500 mg/kg treatment group in the recovery group on Day 52 of administration.

**HISTOPATHOLOGY (PARENTAL ANIMALS)**

In the main group, cast of kidney was observed in one male (1104) of the control group, and sperm granuloma of epididymis was observed in one male (1408) of the 500 mg/kg treatment group. The other abnormal findings were not observed.

In the recovery group, basophilic tubules of kidney was observed in one female (2119) of the control group. The other abnormal findings were not observed.

In the 500 mg/kg treatment group of the main group female, no histopathological change in one dead animal (2403) was observed. In the 500 mg/kg treatment group of the recovery group female, renal tissue in one dead animal (2416) was not observed by severe hydronephrosis of gross findings, and left uterine horn was dilated; however, no histopathological change was observed.

**Observations: offspring*****Clinical signs (offspring)***

no effects

***Body weight (offspring)***

no effects

***Sexual maturation (offspring)***

no effects

***Organ weights (offspring)***

no effects

***Histopathology (offspring)***

no effects

***Details on results (offspring)*****VIABILITY (OFFSPRING)**

Mean litter size and live birth rate in the control, 125, 250, and 500 mg/kg treatment groups were 13.3, 14.4, 14.5, and 15.0 animals and 99.4, 99.0, 100.0, and 97.5 %, respectively. Day 0 and 4 postpartum survival rates in the control, 125, 250, and 500 mg/kg treatment groups were 100 % in all and 99.4, 99.1, 99.3, and 98.4 %, respectively. No statistically significant difference was observed in all animals.

**BODY WEIGHT (OFFSPRING)**

On Day 0 and 4 postpartum, no treatment-related abnormalities in body weight gain of neonate were noted in all animals of the control and treatment groups.

**OTHER FINDINGS (OFFSPRING)**

- Sex ratio and external findings of live neonate: Sex ratio of live neonate in the control, 125, 250, and 500 mg/kg treatment groups were 0.9, 0.8, 0.9, and 1.2, respectively. On Day 0 and 4 postpartum, no treatment-related abnormalities in external findings were noted in all animals.

**Remarks on results including tables and figures****Overall remarks, attachments****Overall remarks****Attached full study report**

TG\_422\_7664-38-2.pdf / 943.57 KB (application/pdf)

### **Applicant's summary and conclusion**

#### **Conclusions**

The NOEL for reproductive toxicity was estimated to be 500 mg/kg bw/day.

#### **Executive summary**

**7.8.2 Developmental toxicity / teratogenicity*****Developmental toxicity / teratogenicity.001***

UUID IUC5-aedebcad-a0cf-4359-b5b8-4c4c6ded6c4f

Dossier UUID 0

Author nier2 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-08-13 17:44:45 KST

Remarks

**Administrative Data**

OECD: HPVC

Purpose flag key study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 1 (reliable without restriction)

Rationale for reliability 1a-Guideline study (OECD, EC, EPA, FDA, etc)

**Data source****Reference**

Reference type study report

Author National Institute of Environmental Research (NIER)

Year 2008

Title Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test of Phosphoric acid in rats

Bibliographic source

Testing laboratory Biototech Co., Ltd.

Report no. B08008

Owner company

Company study no.

Report date

**Data access**

data submitter is data owner

**Data protection claimed**

yes, but willing to share

**Cross-reference to same study**

Repeated dose toxicity: oral.001

Toxicity to reproduction.001

**Materials and methods****Limit test**

no

**Test guideline**

Qualifier according to

Guideline other guideline: OECD Guideline 422 (Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test)

Deviations yes

**GLP compliance**

yes (incl. certificate)

**Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Confidential details on test material**

- Name of test material (as cited in study report): Phosphoric acid

- Molecular formula (if other than submission substance): H<sub>3</sub>PO<sub>4</sub>
- Molecular weight (if other than submission substance): 98.00
- Physical state: VISCOUS COLORLESS LIQUID
- Analytical purity: 99.999 % (metals basis), 85wt. % in H<sub>2</sub>O
- Lot/batch No.: 09405LE, 09411TH
- Storage condition of test material: Stored under refrigeration

