DIDP 1:

- 1 General Information
  - 1.1 Identification
  - 1.2 Composition
  - 1.3 Identifiers
  - 1.4 Analytical information
  - 1.5 Joint submission
  - 1.6 Sponsors
  - 1.7 Suppliers
  - 1.8 Recipients
  - 1.9 Product and process oriented research and development
- 2 Classification and Labelling
  - 2.1 GHS
  - 2.2 DSD - DPD
- 3 Manufacture, use and exposure
  - 3.1 Technological process
  - 3.2 Estimated quantities
  - 3.3 Sites
  - 3.4 Form in the supply chain
  - 3.5 Identified uses and exposure scenarios
  - 3.6 Uses advised against
  - 3.7 Waste from production and use
  - 3.8 Exposure estimates
  - 3.9 Biocidal information
  - 3.10 Application for authorisation of uses

DIDP 2:

" 4 Physical and chemical properties

o 4.1 Appearance/physical state/colour

" General inform Endpoint.001

" General inform Endpoint.002

" General inform Endpoint.003

o 4.2 Melting point/freezing point

" Melting Endpoint.001

o 4.3 Boiling point

" Boiling Endpoint.001

o 4.4 Density

" Density Endpoint.001

o 4.5 Particle size distribution (Granulometry)

" Granulometry Endpoint.001

o 4.6 Vapour pressure

" Vapour Endpoint.001

" Vapour Endpoint.002

o 4.7 Partition coefficient

" Partition Endpoint.001

" Partition Endpoint.002

o 4.8 Water solubility

" Water sol Endpoint.001

" Water sol Endpoint.002

o 4.10 Surface tension

" Surface tension Endpoint.001

- o 4.11 Flash point
- " Flash Endpoint.001
- o 4.12 Auto flammability
- " Auto flamm Endpoint.001
- o 4.13 Flammability
- " Flamm Endpoint.001
- o 4.14 Explosiveness
- " Expl Endpoint.001
- o 4.15 Oxidising properties
- " Oxid Endpoint.001
- " Oxid Endpoint.002
- o 4.17 Stability in organic solvents and identity of relevant degradation products
- " Stability organic Endpoint.001
- o 4.21 Dissociation constant
- " Dissociation Endpoint.001
- o 4.22 Viscosity
- " Viscosity Endpoint.001
- o 4.23 Additional physico-chemical information
- " Other Endpoint.001
- " Other Endpoint.002
- " Other Endpoint.003
- " Other Endpoint.004

DIDP 3:

- " 5 Environmental fate and pathways
- o 5.1 Stability

" 5.1.1 Phototransformation in air

" Phototrans air Endpoint.001

" 5.1.2 Hydrolysis

" Hydrolysis Endpoint.001

" 5.1.3 Phototransformation in water

" Phototrans water Endpoint.001

" 5.1.4 Phototransformation in soil

" Phototrans soil Endpoint.001

o 5.2 Biodegradation

" 5.2.1 Biodegradation in water: screening tests

" Biodeg water screen Endpoint.001

" Biodeg water screen Endpoint.002

" Biodeg water screen Endpoint.003

" Biodeg water screen Endpoint.004

" Biodeg water screen Endpoint.005

" Biodeg water screen Endpoint.006

" Biodeg water screen Endpoint.007

" Biodeg water screen Endpoint.008

" 5.2.2 Biodegradation in water and sediment: simulation tests

" Biodeg water sim Endpoint.001

" Biodeg water sim Endpoint.002

" 5.2.3 Biodegradation in soil

" Stability in soil Endpoint.001

DIDP 4:

o 5.3 Bioaccumulation

" 5.3.1 Bioaccumulation: aquatic / sediment

" Bioaccumulation Endpoint.001

" Bioaccumulation Endpoint.002

" Bioaccumulation Endpoint.003

" Bioaccumulation Endpoint.004

" Bioaccumulation Endpoint.005

" Bioaccumulation Endpoint.006

" Bioaccumulation Endpoint.007

" 5.3.2 Bioaccumulation: terrestrial

" Bioaccu terr Endpoint.001

o 5.4 Transport and distribution

" 5.4.1 Adsorption / desorption

" Adsorption Endpoint.001

" Adsorption Endpoint.002

" 5.4.2 Henry's Law constant

" Henry law Endpoint.001

" 5.4.3 Distribution modelling

" Distribution Endpoint.001

" Distribution Endpoint.002

o 5.5 Environmental data

" 5.5.1 Monitoring data

" Monitoring Endpoint.001

" Monitoring Endpoint.002

" Monitoring Endpoint.003

DIDP 5:

" 6 Ecotoxicological Information

o 6.1 Aquatic toxicity

" 6.1.1 Short-term toxicity to fish

" Fishtox Endpoint.001

" Fishtox Endpoint.002

" Fishtox Endpoint.003

" Fishtox Endpoint.004

" Fishtox Endpoint.005

" 6.1.2 Long-term toxicity to fish

" Chronfishtox Endpoint.001

DIDP 6:

" 6.1.3 Short-term toxicity to aquatic invertebrates

" Daphniatox Endpoint.001

" Daphniatox Endpoint.002

" Daphniatox Endpoint.003

" Daphniatox Endpoint.004

" Daphniatox Endpoint.005

" 6.1.4 Long-term toxicity to aquatic invertebrates

" Chrondaphniatox Endpoint.001

" Chrondaphniatox Endpoint.002

" 6.1.5 Toxicity to aquatic algae and cyanobacteria

" Algaetox Endpoint.001

" 6.1.7 Toxicity to microorganisms

" Bactox Endpoint.001

" Bactox Endpoint.002

DIDP 7:

- 6.2 Sediment toxicity
  - Sedimentdwellingtox Endpoint.001
  - Sedimentdwellingtox Endpoint.002
  - Sedimentdwellingtox Endpoint.003

DIDP 8:

- 6.3 Terrestrial toxicity
  - 6.3.1 Toxicity to soil macroorganisms except arthropods
    - Soildwellingtox Endpoint.001
    - Soildwellingtox Endpoint.002
  - 6.3.2 Toxicity to terrestrial arthropods
    - Honeybeestox Endpoint.001
  - 6.3.3 Toxicity to terrestrial plants
    - Planttox Endpoint.001
    - Planttox Endpoint.002
    - Planttox Endpoint.003
  - 6.3.4 Toxicity to soil microorganisms
    - Soil micro tox Endpoint.001
  - 6.3.5 Toxicity to birds
    - Bird tox Endpoint.001

DIDP 9:

- 7 Toxicological information
  - Data tox Summary
  - 7.1 Toxicokinetics, metabolism and distribution
    - 7.1.1 Basic toxicokinetics

" Meta mam Endpoint.001

" Meta mam Endpoint.002

" 7.1.2 Dermal absorption

" Dermal absorption Endpoint.001

o 7.2 Acute Toxicity

" 7.2.1 Acute toxicity: oral

" Acute oral Endpoint.001

" Acute oral Endpoint.002

" Acute oral Endpoint.003

" 7.2.2 Acute toxicity: inhalation

" Acute inhal Endpoint.001

" Acute inhal Endpoint.002

" 7.2.3 Acute toxicity: dermal

" Acute dermal Endpoint.001

" Acute dermal Endpoint.002

" Acute dermal Endpoint.003

" 7.2.4 Acute toxicity: other routes

" Acute other Endpoint.001

DIDP 10:

o 7.3 Irritation / corrosion

" 7.3.1 Skin irritation / corrosion

" Skin irritation Endpoint.001

" Skin irritation Endpoint.002

" Skin irritation Endpoint.003

" Skin irritation Endpoint.004

" 7.3.2 Eye irritation

" Eye irritation Endpoint.001

" Eye irritation Endpoint.002

o 7.4 Sensitisation

" 7.4.1 Skin sensitisation

" Sensitization Endpoint.001

" Sensitization Endpoint.002

" Sensitization Endpoint.003

DIDP 11:

o 7.5 Repeated dose toxicity

" 7.5.1 Repeated dose toxicity: oral

" Repeated oral Endpoint.001

" Repeated oral Endpoint.002

" Repeated oral Endpoint.003

" Repeated oral Endpoint.004

" 7.5.2 Repeated dose toxicity: dermal

" Repeated dermal Endpoint.001

" 7.5.3 Repeated dose toxicity: inhalation

" Repeated inhal Endpoint.001

DIDP 12:

o 7.6 Genetic toxicity

" 7.6.1 Genetic toxicity in vitro

" Genetic in vitro Endpoint.001

" Genetic in vitro Endpoint.002

" Genetic in vitro Endpoint.003

" Genetic in vitro Endpoint.004

" 7.6.2 Genetic toxicity in vivo

" Genetic in vivo Endpoint.001

o 7.7 Carcinogenicity

" Carcinogenicity Endpoint.001

DIDP 13:

o 7.8 Toxicity to reproduction

" 7.8.1 Toxicity to reproduction

" Reproduction Endpoint.001

" Reproduction Endpoint.002

" Reproduction Endpoint.003

" 7.8.2 Developmental toxicity / teratogenicity

" Developmental Endpoint.001

" Developmental Endpoint.002

" Developmental Endpoint.003

o 7.12 Additional toxicological information

" Other Endpoint.001

" Other Endpoint.002

" Other Endpoint.003

" Other Endpoint.004

" Other Endpoint.005

" 11 Guidance on safe use

o Safe use Endpoint.001

Dossier

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance(seeremarks)

- 0 Related Information
  - 0.1 Templates
  - 0.2 Categories
  - 0.3 Mixtures
- 1 General Information
  - 1.1 Identification
  - 1.2 Composition
  - 1.3 Identifiers
  - 1.4 Analytical information
  - 1.5 Joint submission
  - 1.6 Sponsors
  - 1.7 Suppliers
  - 1.8 Recipients
  - 1.9 Product and process oriented research and development
- 2 Classification and Labelling
  - 2.1 GHS
  - 2.2 DSD - DPD
- 3 Manufacture, use and exposure
  - 3.1 Technological process
  - 3.2 Estimated quantities
  - 3.3 Sites
  - 3.4 Form in the supply chain
  - 3.5 Identified uses and exposure scenarios
  - 3.6 Uses advised against
  - 3.7 Waste from production and use
  - 3.8 Exposure estimates
  - 3.9 Biocidal information
  - 3.10 Application for authorisation of uses
- 4 Physical and chemical properties
  - 4.1 Appearance/physical state/colour
    - General inform Endpoint.001
    - General inform Endpoint.002
    - General inform Endpoint.003
  - 4.2 Melting point/freezing point
    - Melting Endpoint.001
  - 4.3 Boiling point
    - Boiling Endpoint.001
  - 4.4 Density
    - Density Endpoint.001
  - 4.5 Particle size distribution (Granulometry)
    - Granulometry Endpoint.001
  - 4.6 Vapour pressure

- Vapour Endpoint.001
- Vapour Endpoint.002

4.7 Partition coefficient

- Partition Endpoint.001
- Partition Endpoint.002

4.8 Water solubility

- Water sol Endpoint.001
- Water sol Endpoint.002

4.10 Surface tension

- Surface tension Endpoint.001

4.11 Flash point

- Flash Endpoint.001

4.12 Auto flammability

- Auto flamm Endpoint.001

4.13 Flammability

- Flamm Endpoint.001

4.14 Explosiveness

- Expl Endpoint.001

4.15 Oxidising properties

- Oxid Endpoint.001
- Oxid Endpoint.002

4.17 Stability in organic solvents and identity of relevant degradation products

- Stability organic Endpoint.001

4.21 Dissociation constant

- Dissociation Endpoint.001

4.22 Viscosity

- Viscosity Endpoint.001

4.23 Additional physico-chemical information

- Other Endpoint.001
- Other Endpoint.002
- Other Endpoint.003
- Other Endpoint.004

5 Environmental fate and pathways

5.1 Stability

5.1.1 Phototransformation in air

- Phototrans air Endpoint.001

5.1.2 Hydrolysis

- Hydrolysis Endpoint.001

5.1.3 Phototransformation in water

- Phototrans water Endpoint.001

5.1.4 Phototransformation in soil

- Phototrans soil Endpoint.001

5.2 Biodegradation

5.2.1 Biodegradation in water: screening tests

- Biodeg water screen Endpoint.001
- Biodeg water screen Endpoint.002
- Biodeg water screen Endpoint.003

- Biodeg water screen Endpoint.004
- Biodeg water screen Endpoint.005
- Biodeg water screen Endpoint.006
- Biodeg water screen Endpoint.007
- Biodeg water screen Endpoint.008

5.2.2 Biodegradation in water and sediment: simulation tests

- Biodeg water sim Endpoint.001
- Biodeg water sim Endpoint.002

5.2.3 Biodegradation in soil

- Stability in soil Endpoint.001

5.3 Bioaccumulation

5.3.1 Bioaccumulation: aquatic / sediment

- Bioaccumulation Endpoint.001
- Bioaccumulation Endpoint.002
- Bioaccumulation Endpoint.003
- Bioaccumulation Endpoint.004
- Bioaccumulation Endpoint.005
- Bioaccumulation Endpoint.006
- Bioaccumulation Endpoint.007

5.3.2 Bioaccumulation: terrestrial

- Bioaccu terr Endpoint.001

5.4 Transport and distribution

5.4.1 Adsorption / desorption

- Adsorption Endpoint.001
- Adsorption Endpoint.002

5.4.2 Henry's Law constant

- Henry law Endpoint.001

5.4.3 Distribution modelling

- Distribution Endpoint.001
- Distribution Endpoint.002

5.5 Environmental data

5.5.1 Monitoring data

- Monitoring Endpoint.001
- Monitoring Endpoint.002
- Monitoring Endpoint.003

6 Ecotoxicological Information

6.1 Aquatic toxicity

6.1.1 Short-term toxicity to fish

- Fishtox Endpoint.001
- Fishtox Endpoint.002
- Fishtox Endpoint.003
- Fishtox Endpoint.004
- Fishtox Endpoint.005

6.1.2 Long-term toxicity to fish

- Chronfishtox Endpoint.001

6.1.3 Short-term toxicity to aquatic invertebrates

- Daphniatox Endpoint.001
- Daphniatox Endpoint.002
- Daphniatox Endpoint.003
- Daphniatox Endpoint.004
- Daphniatox Endpoint.005

6.1.4 Long-term toxicity to aquatic invertebrates

- Chrondaphniatox Endpoint.001
- Chrondaphniatox Endpoint.002

6.1.5 Toxicity to aquatic algae and cyanobacteria

- Algaetox Endpoint.001

6.1.7 Toxicity to microorganisms

- Bactox Endpoint.001
- Bactox Endpoint.002

6.2 Sediment toxicity

- Sedimentdwellingtox Endpoint.001
- Sedimentdwellingtox Endpoint.002
- Sedimentdwellingtox Endpoint.003

6.3 Terrestrial toxicity

6.3.1 Toxicity to soil macroorganisms except arthropods

- Soildwellingtox Endpoint.001
- Soildwellingtox Endpoint.002

6.3.2 Toxicity to terrestrial arthropods

- Honeybeestox Endpoint.001

6.3.3 Toxicity to terrestrial plants

- Planttox Endpoint.001
- Planttox Endpoint.002
- Planttox Endpoint.003

6.3.4 Toxicity to soil microorganisms

- Soil micro tox Endpoint.001

6.3.5 Toxicity to birds

- Bird tox Endpoint.001

7 Toxicological information

- Data tox Summary

7.1 Toxicokinetics, metabolism and distribution

7.1.1 Basic toxicokinetics

- Meta mam Endpoint.001
- Meta mam Endpoint.002

7.1.2 Dermal absorption

- Dermal absorption Endpoint.001

7.2 Acute Toxicity

7.2.1 Acute toxicity: oral

- Acute oral Endpoint.001
- Acute oral Endpoint.002
- Acute oral Endpoint.003

7.2.2 Acute toxicity: inhalation

- Acute inhal Endpoint.001

- Acute inhal Endpoint.002

7.2.3 Acute toxicity: dermal

- Acute dermal Endpoint.001
- Acute dermal Endpoint.002
- Acute dermal Endpoint.003

7.2.4 Acute toxicity: other routes

- Acute other Endpoint.001

7.3 Irritation / corrosion

7.3.1 Skin irritation / corrosion

- Skin irritation Endpoint.001
- Skin irritation Endpoint.002
- Skin irritation Endpoint.003
- Skin irritation Endpoint.004

7.3.2 Eye irritation

- Eye irritation Endpoint.001
- Eye irritation Endpoint.002

7.4 Sensitisation

7.4.1 Skin sensitisation

- Sensitization Endpoint.001
- Sensitization Endpoint.002
- Sensitization Endpoint.003

7.5 Repeated dose toxicity

7.5.1 Repeated dose toxicity: oral

- Repeated oral Endpoint.001
- Repeated oral Endpoint.002
- Repeated oral Endpoint.003
- Repeated oral Endpoint.004

7.5.2 Repeated dose toxicity: dermal

- Repeated dermal Endpoint.001

7.5.3 Repeated dose toxicity: inhalation

- Repeated inhal Endpoint.001

7.6 Genetic toxicity

7.6.1 Genetic toxicity in vitro

- Genetic in vitro Endpoint.001
- Genetic in vitro Endpoint.002
- Genetic in vitro Endpoint.003
- Genetic in vitro Endpoint.004

7.6.2 Genetic toxicity in vivo

- Genetic in vivo Endpoint.001

7.7 Carcinogenicity

- Carcinogenicity Endpoint.001

7.8 Toxicity to reproduction

7.8.1 Toxicity to reproduction

- Reproduction Endpoint.001
- Reproduction Endpoint.002
- Reproduction Endpoint.003

- 7.8.2 Developmental toxicity / teratogenicity
  - Developmental Endpoint.001
  - Developmental Endpoint.002
  - Developmental Endpoint.003
- 7.12 Additional toxicological information
  - Other Endpoint.001
  - Other Endpoint.002
  - Other Endpoint.003
  - Other Endpoint.004
  - Other Endpoint.005
- 11 Guidance on safe use
  - Safe use Endpoint.001

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Templates

Inherit

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Categories

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Mixtures

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Substance identification

Chemical name 1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich

Reference substance

/ Notavailable;notasingleisomersubstance(seeremarksbelow)

EC number	EC name
271-091-4	1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich

CAS number **CAS name**

IUPAC name

Not available; not a single isomer substance (see remarks below)

Type of substance

Composition multi constituent substance

Origin organic

Trade names

Name
Jayflex DIDP

Substance composition

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich

Name	1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich
Brief description	Reaction mass of di-"isodecyl" phthalate and di-"isononyl" phthalate and diisoundecyl phthalate and isodecyl isononyl phthalate and isodecyl isoundecyl phthalate and isononyl isoundecyl phthalate. See - Multiconstituent Declaration Attachment

Constituents

/ 1,2-benzenedicarboxylicacid,di-isodecylester

/ 1,2-benzenedicarboxylicacid,di-isodecylester

Reference substance	EC number	EC name
	247-977-1	di-"isodecyl" phthalate
	CAS number	CAS name
	IUPAC name	
	1,2-benzenedicarboxylic acid, di-isodecyl ester	

/ 1,2-benzenedicarboxylicacid,isodecyl,isoundecylester

/ 1,2-benzenedicarboxylicacid,isodecyl,isoundecylester

Reference substance	EC number	EC name
	305-701-8	isodecyl isoundecyl phthalate
	CAS number	CAS name

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumente745.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f61b3a36-8bfa-48bc-8572-dc49bd25708e%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&view=view_1_2

Reference substance	IUPAC name 1,2-benzenedicarboxylic acid, isodecyl, isoundecyl ester / 1,2-benzenedicarboxylicacid,isodecyl,isononylester / 1,2-benzenedicarboxylicacid,isodecyl,isononylester	
	EC number 285-916-0	EC name isodecyl isononyl phthalate
	CAS number	CAS name
Reference substance	IUPAC name 1,2-benzenedicarboxylic acid, isodecyl, isononyl ester / 1,2-benzenedicarboxylicacid,isononyl,isoundecylester / 1,2-benzenedicarboxylicacid,isononyl,isoundecylester	
	EC number 285-920-2	EC name isononyl isoundecyl phthalate
	CAS number	CAS name
Reference substance	IUPAC name 1,2-benzenedicarboxylic acid, isononyl, isoundecyl ester / 1,2-benzenedicarboxylicacid,di-isononylester / 1,2-benzenedicarboxylicacid,di-isononylester	
	EC number 249-079-5	EC name di-"isononyl" phthalate
	CAS number	CAS name
Reference substance	IUPAC name 1,2-benzenedicarboxylic acid, di-isononyl ester / 1,2-benzenedicarboxylicacid,di-isoundecylester / 1,2-benzenedicarboxylicacid,di-isoundecylester	

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumente745.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f61b3a36-8bfa-48bc-8572-dc49bd25708e%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&view=view_1_2

EC number	EC name
306-165-8	diisoundecyl phthalate
CAS number	CAS name

IUPAC name

1,2-benzenedicarboxylic acid, di-isoundecyl ester

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Identifiers

Regulatory programme identifiers

Other IT system identifiers

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Analytical information

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Joint submission

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Sponsors

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Suppliers

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Recipients

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Product and process oriented research and development

Classification and Labelling according to GHS

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich

General information

Name	1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich Not classified
Implementation	EU
Remarks	DIDP was evaluated by the Classification and Labelling working group with a determination that classification was not required for any endpoint. Issues related to developmental and reproductive toxicity were considered by the Specialized Expert Group who also determined that data did not meet the standards for classification. The official results on Classification and Labeling are published on the website of the European Chemicals Bureau (Official journal of the European Union version C90/11 dated 13.4.2006). These results are copied below: ECB website (http://ecb.jrc.it/esis/), Classification and Labeling Information: This substance is not classified in the Annex I of Directive 67/548/EEC. Official Journal of the European Union (version C90/11 dated 13.3.2006) Classification and Labeling Information Self classification according to Directive 67/548/EEC criteria is explained in the CSR, Section 3.2, Table 7.

Classification

Physical hazards

	Hazard statement	Reason for no classification
Explosives		conclusive but not sufficient for classification
Flammable gases		conclusive but not sufficient for classification
Flammable aerosols		conclusive but not sufficient for classification
Oxidizing gases		conclusive but not sufficient for classification

Gases under pressure		conclusive but not sufficient for classification
Flammable liquids		conclusive but not sufficient for classification
Flammable solids		conclusive but not sufficient for classification
Self-reactive substances and mixtures		conclusive but not sufficient for classification
Pyrophoric liquids		conclusive but not sufficient for classification
Pyrophoric solids		conclusive but not sufficient for classification
Self heating substances and mixtures		conclusive but not sufficient for classification
Substances and mixtures which in contact with water emits flammable gases		conclusive but not sufficient for classification
Oxidising liquids		conclusive but not sufficient for classification
Oxidising solids		conclusive but not sufficient for classification
Organic peroxides		conclusive but not sufficient for classification
Substance and mixtures corrosive to metals		conclusive but not sufficient for classification

Health hazards

	Hazard statement	Reason for no classification
Acute toxicity - oral		conclusive but not sufficient for classification
Acute toxicity - dermal		conclusive but not sufficient for classification
Acute toxicity - inhalation		conclusive but not sufficient for classification
Skin corrosion/irritation		conclusive but not sufficient for classification

Serious damage/ eye irritation	conclusive but not sufficient for classification
Respiratory sensitization	conclusive but not sufficient for classification
Skin sensitization	conclusive but not sufficient for classification
Aspiration hazard	conclusive but not sufficient for classification

Germ cell mutagenicity

	Hazard statement	Reason for no classification
Germ cell mutagenicity		conclusive but not sufficient for classification

Carcinogenicity

	Hazard statement	Reason for no classification
Carcinogenicity		conclusive but not sufficient for classification

	Hazard statement	Reason for no classification
Reproductive toxicity		conclusive but not sufficient for classification
Effects on or via lactation		conclusive but not sufficient for classification

Specific target organ toxicity - single

	Hazard statement	Reason for no classification
Specific target organ toxicity - single		conclusive but not sufficient for classification

Specific target organ toxicity - repeated

	Hazard statement	Reason for no classification
Specific target organ toxicity - repeated		conclusive but not sufficient for classification

Health hazards

	Hazard statement	Reason for no classification
Hazardous to the aquatic environment		conclusive but not sufficient for classification

Labelling

Signal word no signal word

Classification and Labelling according 67/548/EEC (DSD)

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich

General information

Name	1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich
Status	Not classified other: DIDP was evaluated by the Classification and Labelling working group with a determination that classification was not required for any endpoint. DIDP is not listed in Annex I of 67/548/EEC.
Index number	999-005-00-7
Remarks	DIDP was evaluated by the Classification and Labelling working group with a determination that classification was not required for any endpoint. The official results on Classification and Labeling are published on the website of the European Chemicals Bureau (Official Journal of the European Union version C90/11 dated 13.4.2006). These results are copied below.

Classification

	Classification	Reason for no classification
Explosiveness		conclusive but not sufficient for classification
Oxidising properties		conclusive but not sufficient for classification
Flammability		conclusive but not sufficient for classification
Thermal stability		conclusive but not sufficient for classification
Acute toxicity		conclusive but not sufficient for classification
Acute toxicity - irreversible damage after single exposure		conclusive but not sufficient for classification
Repeated dose toxicity		conclusive but not sufficient for classification
Irritation /		conclusive but not sufficient for classification

Corrosion	
Sensitisation	conclusive but not sufficient for classification
Carcinogenicity	conclusive but not sufficient for classification
Mutagenicity - Genetic Toxicity	conclusive but not sufficient for classification
Toxicity to reproduction - fertility	conclusive but not sufficient for classification
Toxicity to reproduction - development	conclusive but not sufficient for classification
Toxicity to reproduction - breastfed babies	conclusive but not sufficient for classification
Environment	conclusive but not sufficient for classification

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Technological process

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Estimated quantities

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Sites

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Form in the supply chain

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance(seeremarksbelow)

Uses and exposure

Overall use and exposure

Main use category

- [x] Industrial use
- [ ] Professional use
- [ ] Consumer use

Specification for industrial and professional use

- [x] Used in closed system
- [x] Use resulting in inclusion into or onto matrix
- [ ] Non-dispersive use
- [ ] Dispersive use

Significant routes of exposure

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument21e9.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f61b3a36-8bfa-48bc-8572-dc49bd25708e%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&view=view_3_5

Human exposure

- Oral
- Dermal
- By inhalation

Environmental exposure

- Water
- Air
- Solid waste
- Soil

Pattern of exposure

- Accidental / infrequent
- Occasional
- Continuous / frequent

Identified uses and exposure scenarios

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument21e9.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f61b3a36-8bfa-48bc-8572-dc49bd25708e%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&view=view_3_5

Identified use

DIDP is a high molecular weight general purpose plasticiser added to PVC to impart flexibility. Plasticized PVC with DIDP is used in construction, industrial applications, and durable goods. DIDP is also used in non-PVC polymer applications.

DIDP is a plasticiser added to PVC (polyvinylchloride) to impart flexibility.

Application technique / Activity	DIDP is a plasticiser added to PVC (polyvinylchloride) to impart flexibility.

plasticizer

Use category	plasticizer

✔ Available as substance

✔ Substance in mixture

C22.2 - manufacturing: manufacture of plastics products

Industry category	C22.2 - manufacturing: manufacture of plastics products
Type of article	Other articles; specify: General purpose plasticiser added to PVC (polyvinylchloride), used in the following industries: wire and cable (cable filling compounds and sheathing); film and sheet (roofing materials, waterproofing applications ie pool liners); auto (interior trim)

other products: paints, coatings, and inks

Use category	other products: paints, coatings, and inks

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument21e9.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f61b3a36-8bfa-48bc-8572-dc49bd25708e%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&view=view_3_5

✔ Available as substance

Substance in mixture

C20.3 - manufacturing: manufacture of paints, varnishes and similar coatings, printing ink and mastics

Industry category	C20.3 - manufacturing: manufacture of paints, varnishes and similar coatings, printing ink and mastics
Type of article	Other articles; specify:

Exposure scenario

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance(seeremarksbelow)

Uses advised against

Not for use in children's toys and childcare articles that can be placed in the mouth.

DIDP is restricted for use in toys and childcare articles in the European Union...