**Test animals****Species**

rat

**Strain**

Sprague-Dawley

**Details on test animals and environmental conditions****TEST ANIMALS**

- Source: Rat, Sprague-Dawley (CrI:CD(SD)), SPF (Supplier: ORIENTBIO INC., Korea)
- Age at study initiation: Male - 9 weeks old, Female - 8 weeks old
- Weight at study initiation: Male - 288.6–336.7 g, Female - 163.5–188.9 g
- Housing: Stainless wire cage, 260W×350D×210H (mm), Polycarbonate cage 260W×420L×180H (mm), 1 animal per cage (During the mating period: 1 male and 1 female, During the lactation period: 1 female and neonate)
- Diet (e.g. ad libitum): ad libitum
- Water (e.g. ad libitum): ad libitum
- Acclimation period: 1 week

**ENVIRONMENTAL CONDITIONS**

- Temperature (°C): 19.2–23.4 °C
- Humidity (%): 27.6–64.3 %
- Air changes (per hr): 10–15 times/hour
- Photoperiod (hrs dark / hrs light): 12-hour light/dark cycle (lights on at 7 a.m., lights off at 7 p.m.)

**Administration / exposure****Route of administration**

oral: gavage

**Vehicle**

other: Water for injection

**Details on exposure****PREPARATION OF DOSING SOLUTIONS:**

At use, the test substance was diluted to necessary concentration using the Water for injection and prepared.

**VEHICLE**

- Amount of vehicle (if gavage): 5 mL/kg
- Lot/batch no. (if required): GBA8002, GBA8003

**Duration of treatment / exposure**

The males were administrated once daily during 2 weeks prior to mating, the 2 weeks of mating period, and 2 weeks after mating (total 6 weeks).

The females of main group were administrated once daily from 2 weeks before mating to Day 4 post partum (approximately 54 days). The females of recovery group (without mating) were administrated approximately 54 days (applied equally main group females).

Also, coitus was confirmed, but females did not show gestational signs, and were administrated until gestation Day 26.

**Frequency of treatment**

once a day

**Doses / concentrations**

0, 125, 250 and 500 mg/kg

**Basis** actual ingested

**No. of animals per sex per dose**

main group: 13 male and 13 female

recovery group: 6 male and 6 female

**Control animals**

yes, concurrent vehicle

**Further details on study design**

- Dose selection rationale: The dose levels were determined based on the previous dose range finding study (Study No.: B08008P). In result, food consumption of males and females was decreased at 500 mg/kg, and females were observed in inhibition of weight gain. In addition, 1000 mg/kg dose level was observed in salivation and soft stool, and moribund in one male. As a result, 500 mg/kg was selected as the high dose level for this study and sequentially divided by a geometric ratio of 2 to produce two additional lower doses. 250 and 150 mg/kg were selected as the middle and low dose levels, respectively. In the control group, Water for injection was administered the same as dosing volume of the high dose.

## Examinations

### Maternal examinations

CAGE SIDE OBSERVATIONS: Yes

- Time schedule: The parent's animals were observed for clinical signs including abortion, dystocia, premature birth, parturition, and lactation condition once daily. The moribund and mortality were observed twice daily. The recovery groups were observed during 2 weeks after the end of administration.
- Cage side observations checked in table [No.1-1 and 1-2] and appendix [No.1-1 and 1-2] were included.

DETAILED CLINICAL OBSERVATIONS: Yes

- Time schedule: once a week
- Detailed clinical signs were performed the day before the first administration and once a week during the treatment and recovery period for general appearance, posture, activity, response to handling, nervous system, function of autonomic nervous system, and abnormal behavior.