Application technique / Activity	DIDP is restricted for use in toys and childcare articles in the European Union by Directive 2005/84/EC. The above restriction is based on the use of the precautionary principle. New data are included in this dossier which shows that DIDP can be used safely in this application. These data are being considered as part of the Commission and ECHA review of the restrictions as required by Directive 2005/84/EC.

other products: Toys and childcare articles that can be placed in the mouth.

Use category	other products: Toys and childcare articles that can be placed in the mouth.

- Available as substance
- Substance in mixture

C22.2 - manufacturing: manufacture of plastics products

Industry category	C22.2 - manufacturing: manufacture of plastics products
Type of article	

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Waste from production and use

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Exposure estimates

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Biocidal information

1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich / / Notavailable;notasingleisomersubstance (seeremarksbelow)

Application for authorisation of uses

Dissemination Dossier

General inform Endpoint.001

Administrative Data

Purpose flag key study

Study result type experimental result

Study period 2008

Reliability 2 (reliable with restrictions)

Rationale for reliability Standard test method used but no GLP certified lab

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2008							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: ASTM D 1209, Pt-Co	no

GLP compliance

no No certified lab

Test materials

Test material equivalent to submission substance identity

yes

Results and discussion

Physical state at 20°C and 1013 hPa

liquid

Form

other: Liquid at room temperature

Colour

Color, Pt-Co = 10

Substance type

organic

Applicant's summary and conclusion

Conclusions

Color according ASTM D 1209, Pt-Co = 10

Executive summary

Color according ASTM D 1209, Pt-Co = 10

Dissemination Dossier
General inform Endpoint.002

Administrative Data

Purpose flag key study

Study result type experimental result

Study period not applicable

Reliability 2 (reliable with restrictions)

Rationale for reliability Information is from manufacturer's database.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2008							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
no guideline required		

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product
Molecular weight = 447 - C28H46O4(average)

Results and discussion

Physical state at 20°C and 1013 hPa

liquid

Form

other: liquid at roomtemperature

Colour

Clear, colorless liquid

Odour

other: mild

Substance type

organic

Applicant's summary and conclusion

Conclusions

Di-isodecyl phthalate is a clear, colorless liquid with a mild odor at 20 degrees C and 1013 hPa.

Executive summary

Di-isodecyl phthalateis a clear, colorless liquid with a mild odor at 20 degrees C and 1013 hPa.

Dissemination Dossier
General inform Endpoint.003

Administrative Data

Purpose flag supporting study

Study result type read-across based on grouping of substances (category approach)

Reliability 2 (reliable with restrictions)

Rationale for reliability Information is from literature

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Wypych Anna	2004	Plasticizers Database 2nd Electronic Edition						

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
no guideline required		

GLP compliance

no not applicable

Test materials

Test material equivalent to submission substance identity

yes

Results and discussion

Physical state at 20°C and 1013 hPa

liquid at 20°C and 101.3 kPa

Form

other: Liquid at roomtemperature

Substance type

organic

Applicant's summary and conclusion

Conclusions

Substance is a liquid at 20°C and 101.3 kPa

Executive summary

Substance is a liquid at 20°C and 101.3 kPa

Dissemination Dossier
Melting Endpoint.001

Administrative Data

Purpose flag key study

Study result type experimental result **Study period** Not applicable

Reliability 2 (reliable with restrictions)

Rationale for reliability Followed a standard test guideline that is valid for the endpoint. Not GLP lab

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2009							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: ASTM D 5950 modified	no data

Type of method

pour point ASTM D5950 modified

Principles of method if other than guideline

Sample was not preheated before cooling. No influence on result.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Results and discussions

Melting / freezing point

Melt./Freez. pt.	Atm. pressure	Decomposition	Decomp. temp.	Sublimation	Subl. temp.	Remarks
-45 °C	101325 Pa	no		no		

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions

Pour point for di-isodecyl phthalate is -45 degrees C

Executive summary

Pour point for di-isodecyl phthalate is -45 degrees C (228 K).

1. Dissemination Dossier
Boiling Endpoint.001

Administrative Data

Purpose flag key study

Study result type estimated by calculation **Study period** Not applicable

Reliability 2 (reliable with restrictions)

Rationale for reliability The reliability rating is 2 because the data are calculated.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Computer model	U.S. Environmental Protection Agency (USEPA)	2000	EPI SuiteTM, Estimation Program Interface Suite, v3.12	USEPA, Washington, DC, USA					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: Computer model	

Type of method

other: calculation by MPBPWIN ver. 1.41

Principles of method if other than guideline

Boiling point calculation by MPBPWIN ver. 1.41, within EPISuite TM v3.12, using calculation method of Stein and Brown.

GLP compliance

no not applicable, calculation

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

SMILES Notation: O=C(c1ccccc1C(=O)OCCCCCCCC(C)C)OCCCCCCCC(C)C

Results and discussions

Boiling point

Boiling pt.	Atm. pressure	Decomposition	Decomp. temp.	Remarks
463 °C	1013 hPa	no		

Applicant's summary and conclusion

Conclusions

Boiling point for diisodecyl phthalate is 463 degrees C.

Executive summary

Boiling point for diisodecyl phthalate is 463 degrees C.

Dissemination Dossier

Density Endpoint.001

Administrative Data

Purpose flag key study

Study result type experimental result

Study period Not applicable

Reliability 2 (reliable with restrictions)

Rationale for reliability Followed a standard test guideline that is valid for the endpoint.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2008							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: ASTM D4052	

Type of method

oscillating densitimeter Standard Test Method for Density and Relative Density of Liquids by Digital Density Meter

GLP compliance

no No GLP certified lab

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Results and discussion

Density

Type	Density	Temp.
density	0.97 g/cm³	20 °C

Remarks on results including tables and figures

Density = 0.966 g/cm3 at 20°C

Applicant's summary and conclusion

Conclusions

Density for di-isodecyl phthalate is 0.966 g/cm3 at 20 degrees C.

Executive summary

Density for di-isodecyl phthalate is 0.966 g/cm3 at 20 degrees C.

Dissemination Dossier
Granulometry Endpoint.001

Administrative Data

Data waiving study scientifically unjustified

Materials and methods

Test materials

Test material equivalent to submission substance identity

yes

Dissemination Dossier
Vapour Endpoint.001

Administrative Data

Purpose flag key study
Study result type estimated by calculation
Study period 2000
Reliability 2 (reliable with restrictions)
Rationale for reliability Result obtained by calculation

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		2003	European Risk Assessment Report	European Risk Assessment Report - Table 1.8 Pg 12					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: regression using Clausius-clapeyron equation	not applicable

Type of method

other: calculation

Principles of method if other than guideline

Various values of vapour pressure for commercial DIDP-type mixtures have been reported (BASF, 1983; 1987a; 1991a; Hüls, 1996). The determinations have been mostly carried out in the temperature range of 180-340°C. Nevertheless, with extrapolation by linear regression using the Clausius-Clapeyron equation, estimates of vapour pressure values in the temperature range of greatest interest for environmental modelling (20°C to 30° C) can be obtained.

GLP compliance

no not applicable

Test materials

Test material equivalent to submission substance identity

yes

Results and discussions

Vapour pressure

0.000051 Pa at 25 °C

Remarks

Remarks on results including tables and figures

Mean value

Applicant's summary and conclusion

Conclusions

Vapour pressure for DIDP at 25 °C is 0.000051 Pa

Executive summary

Vapour pressure for DIDP at 25 °C is 0.000051 Pa

Administrative Data

Purpose flag	supporting study		
Study result type	estimated by calculation	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is 2 because the data are calculated. The value was calculated based on the QSPR (quantitative structure-property relationship) three-solubility model, which was peer reviewed.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Cousins I and Mackay D	2000	Correlating the physical-chemical properties of phthalate esters using the 'three solubility' approach	Chemosphere 41: 1389-1399					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: Mathematical model	not applicable

Type of method

other: calculation

Principles of method if other than guideline

Physicochemical data for selected commercial phthalate esters from various sources including the public literature, manufacturing specifications, and handbook values were evaluated. Valid values were identified and presented in a phthalate ester environmental fate, peer reviewed publication. These data, including the values for vapor pressure, represent the definitive and currently accepted physicochemical database for selected phthalate esters including diisodecyl phthalate. Quantitative structure-property relationships, significant at the 99.9% level, were developed using the relevant phthalate ester data to estimate solubility in water, air, and octanol, where V = the Le Bas molar volume (cm3 mol-1). The Le Bas molar volume used for diisodecyl phthalate ester was 609.2 cm3 mol-1. Log CS(WL) = -0.012V + 5.8, n = 35 (solubility in water) r2 = 0.98, SE = 0.39 Log CS(AL) = -0.013V - 1.3, n = 15 (solubility in air) r2 = 0.87, SE = 0.33 Log CS(OL) = -0.016V + 3.4, n = 68 (solubility in octanol) r2 = 0.19, SE = 0.41 It was recommended by the authors that the above regressions be used for predicting the three solubilities for phthalate esters with alkyl chain lengths from 1 to 13 carbons.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

yes

Results and discussions

Vapour pressure

0.0000000184 hPa at 25 °C

Remarks

Transition / decomposition

Transition / decomposition	no
at	
Vapour pressure at 10°C above transition temperature	
Vapour pressure at 20°C above transition temperature	

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions

Vapour pressure at 25 deg C is 0.0000000184 hPa

Executive summary

Vapour pressure at 25 deg C is 0.0000000184 hPa

Administrative Data

Purpose flag	supporting study		
Study result type	estimated by calculation	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is 2 because the data are calculated. The value was calculated based on the QSPR (quantitative structure-property relationship) three-solubility model, which was peer reviewed.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Cousins I and Mackay D	2000	Correlating the physical-chemical properties of phthalate esters using the 'three solubility' approach	Chemosphere 41: 1389-1399					

Materials and methods

Partition coefficient type
octanol-water

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: Mathematical model	

Type of method

other: Esitmated from Q!SAR model

Principles of method if other than guideline

Physicochemical data for 22 selected commercial phthalate esters from various sources including the public literature, manufacturing specifications, handbook values, and computer modeling were evaluated. Valid values were identified and presented in a phthalate ester physicochemical properties, peer reviewed publication. These data including the values for octanol-water partitioning represent the definitive and currently accepted physicochemical database for selected phthalate esters including diisodecyl phthalate. Quantitative structure-property relationships, significant at the 99.9% level, were developed using the relevant phthalate ester data to estimate solubility in water, air, and octanol, where V = the Le Bas molar volume (cm3 mol-1). Log CS(WL) = -0.012V + 5.8, n = 35 (solubility in water) r2 = 0.98, SE = 0.39 Log CS(AL) = -0.013V - 1.3, n = 15 (solubility in air) r2 = 0.87, SE = 0.33 Log CS(OL) = -0.016V + 3.4, n = 68 (solubility in octanol) r2 = 0.19, SE = 0.41 It was recommended by the authors that the above regressions be used for predicting the three solubilities for phthalate esters with alkyl chain lengths from 1 to 13 carbons.

GLP compliance

no calculation

Test materials

Test material equivalent to submission substance identity

yes

Analytical method

other: calculation

Results and discussions

Partition coefficient

Type	Partition coefficient	Temp.	pH
log Pow	9.46	25 °C	7

Applicant's summary and conclusion

Conclusions

Log Kow (Pow) for 1,2-benzenedicarboxylic acid, di-C9,C10 and C11 branched alkyl ester, C10 Rich, is 9.46 at 25 deg C

Executive summary

Log Kow (Pow) for 1,2-benzenedicarboxylic acid, di-C9,C10 and C11 branched alkyl ester, C10 Rich, is 9.46 at 25 deg C

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability is rated 2 because the test procedure followed a technically appropriate procedure to determine the octanol/water partition coefficient of substances with very low water solubility, but did not follow GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Ellington J	1999	Octanol/water partition coefficients and water solubilities of phthalate esters	J. Chem. Eng. Data 44(6): 1414-1418					

Materials and methods

Partition coefficient type

octanol-water

Test guideline

Qualifier	Guideline	Deviations
equivalent or similar to	OECD Guideline 123 (Partition Coefficient (1-Octanol / Water), Slow-Stirring Method)	no

Type of method

other: Slow-stirring method

Principles of method if other than guideline

Partition coef ellington Apparatus and Experimental Procedure A Pyrex cylindrical jar, approximate volume 11.5 L, was fitted with a 2-mm i.d. straight bore stopcock that was inserted through the container wall at the bottom and turned down to form a tap for withdrawing water. The jars were cleaned by soaking with an aqueous cleaning solution in laboratory deionized water. The jars were rinsed sequentially with deionized water, with concentrated nitric acid, and again with deionized water. A final rinse was made with the distilled, 0.20-μm-filtered water. A Teflon-coated magnetic stirring bar (2.54 cm) was added and the jar filled to a level of 6 L for water solubility measurements and 10 L for Kow determinations. In the water solubility experiments, 100 μl of the neat phthalate was added to the water surface and a 30 × 30 cm by 6-mm-thick flat glass plate was placed over the smooth ground open end of the jar to form a tight seal. This prevented both the entrance of airborne particulate matter and the evaporation of water. The water for the Kow experiments was presaturated with octanol by adding 5.5 mL of octanol and slow-stirring for 24 h. The reported water solubility of octanol in water is 0.0347 M or approximately 0.5 mL/L. Droplets of octanol were always observed on the water surface at the end of the presaturation. The phthalate, dissolved in 50 mL of octanol at a concentration of 35−75 mg/mL, was carefully layered on the water surface and again covered with the flat glass plate seal. The stirring rate was adjusted in the water solubility experiments in order to move the droplets of phthalate on the surface of the water at approximately 10 cm/min, while in the Kow experiments the rate of stirring was adjusted to create a vortex of approximately 1 cm at the octanol/water interface. To prevent heat transfer from the magnetic stirrer during the experiments, the jar was placed on four 4 × 4 cm by 0.5-cm-thick blocks of wood. The experiments were conducted at a constant room air temperature of 25 ± 0.1 °C, the same temperature that was observed in the octanol/water systems when periodic measurements were made. Solid-Phase Extraction (SPE) Water samples were collected from the cylindrical jars in either 0.5-L (water solubility measurements) or 1-L (Kow measurements) volumetric flasks. Before the collection of the sample, a volume of methanol was added to the collection flask to make the collected sample 0.5% in methanol. The sample flask also contained 100−300 ng of one of the other phthalates (not being measured) that served as an internal standard. The phthalates were extracted from the collected water sample using a solid-phase disk procedure. The solid-phase extractions utilized the 1-L vacuum filtration glassware

commonly used to filter liquid chromatography solvents, which was fitted with a ceramic fritted glass support and a 40/35 joint. The strength of the applied vacuum was adjusted with a bleed valve attached to a tee joint in the vacuum hose. The extraction disk was placed in the filtration apparatus and cleaned by adding 6 mL of acetonitrile to the reservoir and applying gentle vacuum until the disk was saturated. The disk was soaked for 3 min before drying under a full vacuum. The cleaning step was repeated with methanol then the disk was activated by adding 10-mL of methanol to the reservoir and applying slight vacuum to saturate the disk. At the end of 3 min the level of methanol dropped to 3−5 mm above the surface of the disk. Then the water sample was added to the reservoir and the vacuum adjusted to yield a flow of approximately 20 mL/min until all the water passed through the disk. A sheet of clean aluminum foil was placed loosely over the mouth of the reservoir during the extraction. The foil was pressed tightly over the lip of the reservoir to form a seal, before full vacuum was applied for 30 s to dry the disk. The interior surface of the reservoir and the bottom surfaces of the filter holder were rinsed with acetonitrile to remove residual droplets of water; care was taken to avoid rinsing the extraction disk. The sorbed phthalates were eluted into a collection tube with three 2-mL volumes of acetonitrile. The acetonitrile was transferred to a glass-stoppered, 10-mL, tapered tube. In the water solubility experiments, 25 μL of octanol was added to the acetonitrile at this time; this was approximately the same volume of octanol retained by the disk when the Kow water layer samples were extracted. This octanol acted as a "keeper" solvent during the subsequent concentration step. Acetonitrile was removed by gentle, nitrogen-gas blowdown while warming the tube with steam. The final concentrated volume used for the water solubility and Kow determinations was 25−50 μL. Solutions for Quantitative Analysis Stock solutions (5−10 g/L) were prepared by weighing each phthalate into separate 5-mL volumetric flasks and bringing to final volume with methanol. Sequential dilutions were made in methanol to yield 100 mg/L and 20 mg/L standards. Similarly, 100 mg/L, 20 mg/L, and 4 mg/L standards that contained all three phthalates together in octanol were prepared. The three mixed phthalate in octanol standards were used to calibrate detector response and linearity and to determine the optimum temperature and pressure programs for GC analysis. The 20 mg/L solutions of the individual phthalates in methanol were used in spiking experiments designed to determine SPE recoveries, and they were also used as the internal standard spiking solutions. Gas Chromatography (GC) Analyses were performed on a Hewlett-Packard 5890 Series II gas chromatograph (Palo Alto, CA) equipped with a programmable pressure, cool on-column inlet, flame ionization detector (FID) fitted with a 30 m, 0.53-mm i.d., 0.5 μm df XTI-5 Integra-Guard capillary column (Restek, Bellefonte, PA). The on-column inlet was operated in the constant flow mode set at 8.8 psi at the initial column oven temperature of 120 °C. The inlet was programmed to maintain the inlet temperature 3 °C above the column oven temperature. The helium carrier gas velocity was 20 cm/s at this temperature, and nitrogen was used as the FID makeup gas (35 mL/min). The oven was held at 120 °C for 2 min and then programmed at 10 °C/min to 310 °C and held for 10 min. The final pressure was 14.8 psi. Injections (1−5 μL) were made manually. Quantitation The on-column GC inlet makes negligible contributions to deviations and errors in quantitative analyses. Calibration only has to consider detector response and possible losses in the column. On-column injection of the mixture of the three phthalates in octanol at the concentrations 4, 20, and 100 mg/L gave chromatograms in which the relative peak areas in each chromatogram varied <5%. The total amount of each phthalate per injection ranged from 4 ng to 600 ng and the volume of octanol from 1 μL to 5 μL. Typical peak widths in minutes from injection of 5 μl of the 20 mg/L solution were 0.033 (DHP), 0.036 (DnOP), and 0.038 (DnDP). Four separate 1-L samples of water were spiked with 100 ng

each of DnOP and DnDP. The phthalates were extracted from the water samples using C18 disks. Acetonitrile was used to elute the phthalates from the disk. The recoveries of DnOP (96.8 ± 3%) and DnDP (102.2 ± 1.2%) were calculated using each alternately as an internal standard for calculating recovery of the other. The absolute recoveries of DnOP and DnDP, which ranged from 41 to 71 ng, were determined by comparison of their FID area response to DHP (100 ng) that was added after the nitrogen-gas blowdown. In the water solubility and octanol/water partition experiments the phthalate closest in volatility to the phthalate of interest was spiked into the water sample and served as the internal standard to determine the water concentration of the phthalate of interest. A method detection limit (LOD) was calculated using the SPE extracts of the 1-L presaturation samples that were collected as the first samples taken in the DnDP octanol/water partition experiments. The LOD (0.025 μg/L) was calculated as the quantity of DnDP to give a response of 3 times baseline noise at the retention time of DnDP.

GLP compliance

no no GLP lab

Test materials

Test material equivalent to submission substance identity

no

Details on test material

Purity: 99.4% (determined by GC/FT-IR/MS)

Analytical method

GC

Results and discussions

Partition coefficient

Type	Partition coefficient	Temp.	pH
log Pow	8.8	25 °C	7

Remarks on results including tables and figures

The log Pow was measured as 8.8 at 25 degrees C, but the pH at which it was measured was not included by the authors but estimated to be around 7.

Applicant's summary and conclusion

Conclusions

Log Kow (Pow) for di-n-decyl phthalate is 8.8 at 25 degrees C.

Executive summary

Log Kow (Pow) for di-n-decyl phthalate is 8.8 at 25 degrees C.

Dissemination Dossier
Water sol Endpoint.001

Administrative Data

Purpose flag key study

Study result type experimental result

Study period March 1999

Reliability 2 (reliable with restrictions)

Rationale for reliability The reliability is rated 2 because the test procedure followed a technically appropriate procedure to determine the water solubility of substances with very low water solubility, but did not follow GLP.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Study report; company data		1999							1999-07-16

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
equivalent or similar to	OECD Guideline 105 (Water Solubility)	no

Type of method

flask method OECD Guideline 105

GLP compliance

no No GLP lab

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Results and discussions

Water solubility

0.00017 mg/L

Temp. 21 °C

pH 7

Details on results

The test substance water solubility was 0.00017 mg/L with a standard deviation of 0.00002 mg/L. The test substance concentrations were corrected using the control (background) value of 0.0762 ug/L.

Remarks on results including tables and figures

Applicant's summary and conclusion

Interpretation of results

insoluble (< 0.1 mg/L) <0.001 mg/L at 21 deg C

Conclusions

Water solubility for di-isodecyl phthalate is 0.00017 mg/L at 21 degrees C.

Executive summary

Water solubility for di-isodecyl phthalate is 0.00017 mg/L at 21 degrees C.

Administrative Data

Purpose flag	supporting study		
Study result type	estimated by calculation	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is 2 because the data are calculated. The value was calculated based on the QSPR (quantitative structure-property relationship) three-solubility model, which was peer reviewed.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Cousins I and Mackay D	2000	Correlating the physical-chemical properties of phthalate esters using the 'three solubility' approach	Chemosphere 41: 1389-1399					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations

according to	other guideline: Mathematical model	not applicable

Type of method

other: litterature study

Principles of method if other than guideline

Physicochemical data for selected commercial phthalate esters from various sources including the public literature, manufacturing specifications, and handbook values were evaluated. Values were identified and presented in a phthalate ester environmental fate, peer reviewed publication. These data, including the values for water solubility, represent the definitive and currently accepted physicochemical database for selected phthalate esters including diisodecyl phthalate. Quantitative structure-property relationships, significant at the 99.9% level, were developed using the relevant phthalate ester data to estimate solubility in water, air, and octanol, where V = the Le Bas molar volume (cm3 mol-1). The Le Bas molar volume used for diisodecyl phthalate ester was 609.2 cm3 mol-1. Log CS(WL) = -0.012V + 5.8, n = 35 (solubility in water) r2 = 0.98, SE = 0.39 Log CS(AL) = -0.013V - 1.3, n = 15 (solubility in air) r2 = 0.87, SE = 0.33 Log CS(OL) = -0.016V + 3.4, n = 68 (solubility in octanol) r2 = 0.19, SE = 0.41 It was recommended by the authors that the above regressions be used for predicting the three solubilities for phthalate esters with alkyl chain lengths from 1 to 13 carbons.

GLP compliance

no Not applicable

Test materials

Test material equivalent to submission substance identity
yes

Results and discussions

Water solubility

0.0381 µg/L
Temp. 25 °C
pH 7

Details on results

0.0000381 mg/L at 25 °C

Remarks on results including tables and figures

Applicant's summary and conclusion

Interpretation of results

insoluble (< 0.1 mg/L) at 25 deg C

Conclusions

Product is insoluble in water at 25 deg C.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	Followed a standard guideline that is valid for the test.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2006							

Materials and methods

Type of method
plate method

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: Wilhelmy plate	no

Principles of method if other than guideline

A Wilhelmy plate is a thin plate that is used to measure equilibrium surface or interfacial tension at an air-liquid or liquid-liquid interface. In this method, the plate is oriented perpendicular to the interface, and the force exerted on it is measured. The Wilhelmy plate consists of a thin plate usually on the order of a few centimeters square. The plate is often made from glass or platinum which may be roughened to ensure complete wetting. The plate is cleaned thoroughly and attached to a scale or balance via a thin metal wire. The force on the plate due to wetting is measured via a tensiometer or microbalance and used to calculate the surface tension (σ) using the Wilhelmy equation: where l is the wetted length of the Wilhelmy plate and θ is the contact angle between the liquid phase and the plate. In practice the contact angle is rarely measured, instead either literature values are used, or complete wetting ($\theta = 0$) is assumed.

GLP compliance

no no GLP lab

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Results and discussions

Surface tension

30.9 mN/m
Temp. 20 °C
Concentration 100 vol%

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions
Surface tension for di-isodecyl phthalate is 30.9 mN/m at 20 degrees C.

Executive summary

Surface tension for di-isodecyl phthalate is 30.9 mN/m at 20 degrees C.

Dissemination Dossier
Flash Endpoint.001

Administrative Data

Purpose flag key study

Study result type experimental result

Study period Not applicable

Reliability 2 (reliable with restrictions)

Rationale for reliability Followed a standard test guideline that is valid for the endpoint.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2008							2008-09-02

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	ISO No., other: COC ASTM D 92	no

Type of method

open cup

GLP compliance

no no GLP lab

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Results and discussions

Flash point

244 °C

at 1013 hPa

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions

Flash point for di-isodecyl phthalate is 244 degrees C at 1013 hPa.

Executive summary

Flash point for di-isodecyl phthalate is 244 degrees C at 1013 hPa.

Dissemination Dossier

Auto flamm Endpoint.001

Administrative Data

Purpose flag key study

Study result type experimental result

Study period Not applicable

Reliability 2 (reliable with restrictions)

Rationale for reliability Followed a standard test guideline that is valid for the endpoint. certified laboratory.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2008							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: ASTM E 659	no data

GLP compliance

yes certified lab

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Results and discussions

Autoflammability / Self-ignition temperature

405 °C

at 1013 hPa

Applicant's summary and conclusion

Conclusions

The auto ignition temperature for di-isodecyl phthalate is 405 degrees C at 1013 hPa.

Executive summary

The auto ignition temperature for di-isodecyl phthalate is 405 degrees C at 1013 hPa.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	2008
Reliability	2 (reliable with restrictions)		
Rationale for reliability	Followed a standard test guideline that is valid for the endpoint. Certified laboratory.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		2008							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: Intertek method	

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentb56e.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-6aaea936-dd5c-47b9-9fdc-20d06b1e9cd8%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Principles of method if other than guideline

Test performed at atmospheric pressure using vertical flame propagation in a closed 2 litre capacity aluminium alloy vertical tube (100 mm diameter, 260 mm long) held within a temperature-controlled enclosure. Ignition by high tension spark gap mounted 10 mm above the base of the explosion tube.

GLP compliance

no internal method

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

Substance type: commercial product

Results and discussions

Solid/liquid: Ignition on contact with air
no

Gas: Lower explosion limit (%)

0.3

Gas: Upper explosion limit (%)

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentb56e.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-6aaea936-dd5c-47b9-9fdc-20d06b1e9cd8%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

1.6

Remarks on results including tables and figures

Results for lower and upper flammable limits (LFL & UFL)

Applicant's summary and conclusion

Conclusions

Di-isodecyl phthalate has a very low degree of flammability (flash point > 200°C). See also the European Risk Assessment report

Executive summary

Di-isodecyl phthalate has a very low degree of flammability (flash point > 200°C). See also the European Risk Assessment report.

Administrative Data

Purpose flag	key study		
Study result type	other: Company data	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	Recommended value from European Commission risk assessment for 1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich, CAS#: 68515-49-1, EINECS#: 271-091-4.and:di-"isodecyl" phthalate (DIDP), CAS#: 26761-40-0, EINECS#: 247-977-1.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		2003							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations

according to other guideline: EU Risk-Assessment Report Vol. 36 not applicable

Principles of method if other than guideline

Value recommended by European Commission risk assessment.

GLP compliance

no Not applicable

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

Substance type: commercial product

Results and discussions

Explosive under influence of flame
no

More sensitive to shock than m-dinitrobenzene

no

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument2c14.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-efa0cd92-88db-4dbd-9c6a-347d63717845%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

More sensitive to friction than m-dinitrobenzene

no

Explosive (not specified)

no value EU commission

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions
Di-isodecyl phthalate does not have explosion limits under standard conditions.

Executive summary

Di-isodecyl phthalate does not have explosion limits under standard conditions.