BODY WEIGHT: Yes

- Time schedule for examinations: once a week

Body weights of males were measured just before administration and once a week during the treatment and recovery period. Body weights of females were measured just before administration, on Day 0, 7, 14, and 20 of gestation and on Day 0 and 4 of lactation. During the administration and recovery period, body weights were measured once a week. Only, body weights were not measured during the mating period.

### Ovaries and uterine content

The ovaries and uterine content was examined after termination: Yes

Examinations included:

- Number of corpora lutea: Yes
- Number of implantations: Yes
- Number of early resorptions: Yes
- Number of late resorptions: Yes

The corpora lutea of all ovaries from pregnant females were counted at necropsy. Also, the uterine implantation sites were counted and calculated as follows:

- Pre-implantation loss rate (%) =  $(1 - (\text{No. of implantations} / \text{No. of corpus lutea})) \times 100$
- Post-implantation loss rate (%) =  $(1 - (\text{No. of live neonates} / \text{No. of implantations})) \times 100$

### Fetal examinations

- External examinations: Yes: all per litter

- Soft tissue examinations: No
- Skeletal examinations: No
- Head examinations: No

### Statistics

Statistical analysis of this study was performed by the SAS program (SAS 9.1.3, SAS Institute Inc., U.S.A.).

For the data including body weights, food consumption, urine, hematology, blood biochemistry parameters, organ weights, mating results, birth and survival rates, sensory reflex, and motor function test, the Bartlett test was conducted to test for variance homogeneity at the 5.0% one-tailed probability level. One-way analysis of variance (ANOVA) test was employed on homogeneity, if significant, followed by Dunnett's t-test for multiple comparisons. Kruskal-wallis was employed on heterogeneity, if significant, followed by Mann-whitney u-test for multiple comparisons. Group comparison was performed at the 5.0 and 1.0% two-tailed probability level. For the data of recovery, Folded-F test was conducted to test for variance homogeneity at the 5.0% two-tailed probability level. Student t-test was employed on homogeneity, if overrule, Aspin-Welch t-test was performed at the 5.0 and 1.0% two-tailed probability level.

Non pregnancy animals were excluded.

### Indices

- Mating rate (%) =  $(\text{No. of coitus confirmed females} / \text{No. of mated males}) \times 100$
- Mating period = The day observed positive evidence of mating – The day of initial pairing (based on administration day)
- Gestation period = Day 0 of parturition – Day 0 of gestation (based on administration day)
- Male fertility rate (%) =  $(\text{No. of pregnant females} / \text{No. of mated males}) \times 100$
- Female fertility rate (%) =  $(\text{No. of pregnant females} / \text{No. of coitus confirmed females}) \times 100$
- Parturition rate (%) =  $(\text{No. of dams} / \text{No. of coitus confirmed females}) \times 100$
- Mean litter size
- Live birth index =  $(\text{No. of live neonates at parturition} / \text{total No. of neonates at parturition}) \times 100$
- Day 0 post partum survival rate =  $(\text{No. of live neonates on day 0 post partum} / \text{No. of live neonates at parturition}) \times 100$
- Day 4 post partum survival rate =  $(\text{No. of live neonates on day 4 post partum} / \text{No. of live neonates on day 0 post partum}) \times 100$

## Results and discussions

### Effect levels

Endpoint NOAEL

Effect type developmental toxicity

Effect level 500 mg/kg bw/day

Basis

for  
effect  
level /  
Remarks

**Maternal toxic effects**

no effects

**Details on maternal toxic effects**

In the examination for reproductive and development toxicity, effects of test substance were not considered to sensory reflex, motor function, and reproductive function of females including mating, pre- and post-implantation loss rates, litter size, live birth rate, and survival rate.

**Embryotoxic / teratogenic effects**

no effects

**Details on embryotoxic / teratogenic effects**

In the examination for reproductive and development toxicity, there were not considered to neonate body weights on Day 0 and 4 and external examination.

**Remarks on results including tables and figures****Overall remarks, attachments****Attached full study report**

TG 422\_7664-38-2.pdf / 943.57 KB (application/pdf)

**Applicant's summary and conclusion****Conclusions**

The NOEL for reproductive and development toxicity was estimated to be 500 mg/kg bw/day.