Dissemination Dossier
Oxid Endpoint.001

Administrative Data

Data waiving study technically not feasible

Materials and methods

Test materials

Test material equivalent to submission substance identity

yes

Administrative Data

Purpose flag	supporting study		
Study result type	other: Company data	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	Recommended value from European Commission risk assessment for 1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich, CAS#: 68515-49-1, EINECS#: 271-091-4.and:di-"isodecyl" phthalate (DIDP), CAS#: 26761-40-0, EINECS#: 247-977-1.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		2003							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations

according to other guideline: EU Risk-Assessment Report Vol. 36 not applicable

GLP compliance

no Not applicable

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

Substance type: commercial product

Results and discussions

Test result
other: Not oxidizing
other:
Remarks Not oxidizing

Remarks on results including tables and figures

Not oxidizing

Applicant's summary and conclusion

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentf078.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-3f9190e6-a5e1-49d6-9b1b-8b1f81911e26%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Conclusions

Di-isodecyl phthalate ester has no oxidizing properties.

Executive summary

Di-isodecyl phthalate ester has no oxidizing properties.

Dissemination Dossier

Stability organic Endpoint.001

Administrative Data

Purpose flag key study

Study result type experimental result

Study period 2009

Reliability 2 (reliable with restrictions)

Rationale for reliability Laboratory testing within laboratory without GLP certification.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2009							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
no guideline followed	other guideline: stability testing over time	

Principles of method if other than guideline

The substance is placed in contact with organic solvents (THF, Acetone, White Spirit) in a ratio 50/50 in a glass bottle under the light.
A GC light ends will be performed at regular times to compare it with the GC of a fresh sample.

GLP compliance

no No GLP lab

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Results and discussions

Test substance stable

yes

Degradation products

no

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions

Di-isodecyl phthalate is stable in organic solvents.

Executive summary

Di-isodecy phthalate is stable in organic solvents.

Dissemination Dossier
Dissociation Endpoint.001

Administrative Data

Data waiving study scientifically unjustified

Materials and methods

Test materials

Test material equivalent to submission substance identity
yes

Dissemination Dossier
Viscosity Endpoint.001

Administrative Data

Purpose flag key study
Study result type experimental result
Study period 2008
Reliability 2 (reliable with restrictions)
Rationale for reliability Company data

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2008							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: ASTM D445	no

Type of method

capillary method

GLP compliance

no No GLP lab

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Results and discussions

Viscosity

116 mPa s (dynamic)

Temp. 20 °C

Remarks

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions

Dynamic viscosity is 116 mPa.s at 20°C

Executive summary

Dynamic viscosity is 116 mPa.s at 20°C

Dissemination Dossier
Other Endpoint.001

Administrative Data

Purpose flag supporting study

Study result type experimental result

Study period 2008

Reliability 2 (reliable with restrictions)

Rationale for reliability Company data developed using a standard procedure for the endpoint.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2008							

Materials and methods

Endpoint investigated

other: Water content

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: ASTM E 1064	no

GLP compliance

no No certified lab

Test materials

Test material equivalent to submission substance identity

yes

Results and discussions

Results

Water content = 0.01% (wt.)

Applicant's summary and conclusion

Conclusions

Water content = 0.01% (wt.)

Executive summary

Water content = 0.01% (wt.)

Dissemination Dossier
Other Endpoint.002

Administrative Data

Purpose flag supporting study
Study result type experimental result
Study period Not applicable
Reliability 2 (reliable with restrictions)
Rationale for reliability Company data developed using a standard procedure for the endpoint.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2008							

Materials and methods

Endpoint investigated

other: Coefficient of thermal expansion

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: density measurements at different temperatures.	not applicable

Principles of method if other than guideline

Plz Physical Parameters - Coefficient of thermal expansion

GLP compliance

no No certified lab

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Results and discussions

Results

Coefficient of thermal expansion = 0.00076 (vol/vol/degree C)

Applicant's summary and conclusion

Conclusions

Di-isodecyl phthalate coefficient of thermal expansion is 0.00076 (vol/vol/degree C).

Executive summary

Di-isodecyl phthalate coefficient of thermal expansion is 0.00076 (vol/vol/degree C).

Dissemination Dossier

Other Endpoint.003

Administrative Data

Purpose flag supporting study

Study result type experimental result

Study period 2008

Reliability 2 (reliable with restrictions)

Rationale for reliability Company data developed using a standard procedure for the endpoint.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2008							

Materials and methods

Endpoint investigated

refractive index

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: ASTM D 1045	no

GLP compliance

no No certified lab

Test materials

Test material equivalent to submission substance identity

yes

Results and discussions

Results

Refractive index = 1.485 at 20°C

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions

Refractive index = 1.485 at 20°C

Executive summary

Refractive index = 1.485 at 20°C

Dissemination Dossier
Other Endpoint.004

Administrative Data

Purpose flag supporting study
Study result type experimental result
Study period 2008
Reliability 2 (reliable with restrictions)
Rationale for reliability Company data developed using a standard procedure for the endpoint.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2008							

Materials and methods

Endpoint investigated
other: Acidity mg KOH/g

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: ASTM D1045	no

GLP compliance

no no certified lab

Test materials

Test material equivalent to submission substance identity
yes

Results and discussions

Results
Acidity = 0.05 mg KOH/g

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions

Acidity = 0.05 mg KOH/g

Executive summary

Acidity = 0.05 mg KOH/g

Administrative Data

Purpose flag	key study		
Study result type	estimated by calculation	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is 2 because the data are calculated.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Computer model	U.S. Environmental Protection Agency (USEPA)	2000	EPI SuiteTM, Estimation Program Interface Suite, v3.12	USEPA, Washington, DC, USA					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
no guideline followed	other guideline: Computer model	

Principles of method if other than guideline

Calculated values using AOPWIN version 1.91, a subroutine of the computer program EPI SuiteTM version 3.12. Indirect photodegradation, or atmospheric oxidation potential, is based on the structure-activity relationship methods developed by R. Atkinson under the following conditions: Temperature: 25°C Sensitizer: OH- radical Concentration of Sensitizer: 1.5E6 OH-radicals/cm3

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

SMILES notation used: O=C(c1ccccc1C(=O)OCCCCCCCCC(C)C)OCCCCCCCCC(C)C

Study design

Light source
sunlight

Results and discussions

Dissipation half-life of parent compound

DT50	4.9 h

Test condition Estimated value

Transformation products

not measured

Remarks on results including tables and figures

Rate constant: 0.0000000000262 cm3/molecule*sec Degradation: 50% after 4.9 hours (0.41 days)

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Rate constant: 0.0000000000262 cm3/molecule*sec Degradation: 50% after 4.9 hours (0.41 days)

Executive summary

Indirect photochemical degradation of DIDP as mediated byOH-attack is estimated to have ahalf-life of 0.41 days or 4.9 hours based on a 12-hour sunlight day, a rate of 2.62E-11 cm3/molecule*sec, and an average OH- concentration of 1.5E6 OH-/cm3. A 12-hour day half-life value normalizes degradation to a standard day light period during which hydroxyl radicals needed for photolysis are generated in the atmosphere. AlthoughDIDP has the potential to degrade rapidly byOH-attack,multimedia distribution modeling indicates DIDP is predicted to partition negligibly (0.1%) to the air compartmentbecause it has a low vapor pressure (0.000051 Pa). Although DIDP has a relatively short atmospheric oxidation half-life (4.9 hours),this process is unlikely to contribute significantly to the loss of DIDP from the environment.

Administrative Data

Purpose flag	key study		
Study result type	estimated by calculation	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is 2 because the data are calculated.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Computer model	U.S. Environmental Protection Agency (USEPA)	2000	EPI SuiteTM, Estimation Program Interface Suite, v3.12	USEPA, Washington, DC, USA					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
no guideline followed	other guideline: Computer model	

Principles of method if other than guideline

Hydrolysis rate calculated by HYDROWIN version 1.67 based on work for EPA by T. Mill et al., a subroutine of the computer program EPI SuiteTM version 3.12.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
yes

Radiolabelling

no

Details on test material

SMILES Notation used: O=C(c1ccccc1C(=O)OCCCCCCCCC(C)C)OCCCCCCCCC(C)C

Results and discussion

Transformation products
not measured

Dissipation half-life of parent compound

pH	Temp.	Hydrolysis rate constant	Half-life	St. dev.	Type	Remarks (e.g. regression equation, r^2, DT90)
7	25 °C		3.4 yr			
8	25 °C		125.2 d			

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Hydrolysis will not significantly contribute to the removal of DIDP from the environment. The DIDP hydrolysis half-life (25 degrees C) is calculated as: pH 7 = 3.4 years pH 8 = 125.2 days

Executive summary

Results from the EQC (Equilibrium Criterion) Levels I and III distribution models (Mackay, 2001) show that because of its low water solubility, DIDP is not expected to partition to the water compartment (see Section 4.2.2). However, abiotic degradation of any trace amounts of DIDP which may be present in aquatic environments is unlikely to occur at a significant rate based on modeled data. The HYDROWIN model, a subroutine within the USEPA (2000) computer program, estimates a hydrolysis half-life for DIDP of 3.4 years at pH 7 (25°C) and 125.2 days at pH 8 (25°C).

Administrative Data

Purpose flag	key study		
Study result type	other: Technical discussion	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability is rated 2 because the information presents a technical summary rather than the results of a specific study.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Zepp R and Cline D	1977	Rates of direct photolysis in the aqueous environment	Environ. Sci. Technol. 11: 359-366					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
no guideline followed	other guideline: Technical discussion	

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
yes

Radiolabelling

no

Results and discussions

Transformation products
not measured

Applicant's summary and conclusion

Validity criteria fulfilled
yes

Conclusions

DIDP does not absorb light within a range of 290 to 750 nm. Therefore, direct photolysis will not contribute to the degradation of DIDP in the aquatic environment because it does not absorb light at wavelengths >290 nm, i.e., in the range that contribute to this process.

Executive summary

Direct photochemical degradation in water occurs through the absorbance of solar radiation by a chemical substance. If the absorbed energy is high enough, then, in the resultant excited state, the chemical may undergo a transformation. A prerequisite for direct photodegradation is the ability of one or more bonds within a molecule to absorb ultraviolet (UV)/visible light in the 290 to 750 nm range. Light wavelengths longer than 750 nm do not contain sufficient energy to break chemical bonds, and wavelengths below 290 nm are shielded from the earth by the stratospheric ozone layer. An approach to assessing the potential for DIDP to undergo direct photochemical degradation is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by DIDP molecules. DIDP does not absorb light within a range of 290 to 750 nm. Therefore, direct photolysis will not contribute to the degradation of DIDP in the aquatic environment because it does not absorb light at wavelengths >290 nm, i.e., in the range that contribute to this process.

Administrative Data

Purpose flag	key study		
Study result type	other: Technical discussion	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability is rated 2 because the information presents a technical summary rather than the results of a specific study.		

Materials and methods

Test materials

Test material equivalent to submission substance identity
yes

Applicant's summary and conclusion

Validity criteria fulfilled
yes

Conclusions

Di-isodecyl phthalate ester (DIDP; CAS #68515-49-1) does not absorb light within a range of 290 to 750 nm. Therefore, direct photolysis will not contribute to the degradation of DIDP in the terrestrial environment because it does not absorb light at wavelengths >290 nm, i.e., in the range that contribute to this process.

Executive summary

Direct photochemical degradation in soil occurs through the absorbance of solar radiation by a chemical substance. If the absorbed energy is high enough, then, in the resultant excited state, the chemical may undergo a transformation. A prerequisite for direct photodegradation is the ability of one or more bonds within a molecule to absorb ultraviolet (UV)/visible light in the 290 to 750 nm range. Light wavelengths longer than 750 nm do not contain sufficient energy to break chemical bonds, and wavelengths below 290 nm are shielded from the earth by the stratospheric ozone layer. An approach to assessing the potential for di-isodecyl phthalate ester (DIDP; CAS #68515-49-1)to undergo direct photochemical degradation is to assume that degradation will occur in proportion to the amount of light wavelengths >290 nm absorbed by DIDP molecules. DIDP does not absorb light within a range of 290 to 750 nm. Therefore, direct photolysis will not contribute to the degradation of DIDP in the terrestrial environment because it does not absorb light at wavelengths >290 nm, i.e., in the range that contribute to this process.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	March 2009
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is a 2 because the study followed an OECD standard guideline, which describes a procedure designed to evaluate this endpoint, and the results were reviewed for reliability and assessed as valid. However, the study was not conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Study report; company data		2009							2009-05-29

Materials and methods

Test type

ready biodegradability

Test guideline

Qualifier	Guideline	Deviations
according to	OECD Guideline 301 F (Ready Biodegradability: Manometric Respirometry Test)	no

GLP compliance

no Study was not conducted under GLP, however, a standard OECD guideline was used with no deviations from the protocol. The laboratory has auditable recieving records, quality assurance coordination, and all data are documented in the raw data set.

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

Substance type: technical product

Study design

Oxygen conditions
aerobic

Inoculum or test system

activated sludge, domestic, non-adapted

Details on inoculum

Fresh activated sludge was used as the inoculum. The activated sludge was obtained from the Somerset Raritan Valley Sewage Authority, Bridgewater, New Jersey, USA. This treatment facility was selected because it deals predominantly with domestic sewage as specified in the guideline. There were no known contaminants in the fresh activated sludge believed to be present at levels high enough to interfere with this study. Fresh activated sludge was obtained on day -1 of the test. Duplicate 10 mL aliquots of the activated sludge were filtered through pre weighed Whatman 934-AH filter pads in a Buchner funnel and vacuum flask set up. The filter pads were placed in an aluminum pan and dried in an oven for sixty minutes at 102 degrees C. After cooling the filters were reweighed and the mean total suspended solids concentration was determined to be 4.73 g/L. The activated sludge was then homogenized in a blender for two minutes at low speed. The homogenated sample was allowed to settle for approximately ninety-five minutes, after which the supernatant was decanted (avoiding carry-over of sludge solids). An aliquot of the supernatant was used to determine microbial activity. The microbial activity was determined using an Easicult®-TTC dip slide. The agar stick was removed from the culturing tube and the agar dipped into the supernatant aliquot. Excess supernatant was blotted off with a clean paper towel, and the agar stick was then placed back into the culture tube. The whole unit was placed into a dark environmental chamber for 48 hours at 20 +/- 1 degrees C monitored by the Watchdog V5 monitoring system. Based on comparison of the density of colonies growing on the agar with the model density chart provided by the supplier, the microbial activity was determined to be 10E5 CFU/mL. The remaining decanted sludge supernatant was used for final preparation of the test medium on day -1.

Duration of test (contact time)

28 d

Initial test substance concentration

Initial conc.	Based on
ca. 50.3 mg/L	test mat.

Parameter followed for biodegradation estimation

Parameter followed for biodegradation estimation
O2 consumption

Details on study design

Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test substance as calculated using results of an elemental analysis of the test substance. The empirical formula and the theoretical oxygen demand (ThOD) of the test substance was calculated from elemental analysis data (assuming 100 gram test substance). Sodium benzoate ThOD was calculated using the empirical formula and was determined to be 1.67 mg O2/mg sodium benzoate. The ThOD calculation of the test and positive control substance was based on Annex IV of OECD 301F guideline. The total suspended solids (TSS) of the activated sludge was 4.73 g/L of and the microbial count was 105 CFU/mL. The sludge supernatant was added at a 1% loading volume of to test medium. Test medium consisted of glass distilled water and mineral salts (phosphate buffer, ferric chloride, magnesium sulfate, calcium chloride). One liter of test medium and activated sludge, which was aerated for 24 hours with carbon dioxide free air, was added to each one liter respirometer flask. Test vessels were 1L glass flasks placed in a water bath and electronically monitored for oxygen consumption. The test substance, positive control, and blanks were tested in triplicate. Test substance (1,2-benzenedicarboxylic acid, diiso-C10 alkyl esters) concentration was 50.3 mg/L. The positive control (sodium benzoate) concentration was 53.21 mg/L. Test temperature was 22 +/- 1 Deg C. All test vessels were stirred constantly for 28 days using magnetic stir bars.

Reference substance

benzoic acid, sodium salt

Results and discussions

Preliminary study

A preliminary study was not conducted.

Test performance

No deviations from the protocol occurred that affected the integrity of the study data.

% Degradation of test substance

%Degr.	St. dev.	Parameter	Sampling time	Remarks
5.4	1.9	O2 consumption	10 d	

11.6	1.6	O2 consumption	11 d
49.7	2.4	O2 consumption	16 d
60.5	1.8	O2 consumption	19 d
74	3.9	O2 consumption	28 d

Details on results

10% biodegradation was achieved between sampling days 10 and 11, 50% biodegradation occurred on day 16, and >60% biodegradation between sampling days 18 and 19. On day 28, 74% biodegradation of the test substance was observed. By day 4, >60% biodegradation of positive control was observed, which meets the guideline requirement. Oxygen uptake in the blanks was within guideline limits. No excursions from the protocol were noted.

BOD5 / COD results

Results with reference substance

Positive reference substance (Na Benzoate) biodegradation data: Day % Degradation* 1 24.1 2 56.6 4 58.8 5 65.0 * mean of triplicate test systems

Overall remarks

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Interpretation of results

readily biodegradable

Conclusions

The test substance biodegraded to a high extent, 74% , met the 10-day window criterium, and is considered readily biodegradable.

Executive summary

The test substance biodegraded to a high extent, 74%, met the 10 -day window criterium, and is considered readily biodegradable.

Administrative Data

Purpose flag	supporting study		
Study result type	read-across from supporting substance (structural analogue or surrogate)	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is a 2 because the study followed a test procedure that was similar to a current standard guideline, which describes a procedure designed to evaluate this endpoint, and the results were reviewed for reliability and assessed as valid.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	O'Grady D, Howard P and Werner A	1985	Activated sludge biodegradation of 12 commercial phthalate esters	Appl. Environ. Microbiol. 49(2): 443-445					
secondary source		1984							1984-12-15

Materials and methods

Test type
other: Simulation study

Test guideline

Qualifier	Guideline	Deviations
equivalent or similar to	EPA OPPTS 835.5045 (Modified SCAS Test for Insoluble and Volatile Chemicals)	

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
no

Details on test material

Diisodecyl phthalate ester with unknown CAS number. Substance type: commercial product Analytical purity: unknown

Study design

Oxygen conditions
aerobic

Inoculum or test system

activated sludge, adapted

Details on inoculum

The acclimation period was 3 weeks.

Initial test substance concentration

Initial conc.	Based on
1 mg/L	test mat.

Parameter followed for biodegradation estimation

Parameter followed for biodegradation estimation
Test mat. analysis

Details on study design

Daily operation of the semi-continuous activated sludge (SCAS) unit was conducted according to the Soap and Detergent Association procedure except the total volume was 2 liters instead of 1.5 liters. After the sludge was acclimated to the synthetic sewage feed and the dissolved organic carbon removal efficiency remained at >70%, the test substance feeding began. Once feeding began, a draw-and-fill procedure was started and maintained for 3 weeks. The test substance was added to the test system in an acetone stock solution to provide a concentration of 1 mg/L during week 1 and 3 mg/L during weeks 2 and 3. 24-hour test substance biodegradation was determined once a week during the 3-week draw-and-fill period, in the middle of each week by analyzing a 50 ml aliquot for each unit after feeding of test substance, synthetic sludge, and followed by a 23-hour aeration period.

Reference substance

ethylene glycol

Results and discussions

% Degradation of test substance

%Degr.	St. dev.	Parameter	Sampling time	Remarks
68	4.9	Test mat. analysis	24 h	

BOD5 / COD results

Results with reference substance

No information was provided on the performance of the reference substance.

Overall remarks

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Interpretation of results

other: Rapidly biodegradable under acclimated conditions.

Conclusions

Di-isodecyl phthalate ester can biodegrade rapidly under wastewater treatment simulation conditions, based on a 68% loss of test substance after 24 hours in a semi-continuous activated sludge test system.

Executive summary

Di-isodecyl phthalate ester can biodegrade rapidly under wastewater treatment simulation conditions, based on a 68% loss of test substance after 24 hours in a semi-continuous activated sludge test system.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability rating is a 1 because the study followed an OECD standard guideline, which describes a procedure designed to evaluate this endpoint. The study was conducted under GLP and the results were reviewed for reliability and assessed as valid.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		2003							

Materials and methods

Test type

ready biodegradability

Test guideline

Qualifier	Guideline	Deviations
according to	OECD Guideline 301 B (Ready Biodegradability: CO2 Evolution Test)	

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity
no

Details on test material

The test substance was an alky mono ester of phthalic acid. The mono ester alkyl group distribution of the test substance was approximately a 1:1 ratio of C8 and C10. The test substance was clear and purity ranged between 92 and 94% with the remaining impurities composed of the diester, and the phthalic acid and C8 and C10 alkyl alcohols used in the esterification process.

Study design

Oxygen conditions
aerobic

Inoculum or test system

activated sludge, domestic, non-adapted

Duration of test (contact time)

28 d

Parameter followed for biodegradation estimation

Parameter followed for biodegradation estimation
CO2 evolution

Reference substance

other: no data

Results and discussions

% Degradation of test substance

%Degr.	St. dev.	Parameter	Sampling time	Remarks
ca. 90		CO2 evolution	28 d	

Applicant's summary and conclusion

Validity criteria fulfilled
yes
Interpretation of results: readily biodegradable

Conclusions

The test substance was readily biodegradable.

Executive summary

Mono-n-octyl/n-decyl-phthalate was shown to biodegrade to approximately 90% after 28 days and the results met the ready biodegradable criteria.

Administrative Data

Purpose flag	supporting study		
Study result type	read-across from supporting substance (structural analogue or surrogate)	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is a 2 because the study followed a standard guideline, which describes a procedure designed to evaluate this endpoint and the results were reviewed for reliability and assessed as valid, but the study did not follow GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: publication; handbook	Chemicals Inspection & Testing Institute	1992	Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan	Japan Chemical Industry Ecology-Toxicology & Information Center, Japan					

Materials and methods

Test type
inherent biodegradability

Test guideline

Qualifier	Guideline	Deviations
according to	OECD Guideline 302 C (Inherent Biodegradability: Modified MITI Test (II))	

GLP compliance

no data

Test materials

Test material equivalent to submission substance identity
no

Details on test material

Substance type: Commercial substance may have been tested. Analytical purity: unknown

Study design

Oxygen conditions
aerobic

Inoculum or test system

activated sludge, non-adapted

Duration of test (contact time)

21 d

Initial test substance concentration

Initial conc.	Based on
100 mg/L	test mat.

Results and discussions

% Degradation of test substance

%Degr.	St. dev.	Parameter	Sampling time	Remarks
42		CO2 evolution	21 d	

BOD5 / COD results

Overall remarks

The biodegradation curve was continuing to increase when the study was terminated on day 21.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Interpretation of results

other: DIDP is rapidly biodegradable under non acclimated conditions.

Conclusions

DIDP is rapidly biodegradable under non acclimated conditions.

Executive summary

DIDP is rapidly biodegradable under non acclimated conditions.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability rating is a 1 because the study followed a standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study followed GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1983							
publication	Sugatt R, O'Grady D, Banerjee S, Howard P and Gledhill W	1984	Shake flask biodegradation of 14 commercial phthalate esters	Appl. Environ. Microbiol. 47(4):601-606					

Materials and methods

Test type
other: Simulation

Test guideline

Qualifier	Guideline	Deviations
according to	EPA OPPTS 835.3170 (Shake Flask Die-away Test)	

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

Substance type: technical product

Study design

Oxygen conditions
aerobic

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument46f8.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-bf2a3a07-c6b4-4dea-a256-e0e5b6a5da33%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Inoculum or test system

activated sludge, adapted

Initial test substance concentration

Initial conc.	Based on
20 mg/L	test mat.

Results and discussions

% Degradation of test substance

%Degr.	St. dev.	Parameter	Sampling time	Remarks
5		CO2 evolution	7 d	
17		CO2 evolution	9 d	
39		CO2 evolution	14 d	
53		CO2 evolution	21 d	
56		CO2 evolution	28 d	

Details on results

Day % Biodegradation 3 1 7 5 9 17 14 39 21 53 28 56

BOD5 / COD results

Overall remarks

Primary degradation was also determined based on measured disappearance of test substance. The result was > 99% after 28 days.

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument46f8.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-bf2a3a07-c6b4-4dea-a256-e0e5b6a5da33%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Applicant's summary and conclusion

Validity criteria fulfilled
yes

Interpretation of results

other: Rapidly biodegradable under acclimated conditions.

Conclusions

DIDP is rapidly biodegradable under acclimated conditions.

Executive summary

DIDP is rapidly biodegradable under acclimated conditions.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	January 1995
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is a 2 because the study followed an OECD standard guideline, which describes a procedure designed to evaluate this endpoint, and the results were reviewed for reliability and assessed as valid. However, the study was not conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1995							1995-05-19

Materials and methods

Test type

ready biodegradability

Test guideline

Qualifier	Guideline	Deviations
according to	OECD Guideline 301 F (Ready Biodegradability: Manometric Respirometry Test)	no

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

Substance type: technical product

Study design

Oxygen conditions
aerobic

Inoculum or test system

activated sludge, domestic, non-adapted

Details on inoculum

Fresh activated sludge was used as the inoculum. The activated sludge was obtained from the Clinton Sanitary Wastewater Treatment

Plant, Annandale, New Jersey. This treatment facility was selected because it deals predominantly with domestic sewage as specified in the guideline. There were no known contaminants in the fresh activated sludge believed to be present at levels high enough to interfere with this study. Fresh activated sludge was obtained on day -1 of the test. Duplicate 10 mL aliquots of the activated sludge were filtered through pre weighed Whatman 934-AH filter pads in a Buchner funnel and vacuum flask set up. The filter pads were placed in an aluminum pan and dried in an oven for ninety minutes at 103 degree C. After cooling the filters were reweighed and the mean total suspended solids concentration was determined to be 3.61 g/L. The activated sludge was then homogenized in a blender for two minutes at low speed. The homogenated sample was allowed to settle for sixty minutes, after which the supernatant was decanted (avoiding carry-over of sludge solids). An aliquot of the supernatant was used to determine microbial activity. The microbial activity was determined using an Easicult®-TTC dip slide. The agar stick was removed from the culturing tube and the agar dipped into the supernatant aliquot. Excess supernatant was blotted off with a clean paper towel, and the agar stick was then placed back into the culture tube. The whole unit was placed into a dark environmental chamber for 48 hours at 20 +/- 1 degree C monitored by Aquatic Toxicology Data Systems (ATDS). Based on comparison of the density of colonies growing on the agar with the model density chart provided by the supplier, the microbial activity was determined to be 10E5 CFU/mL. The remaining decanted sludge supernatant was used for final preparation of the test medium on day -1.

Duration of test (contact time)

28 d

Initial test substance concentration

Initial conc.	Based on
ca. 50 mg/L	test mat.

Parameter followed for biodegradation estimation

Parameter followed for biodegradation estimation
O2 consumption

Details on study design

Biodegradation was based on oxygen consumption and the theoretical oxygen demand of the test substance as calculated using results of an elemental analysis of the test substance. The empirical formula and the theoretical oxygen demand (ThOD) of the test substance were calculated from elemental analysis data (assuming 100 gram test substance). Sodium benzoate ThOD was calculated using the empirical formula and was determined to be 1.67 mg O2/mg sodium benzoate. The ThOD calculation of the test and positive control substance was based on Annex IV of OECD 301F1 guideline. Activated sludge and test medium were combined prior to test substance addition. Test medium consisted of glass distilled water and mineral salts (phosphate buffer, ferric chloride, magnesium sulfate, calcium chloride). Test vessels were 1L glass flasks placed in a water bath and electronically monitored for oxygen consumption. Test substance was tested in triplicate, controls and blanks were tested in duplicate. Test substance (1,2-benzenedicarboxylic acid, diiso-C10 alkyl esters) concentration was approximately 50 mg/L. The positive control (sodium benzoate) concentration was approximately 50 mg/L. Test temperature was 22 +/- 1 Deg C. All test vessels were stirred constantly for 28 days using magnetic stir bars.