**Executive summary**



**7.10 Exposure related observations in humans****7.10.1 Health surveillance data*****Health surveillance data.001***

UUID IUC5-c1d7ae04-56f9-48a6-ab49-616301deb03c  
Dossier UUID 0  
Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of  
Date 2011-04-11 14:17:37 KST  
Remarks

**Administrative Data**

[IP] OECD: HPVC

Purpose flag ( ) robust study summary ( ) used for classification ( ) used for MSDS

**Materials and methods****Test materials**

Test material equivalent to submission substance identity

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Method**

Any other information on materials and methods incl. tables

**Overall remarks, attachments****Overall remarks**

No information on health surveillance is available.

**Applicant's summary and conclusion****Executive summary**

No information on health surveillance is available.

**7.10.2 Epidemiological data*****Epidemiological data.001***

UUID IUC5-a50c4b03-ec8e-4476-af4b-f835e6e23e3f

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 14:17:51 KST

Remarks

**Administrative Data****[IP] OECD: HPVC**

Purpose flag ( ) robust study summary ( ) used for classification ( ) used for MSDS

**Materials and methods****Test materials**

Test material equivalent to submission substance identity

yes

Test material identity

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Overall remarks, attachments**

Overall remarks

No information on epidemiological data is available.

**Applicant's summary and conclusion**

Executive summary

### 7.10.3 Direct observations: clinical cases, poisoning incidents and other *Direct observations: clinical cases, poisoning incidents and other.001*

UUID IUC5-5b0c3971-9bcb-4117-8361-56216b6806c4

Dossier UUID 0

Author nier1 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-07-01 10:46:00 KST

Remarks

#### Administrative Data

[IP] OECD: HPVC

Purpose flag supporting study ( ) robust study summary ( ) used for classification ( ) used for MSDS

Study result type experimental result

Reliability 3 (not reliable)

Rationale for reliability 3a - Documentation insufficient for assessment

#### Data source

##### Reference

Reference type publication

Author Cello JP, Fogel RP and Boland R Year 1980

Title Liquid caustic ingestion - spectrum of injury

Bibliographic source Arch. Intern. Med. 140: 501-504.

Testing laboratory Report no.

Owner company

Company study no. Report date

##### Data access

data published

#### Materials and methods

##### Study type

poisoning incident

##### Endpoint addressed

acute toxicity: oral

##### Test guideline

Qualifier no guideline followed

Guideline

Deviations

##### Test materials

##### Test material equivalent to submission substance identity

yes

##### Test material identity

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

##### Details on test material

Phosphoric acid

##### Confidential details on test material

240 mL of the test material were admitted.

##### Method

##### Type of population

general

**Subjects**

male, 42 years old

(This patient was seen in the emergency service of the San Francisco General Hospital following liquid corrosive ingestion.)

**Ethical approval**

no data

**Route of exposure**

oral

**Reason of exposure**

other: no data

**Exposure assessment**

no data

**Details on exposure**

Time to admission: 1 hr

Volume of admitted: 240 mL

**Examinations**

After initial stabilization with fluids, patients underwent fiberoptic endoscopy. The extent and severity of injury were determined at endoscopy. The endoscope was passed under direct vision through the posterior region of the pharynx into the upper portion of the esophagus. The endoscope routinely was passed into the stomach unless deep, circumferential, severe, esophageal burns were encountered. A nasogastric tube usually was inserted to administer antacids as well as to serve as a stent if bougienage became necessary. Steroids (prednisolone, 40 to 60 mg/day by intravenous infusion) were given for ten to 14 days in those patients with extensive, severe, erosive esophagitis. Patients with minimal esophagitis or superficial gastric mucosal injury were treated with antacids alone.