Reference substance

benzoic acid, sodium salt

Results and discussions

% Degradation of test substance

%Degr.	St. dev.	Parameter	Sampling time	Remarks
9.9		O2 consumption	12 d	
19.2		O2 consumption	13 d	
57.9		O2 consumption	22 d	
60		O2 consumption	23 d	
67.1		O2 consumption	28 d	

Details on results

10% biodegradation was achieved between sampling days 12 and 13, 50% biodegradation between sampling days 19 and 20, and >60% biodegradation between sampling days 22 and 23. On day 28, 67% degradation of the test substance was observed. By day 14,

>60% biodegradation of positive control was observed, which meets the guideline requirement. Oxygen uptake in the blanks was within guideline limits. No excursions from the protocol were noted. Test Substance: Day % Degradation* 7 0, 0, 0 12 4, 14, 11 13 11, 26, 20 14 20, 36, 27 19 55, 41, 65 22 46, 73, 55 23 48, 76, 57 28 57, 81, 64 Positive Reference Substance (Na Benzoate): Day % Degradation* 1 32, 36 2 56, 66 5 76, 89, 82 * replicate data

BOD5 / COD results

Overall remarks

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Interpretation of results

readily biodegradable, but failing 10-day window

Conclusions

The test substance biodegraded to a high extent, 67% , but did not meet the 10-day window requirement to be considered readily biodegradable.

Executive summary

The test substance biodegraded to a high extent, 67% , but did not meet the 10-day window requirement to be considered readily biodegradable.

Administrative Data

Purpose flag	supporting study		
Study result type	read-across from supporting substance (structural analogue or surrogate)	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is a 2 because the study followed a test procedure that was similar to a current standard guideline, which describes a procedure designed to evaluate this endpoint, and the results were reviewed for reliability and assessed as valid.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	O'Grady D, Howard P and Werner A	1985	Activated sludge biodegradation of 12 commercial phthalate esters	Appl. Environ. Microbiol. 49(2): 443-445					
secondary source		1984							1984-12-15

Materials and methods

Test type
other: 19-day die-away test

Test guideline

Qualifier	Guideline	Deviations
equivalent or similar to	EPA OPPTS 835.3100 (Aerobic Aquatic Biodegradation)	

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
no

Details on test material

Diisodecyl phthalate ester with unknown CAS number. Substance type: commercial product Analytical purity: unknown

Study design

Oxygen conditions
aerobic

Inoculum or test system

activated sludge, adapted

Details on inoculum

The inoculum was developed from a sewage sludge sample that was used in a semi-continuous activated sludge (SCAS) test system conducted for 3 weeks. After the SCAS test was completed, the suspended solids from the SCAS units were adjusted to 500 mg/L and added to the test units used in the 19-day die-away test.

Duration of test (contact time)

19 d

Initial test substance concentration

Initial conc.	Based on
3 mg/L	test mat.

Parameter followed for biodegradation estimation

Parameter followed for biodegradation estimation
Test mat. analysis

Results and discussions

% Degradation of test substance

%Degr.	St. dev.	Parameter	Sampling time	Remarks
>= 90		Test mat. analysis	9 d	

Details on results

Two trials were conducted. The test substance biodegraded greater than or equal to 90% after 9 days in each trial.

BOD5 / COD results

Results with reference substance
A reference substance was not tested because the study used an acclimated inoculum.

Overall remarks

Applicant's summary and conclusion

Validity criteria fulfilled
yes

Interpretation of results

other: Rapidly biodegradable under acclimated conditions.

Conclusions

Di-isodecyl phthalate ester can be rapidly biodegraded after acclimation.

Executive summary

Di-isodecyl phthalate ester can be rapidly biodegraded after acclimation, exhibiting >/=90% biodegradation after 9 days.

Dissemination Dossier
Biodeg water screen Endpoint.008

Administrative Data

Purpose flag supporting study

Study result type read-across from supporting substance (structural analogue or surrogate)

Study period 1983

Reliability 2 (reliable with restrictions)

Rationale for reliability The reliability rating is a 2 because the study followed a standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, but the study did not follow GLP and the inoculum was adapted.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1984							

Materials and methods

Test type

inherent biodegradability

Test guideline

Qualifier	Guideline	Deviations
equivalent or similar to	OECD Guideline 301 C (Ready Biodegradability: Modified MITI Test (I))	

Principles of method if other than guideline

The OECD Guideline 301C was amended to include a determination of biodegradability by measuring carbon dioxide (14CO2) evolution using an acclimated inoculum.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

no

Details on test material

Di-isodecyl Phthalate mixed with a small quantity of the equivalent 14C carbonyl group radiolabelled substance in acetone solution. The acetone was removed by evaporation.
Analytical purity: unknown

Study design

Oxygen conditions

aerobic

Inoculum or test system

activated sludge, adapted

Initial test substance concentration

Initial conc.	Based on
100 mg/L	test mat.

Results and discussions

% Degradation of test substance

%Degr.	St. dev.	Parameter	Sampling time	Remarks
86		CO2 evolution	28 d	

BOD5 / COD results

Overall remarks

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Interpretation of results

other: DIDP is rapidly biodegradable under acclimated conditions.

Conclusions

DIDP is rapidly biodegradable under acclimated conditions.

Executive summary

DIDP is rapidly biodegradable under acclimated conditions.

Dissemination Dossier
Biodeg water sim Endpoint.001

Administrative Data

Purpose flag supporting study

Study result type experimental result

Study period Not applicable

Reliability 2 (reliable with restrictions)

Rationale for reliability Value cited in the European Commission risk assessment for 1,2-Benzenedicarboxylic acid, di-C8-11-branched alkyl esters, C10-rich, CAS#: 68515-49-1, EINECS#: 271-091-4 and di-"Isodecyl" phthalate (DIDP), CAS#: 26761-40-0, EINECS#: 247-977-1.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: PhD dissertation	Furtmann K	1993	Phthalates in the aquatic environment	Regional Water and Wastewater Authority, Nordrhein-Westfalen, Germany					
publication		2003							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
no guideline followed	other guideline: The test guideline generally followed an aerobic sewage treatability procedure.	not applicable

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

no

Radiolabelling

no

Study design

Oxygen conditions

aerobic

Inoculum or test system

other: Treated wastewater

Duration of test (contact time)

7 d

Initial test substance concentration

Initial conc.	Based on
7.8 µg/L	test mat.

Results and discussions

% Degradation of test substance

%Degr.	St. dev.	Parameter	Sampling time	Remarks
82		Test mat. analysis	7 d	

Half-life of parent compound / 50% disappearance time (DT50)

Compartment	Half-life	St. dev.	Type	Remarks (e.g. regr. equ., r^2, DT90)
other: Wastewater	ca. 1 d		(pseudo-)first order (= DT50)	

Transformation products

not measured

Evaporation of parent compound

not measured

Volatile metabolites

not measured

Residues

not measured

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-n decyl phthalate degraded 82% after 7 days incubation with wastewater at 25 degrees C.

Executive summary

Di-n-decyl phthalate degraded 82% after 7 days incubation with wastewater at 25 degrees C.

Administrative Data

Purpose flag	key study		
Study result type	read-across from supporting substance (structural analogue or surrogate)	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is a 2 because, although the data were developed using a non standard test procedure, the information is well documented and the testing followed accepted scientific procedures.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Otton V, Sura S, Blair J, Ikonomou M and Gobas F	2008	Biodegradation of mono-alkyl phthalate esters in natural sediments	Chemosphere					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations

no guideline followed	other guideline: Followed sound scientific testing principles for determining biodegradability in sediment.

Principles of method if other than guideline

Aerobic biodegradation in natural sediment as determined in closed glass test systems and based on analytical measurements of the parent test substance over time.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
no

Radiolabelling

no

Details on test material

The test substance was synthesized by Chemsyn Science Laboratories (Lenexa, KS) and had 97–99% purity as esters as determined by HPLC. The test subsance was produced from an isomeric mixture of isodecyl alcohols.

Study design

Oxygen conditions
aerobic

Inoculum or test system

natural sediment

Details on source and properties of sediment

Surface sediment samples were collected using a petit ponar grab sampler from two locations in False Creek (called 'North Central' and 'Marina South' in Mackintosh et al., 2004), an urbanized marine inlet in Vancouver. The top layer (0.5–1.0 cm) of each grab sample was transferred to cleaned 250 ml glass jars with foil-lined lids. The filled jars were immediately placed on ice for transport to the laboratory. Sediments were either used immediately or were stored at −20 °C in the dark until use. The pH of the sediments was measured in the field using pHydrion pH-indicator strips. Frozen sediments were thawed at room temperature and any pebbles or vegetative material were removed. Autoclaved sediments were used as controls to measure any degradation or loss of chemical not due to microbial degradation. They were prepared by autoclaving three consecutive times at 120 °C for 20 min, followed by 24 h cooling periods at 22 ± 1 °C. The total organic carbon content and moisture content of the sediments were measured at the Institute of Ocean Sciences (Sidney, BC) using a Control Equipment Corporation 440 Elemental Analyzer according to Van Iperen and Helder, 1985 J. Estimates of the number of bacteria culturable on agar under aerobic conditions were obtained using EasiCult® dip-slides (Orion Diagnostica, Espoo, Finland). The agar dipslides were inoculated by dipping into a 1:2000 dilution of sediment with sterilized milli-Q water. The organic carbon content of the sediment was 2.90 ± 0.17% (mean ± SD, n = 4) for the marine sediments from False Creek. The pH of the sediment was 6 ± 0.2. The number of culturable bacteria was high in marine sediment samples (i.e. >108 g−1 sediment, wet weight). The agar slides inoculated with autoclaved marine or freshwater sediment were blank, verifying the effectiveness of the sterilization procedure.

Details on inoculum

The inoculum consisted of the natural microorganisms found in the sediment samples. No outside source of bacteria were added.

Duration of test (contact time)

ca. 72 h

Initial test substance concentration

Initial conc.	Based on
ca. 2 µg/g sediment (wet weight)	test mat.

Details on study design

Sediment samples (4.0 g wet weight) were transferred to solvent-rinsed 20 ml glass scintillation vials. Autoclaved sediment samples were used as a control to determine loss of the mono phthalate ester (MPE) by processes other than biotic. A small volume (8 µl) of a 1 g l−1 MPE solution in acetonitrile was added to the sediment slurry and gently mixed on a vortex mixer. Sediments were exposed to the MPE in the dark. The final concentration of the MPE was approximately 2 µg g−1 sediment (wet weight). The incubation vials were capped with foil-lined caps and wrapped in foil to eliminate the potential of photolysis. The proportion of headspace air-to-sediment at the beginning of the incubation was 4.5:1, based on the volume of sediment in the scintillation vial. The spiked sediments were incubated in triplicate at 22 ± 1 °C and at 5 ± 1 °C. At various time points, 0.5 g subsamples were removed and transferred to clean glass scintillation vials for analysis. A 10 ml volume of acetonitrile was added to 0.5 g subsamples to stop biodegradation. The sediments were not agitated or actively oxygenated during the incubations, except when removing subsamples. Incubation experiments were repeated up to nine times.

Results and discussions

Test performance

After an initial lag phase, MiDP concentration followed an exponential decay pattern during incubation, while no significant change in concentration was observed in treatments with autoclaved sediments. This indicates that microbial activity was responsible for the observed degradation of the MIDP. The lag phase varied from 22 to 30 h among individual incubations. After the initial lag phase, MiDP concentration in sediments dropped quickly over time. First-order biodegradation half-life for MiDP was 25 ± 6 h based on 2 replicates.

% Degradation of test substance

%Degr.	St. dev.	Parameter	Sampling time	Remarks
50		Test mat. analysis	25 h	

Half-life of parent compound / 50% disappearance time (DT50)

Compartment	Half-life	St. dev.	Type	Remarks (e.g. regr. equ., r^2, DT90)
other: marine sediment	25 h	6	(pseudo-)first order (= DT50)	

Other kinetic parameters

first order rate constant The kinetics of biodegradation were determined from linear regression of the slope (after the lag phase) on a plot of the logarithm of concentration in subsamples of the sediment incubation versus time.

Transformation products

yes

Identity of degradation products

No.	Identifier	Identity
#1	other: monoisodecyl phthalate	monoisodecyl phthalate
#2	other: isodecyl alcohol	isodecyl alcohol

Details on transformation products

See Executive Summary below.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

The mono ester of di-isodecyl phthalate (mono isodecyl phthalate) exhibited a relatively rapid rate of biodegradation in a natural aerobic marine sediment, with a measured half-life of 25 ± 6 hours, based on the results of two replicates.

Executive summary

The mono ester of di-isodecyl phthalate (mono isodecyl phthalate) was found to biodegrade at a relatively rapid rate in a natural aerobic marine sediment, with a measured half-life of 25 ± 6 hours, based on the results of two replicates. The investigators also evaluated the biodegradability of other mono phthalate esters (MPEs) in marine sediment and some MPEs in freshwater sediments and found that, in general, all the MPEs exhibited relatively similar half-lives in marine and freshwater sediment, ranging from 16 to 39 hours. Although the biodegradability of mono isodecyl phthalate was not evaluated in freshwater sediment, based on biodegradation data for other MPEs in both sediments, mono isodecyl phthalate would also be expected to exhibit a half-life in freshwater sediment equivalent to its half-life in marine sediment. Although transformation products were not measured in this study the two transformation products identified are well known from the literature to be transformation products of DIDP.

Dissemination Dossier
Stability in soil Endpoint.001

Administrative Data

Data waiving other justification

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	June to September 1999
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is a 2 because, although the data were developed using a non standard test procedure, the information is well documented and the testing followed accepted scientific procedures.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Mackintosh C, Maldonado J, Hongwu J, Hoover N, Chong A, Ikonomou M and Gobas F	2004	Distribution of phthalate esters in a marine aquatic food-web: Comparison to polychlorinated biphenyls	Environ Sci Technol 38, 2011-2020					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
no guideline available		

Principles of method if other than guideline

Various marine species were field collected and their tissues anylzed for phthalate diesters including diisodecyl phthalate ester congeners. The sum of diisodecyl phthalate ester congeners analyzed in tissue from each species was used to define the food-web and calculate food-web magnification factors.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

no

Radiolabelling

no

Details on test material

The field study analyzed sample tissues for phthalate diesters including diisodecyl phthalate ester congeners.