**Medical treatment**

Patients were confined to the stomach were treated with antacids alone without subsequent complications. Short course of corticosteroids were employed in two instances prior to endoscopic assessment. All patients with gastric injury, excluding patient 9, had complete healing of these lesions as determined by repeat endoscopy, roentgenography, or long-term follow-up.

**Any other information on materials and methods incl. tables****Results and discussions****Clinical signs**

Symptoms and physical findings ingesting liquid caustics: Hematemesis, Oral pharyngeal burns.

**Results of examinations**

Esophagus: Moderate distal esophagitis

Stomach: Severe proximal gastritis

Duodenum: Normal

**Effectivity of medical treatment**

Unavailable for follow-up.

**Remarks on results including tables and figures****Overall remarks, attachments****Overall remarks****Applicant's summary and conclusion****Conclusions**

Strong acids such as phosphoric acid produced some evidence of esophageal damage.

**Executive summary**

**7.10.4 Sensitisation data (humans)*****Sensitisation data (humans).001***

UUID IUC5-a946577a-3662-4dff-8393-a5c344a0c8ca

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 14:18:30 KST

Remarks

**Administrative Data****[IP] OECD: HPVC**

Purpose flag ( ) robust study summary ( ) used for classification ( ) used for MSDS

**Materials and methods****Test materials**

Test material equivalent to submission substance identity

yes

Test material identity

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Overall remarks, attachments**

Overall remarks

No information on skin or respiratory sensitisation is available.

**Applicant's summary and conclusion**

Executive summary

**7.10.5 Exposure related observations in humans: other data*****Exposure related observations in humans: other data.001***

UUID IUC5-8f5acb60-5d6b-4459-a4ef-bdd213b364f1

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2011-04-11 14:18:42 KST

Remarks

**Administrative Data****[IP] OECD: HPV**

Purpose flag ( ) robust study summary ( ) used for classification ( ) used for MSDS

**Materials and methods****Test materials****Test material equivalent to submission substance identity**

yes

**Test material identity**

Identifier CAS number

Identity 7664-38-2

Identifier IUPAC name

Identity phosphoric acid

**Overall remarks, attachments****Overall remarks**

No information on exposure related observation data is available.

**Reference substance: Phosphoric acid**

UUID IUC5-0578b8c4-e5dc-4752-bb9e-6d803161fa00

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-09-01 16:12:41 KST

Remarks

**General information**

Reference substance name Phosphoric acid

**Reference substance information****CAS information**

CAS number 7664-38-2

CAS name Phosphoric Acid

**IUPAC name**

IUPAC name Phosphoric Acid

**Synonyms**

Name White phosphoric acid

Name Orthophosphoric acid

Name Amberphos 54

Name 3M Etching liquid

Name Ultra-Etch Gel

Name WC-Reiniger

Name Hydrogen phosphate

Name o-phosphoric acid

**Molecular and structural information**

[IP] OECD: HPVC

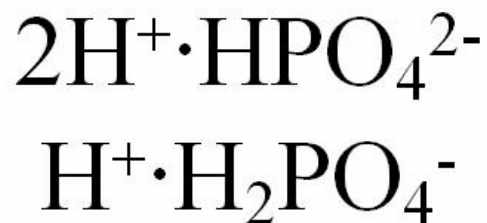
Molecular formula H3O4P

Molecular weight range 98

SMILES notation O=P(O)(O)O

InChI 1/H3O4P/c1-5(2,3)4/h(H3,1,2,3,4)/i1-16,2-16,3-16,4-16,5-31

Structural formula



**Legal entity: National Institute of Environmental Research**

UUID IUC5-b24d7ad5-50ed-4036-ad08-697d62b59689

Dossier UUID 0

Author nier4 / National Institute of Environmental Research / Incheon / Korea, Republic Of

Date 2010-12-09 10:41:48 KST

Remarks

**General information**

Legal entity name National Institute of Environmental Research

**Identifiers****Other IT system identifiers**

IT system LEO

ID 10567

**Contact information****Contact address**

Address flags [IP] OECD: HPVC

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