Test organisms

Details on test organisms

18 species were field collected including: Green Algae - Enteromorpha intestinalis Brown Algae - Nereocystis leutkeana; Fucus gardneri Plankton - various species Blue Mussel - Mytilus edulis Pacific Oyster - Crassostrea gigas Geoduck Clam - Panope abrupta Manila Clam - Tapes philippinarum Dungeness Crab - Cancer magister Purple Seastar - Pisaster ochraccus Juv. Shiner Perch - Cymatogaster aggregata Pacific Herring - Clupea harengus Pile Perch - Rhacochilus vacca Striped Sea Perch - Embiotoca lateralis Pacific Staghorn Sculpin - Leptocottus armatus English Sole - Pleuronectes ventulus Whitespotted Greenling - Hexogrammos stelleri Spiny Dogfish - Squalus acanthias Surf Scoter - Melanitta perspicillata

Study design

Route of exposure
feed

Test type

field study

Water media type

saltwater

Test conditions

Reference substance (positive control)
yes polychlorinated biophenyl congeners

Results and discussions

Details on results
Isotope analysis revealed a general pattern of enrichment of analyzed isotopes beginning with the sediment and moving through the

food web to plankton, macroalgae and bivalves, small forage fish, large fish, marine birds, dungeness crabs, and dogfish. There was a 3-4% increase on average for each succeeding trophic level. Which illustrates that the food web investigated is sufficiently long to test for the occurrence of biomagnification. Concentrations of twenty target PCB (polychorinated biphenyl) congeners and thirteen phthalate diesters were detected at levels above the MDL (minimum detection limit) in the majority of biota species. The lipid equivalent concentrations of the high molecular phthalate esters (DEHP [diethylhexyl phthalate], DnOP [di-n-octyl phthalate], C8 [di-iso-ocytyl phthalate], DnNP [di-n-nonyl phthalate], C9 [di-iso-nonyl phthalate], and C10 (di-iso-decyl phthalate]) significantly declined with increasing trophic position and isotope levels in the food-web. FWMF (food web magnification factor) values for the PCBs ranged from 1.7 to 8.8, indicating biomagnification. FWMF values for the high molecular weight phthalate esters (C8 to C10) ranged from 0.28 to 0.50, indicating that these phthalate diesters did not biomagnify in the aquatic food web studied.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

The data from this food-web study show that diisodecyl phthalate ester did not biomagnify through a food-web that included 18 species, but rather decreased in tissue concentration with increasing trophic position.

Executive summary

The authors concluded that high molecular weight phthalate diesters, including diisodecyl phthalate ester, do not biomagnify through the food-web, but rather decrease in tissue concentration with increasing trophic position. Decreasing concentrations, also referred to as biodilution, can be quantified by food-web magnification factors (FWMFs). A FWMF that is greater than 1.0 is an indication of chemical biomagnification within a food web, whereas a value of less than 1.0 indicates biodilution or dilution from lower to higher trophic levels. The authors showed that lipid equivalent concentrations of the high molecular weight phthalate diesters significantly declined with increasing trophic level and that FWMFs ranged from 0.29 for DEHP, a C8 PE, to 0.50 for a di-iso-octyl phthalate ester. The FWMF for di-iso-decyl phthalate was 0.44.

Administrative Data

Purpose flag	supporting study		
Study result type	other: summary	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability is rated 2 because the information presents the summary of an evaluation of data for a group of phthalate diesters rather than the results of a specific study.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Gobas F, Mackintosh C, Webster G, Ikonomou M, Parkerton T and Robillard K	2003	Bioaccumulation of Phthalate Esters in Aquatic Food-Webs	In: Phthalate Esters. Staples C (Ed.) Springer-Verlag, Berlin, Germany					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
no guideline followed	other guideline: Technical discussion	

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

no

Radiolabelling

no

Details on test material

Various high molecular weight phthalate diesters

Results and discussions

Bioaccumulation factor

Conc. in environment / dose	Type	Value	Basis	Time of plateau	Calculation basis	Remarks
						Higher molecular weight phthalate esters show evidence of trophic dilution in aquatic food-webs, which is consistent with findings from laboratory

studies and modeling studies which indicate that metabolic transformation is a key mitigating factor.

Applicant's summary and conclusion

Validity criteria fulfilled

not applicable summary from book chapter titled Bioaccumulation of Phthalate Esters in Aquatic Food-Webs.

Executive summary

Organisms from various trophic levels in sediment and water samples taken from various sampling sites in False Creek Harbor, Vancouver, BC, Canada,were examined for high molecular weight phthalate ester content. The conclusions on high molecular weight phthalateester biomagnification from this study are summarized in the following abstract taken from a book chapter titledBioaccumulation of Phthalate Esters in Aquatic Food-Webs.

This chapter explores the bioaccumulation behavior ofseveral phthalate esters in aquatic food-webs. It includes (i) a compilation of bioconcentration data from reportedlaboratory studies in the literature, (ii) an overview and discussion of the results from a recently completed food-webbioaccumulation field study and (iii) an analysis of the results of a bioaccumulation modeling study. The study concludesthat laboratory and field studies indicate that phthalate esters do not biomagnify in aquatic food-webs. Higher molecularweight phthalate esters (DEHP [diethylhexyl phthalate], DnOP [di-n-octyl phthalate] and DnNP [di-n-nonyl phthalate])show evidence of trophic dilution in aquatic food-webs, which is consistent with findings from laboratory studies andmodeling studies which indicate that metabolic transformation is a key mitigating factor. Bioaccumulation patterns ofDBP [dibutyl phthalate], DiBP [diisobutyl phthalate] and BBP [butyl benzyl phthalate] indicate no significant relationshipwith trophic position consistent with a lipid-water partitioning model. The lowest molecular weight phthalate esters(DMP[dimethyl phthalate] and DEP [diethyl phthalate]) show bioaccumulation factors in laboratory and field studies thatare greater than predicted from a lipid-water partitioning model. The considerable variability in the field-derivedbioaccumulation factors (BAFs) for lower molecular weight phthalate esters across aquatic species suggests thatspecies-specific differences in metabolic transformation can have a significant effect on observed bioaccumulation. Withsome exceptions discussed below, the bioconcentration and bioaccumulation factors of the phthalate esters, discussedin this paper, are below the UNEP [United Nations Environment Programme] bioaccumulation criterion of 5,000. The lowbioavailability of the high molecular weight phthalate esters in natural waters is the main reason why the BAFs of thehigher molecular weight phthalate esters are below the UNEP bioaccumulation criterion. Since the intention of thebioaccumulation criteria is to identify substances as being "bioaccumulative" if they (like PCBs [polychlorinatedbiphenyls]) biomagnify in the food-web current evidence supports the conclusion that phthalate esters do not appearto be "bioaccumulative.".

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	August - September 2000
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is a 2 because, although the data were developed using a non standard test procedure, the information is well documented and the testing followed accepted scientific procedures.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Study report; company data		2002							2002-07-22

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
no guideline followed		no

Principles of method if other than guideline

This study was performed to determine the elimination rate constant for the test substance from rainbow trout (Oncorhynchus mykiss) tissue. The test substance was administered to the test system via the diet. The low water solubility and high Kow of DIDP prevent conducting an aqueous exposure BCF study.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

yes

Radiolabelling

no

Details on test material

Substance type: commercial product The test substance was used approximately 1 year beyond its listed expiration date. This was not believed to have had an impact on the outcome of the study as the test substance was stored in a controlled environment and appeared stable during the additional storage time.

Details on sampling

Fish samples were collected from each treatment and the control on days 7 and 14 of the uptake phase and on days 0, 1, 3, and 8 of the depuration phase. Day 0 depuration samples were removed approximately 5 hours after the beginning of depuration. Ten fish were removed from each tank at each sampling interval with the exception of day 7 of the uptake phase. Only four fish were removed at this sample interval.

Vehicle

yes

Details on preparation of test solutions or sediment

As this was a dietary study, the vehicle was Salmon Starter obtained from Zeigler Bros., Inc., Gardners, PA, USA. A semi-static exposure system was constructed to provide a sufficient volume of test water to the test tanks. The test water was delivered to the test chambers at a rate of approximately 56 ml/min using a peristaltic pump. This allowed for at least five volume replacements through each test chamber per day. The appropriate amount of the test substance was added to the test feed to achieve a nominal concentrations of 1200 ppm. Untreated food was fed to the control fish. The treated and untreated diets were measured daily and fed to the fish as a single feeding. After 14 days of exposure to the treated feed, the fish were transferred to clean tanks and fed untreated food for 8 days. Transfer of the fish, treated and untreated, marked the beginning of the depuration phase.

Test organisms

Test organisms (species)
Oncorhynchus mykiss

Details on test organisms

The test organisms were supplied by Pierce Associates, Inc., West Buxton, ME, USA. The test organisms were quarantined and observed for parasites and disease for 14 days prior to use in the test, and were held in test water at approximately 15 degrees C, that was continuously aerated to provide a dissolved oxygen concentration of at least 80% of the air saturation value. Fish were not treated for disease or parasites before use in this study. Fish were held under static conditions using biological and mechanical filtration, and were fed Salmon Starter and Artemia nauplii (<24 hours old). Test organism loading at test initiation was 0.32 grams of fish per liter; 55 organisms were used in the control system and 55 organisms in the treatment system. Test organisms length and weight measurements of a subsample of the stock population were recorded prior to the start of the study to estimate a mean organism weight. Length and weight measurements were also recorded on fish removed at each sampling period. Total length was measured in all instances.

Study design

Route of exposure
feed

Test type

semi-static

Water media type

freshwater

Total exposure / uptake duration

14 d

Total depuration duration

8 d

Test conditions

Hardness
Hardness as CaCO3 (mg/L) in water batches used during the test ranged from 100 to 122 with one value as low as 96. Water quality results for one of the water batches had one hardness value outside of the recommended range. Because there was no mortality in the study, those waters are not believed to have adversely affected the study.

Test temperature

Parameter Test Day Control Treated Diet (°C) 0 14.9 14.9 2 14.0 14.0 7 14.3 14.2 9 13.8 13.7 14 14.7 14.6 2 dep 14.1 14.0 8 dep 14.2 14.1

pH

Parameter Test Day Control Treated Diet pH 0 7.5 7.5 2 6.8 6.8 7 6.9 7.0 9 6.9 6.9 14 6.7 6.7 2 dep 7.1 7.1 8 dep 7.6 7.6

Dissolved oxygen

Dissolved oxygen concentrations did not fall below 60% saturation. Parameter Test Day Control Treated Diet (mg/L) 0 9.4 9.4 2 7.2 7.2 7 8.1 7.7 9 7.0 6.4 14 6.7 6.2 2 dep 8.1 7.9 8 dep 8.6 8.1

TOC

TOC in water batches used during the test were all <0.1 ppm.

Nominal and measured concentrations

The nominal diet loading was 1200 mg/kg feed. Analyses of feed for the uptake phase of the test was as follows: Pre-Study Day 14 Control ND ND Treated 1160 1130 Feed 1160 1190 1170 Mean 1160 1160

Details on test conditions

The test water is prepared from UV-sterilized, deionized well water that is treated and distributed throughout the testing facility via PVC and stainless-steel pipes. Batches of 500 to 1000 L of this deionized water are then reconstituted in the laboratory to meet aquatic toxicity testing needs, following Method 8010E of Standard Methods for the Examination of Water and Wastewater, 18th edition. Diurnal light was approximately 16 hours light and 8 hours dark with a gradual intensity conversion between periods. Daylight intensity ranged from 504 to 733 Lux during full daylight periods of the study. Observations for mortality, abnormal behavior and appearance of the fish were performed on all test chambers daily. Water quality measurements (pH, dissolved oxygen, specific conductance and temperature) were performed twice per week on the test treatment and the control. No un-dissolved test substance was observed in the test chambers during the study. To maintain good hygiene, fecal material and uneaten food were siphoned from

the bottom of each test chamber approximately 30 minutes to 1 hour after feeding. The test chambers were 60 L glass aquaria containing approximately 16 L of test water. The test chambers were covered with glass tank lids to minimize contamination or evaporation. A stainless steel screen was placed over the standpipe to prevent fish from becoming trapped in the drain.

Reference substance (positive control)

no

Details on estimation of bioconcentration

Test results were used to derive the elimination rate constant (KElim) as a function of the concentration of the test substance in fish versus time. Calculations were performed using MicroSoft® Excel 97 software and are consistent with methods outlined in the OECD test guidelines [Bioconcentration: Flow-Through Fish Test. OECD Guidelines for Testing of Chemicals. Section 3: Degradation and Accumulation, Guideline 305, adopted 14-Jun-96].

Results and discussions

Lipid content

2.47 %

Time point	other: The percentage lipid in the fish did not vary significantly between the beginning and the end of the uptake phase or between treatments.
Remarks	The percentage lipid in the fish did not vary significantly between the beginning and the end of the uptake phase or between treatments. The mean percent lipid was 2.47% and was determined using three measurements.

Bioaccumulation factor

Conc. in environment / dose	Type	Value	Basis	Time of plateau	Calculation basis	Remarks
1160 ug/g feed	other: Biomagnification factor; lipid	ca.	whole	14 d	kinetic	The half-life value of <1 day

	normalized (concentration ratio in tissue to that in diet)	0.1	body w.w.	was used to calculate a BCF in fish of <1 L/kg

Depuration

Elimination	Endpoint	Depuration time (DT)
yes	other: Elimination rate constant = 0.83 ug/g day-1	

Kinetic parameters

Elimination rate constant = 0.83 ug/g day-1

Metabolites

Metabolites were not measured.

Results with reference substance (positive control)

A reference substance was not tested.

Details on results

There was no difference in mortality, growth, or lipid content between the treatment and the control after 14 days of exposure or at the end of the study (22 days). The following presents the mean weights, percent survival, and final lipid content. Initial Weight (g) Final Weight (g) Survival (Day 14 Uptake) (Day 8 Depuration) After 14 days Final Lipid Content Treatment Mean SD N Mean SD N % Control 1.035 0.212 10 1.504 0.298 10 100 2.42 Treated Diet 1.046 0.168 10 1.499 0.181 10 100 2.37 The calculated elimination rate constants for the test substance is 0.83 ug/g day-1.

Reported statistics

Test results were used to derive the elimination rate constant (KElim) as a function of the concentration of the test substance in fish

versus time. Calculations were performed using MicroSoft® Excel 97 software and are consistent with methods outlined in the OECD test guidelines [Bioconcentration: Flow-Through Fish Test. OECD Guidelines for Testing of Chemicals. Section 3: Degradation and Accumulation, Guideline 305, adopted 14-Jun-96].

Remarks on results including tables and figures

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) has a low potential to bioaccumulate in the environment based on results from a fish dietary lab study. The elimination rate constant was calculated as 0.83 ug/g day-1. The low water solubility and high Kow of DIDP prevent conducting an aqueous exposure BCF study. At the end of the exposure period, fish were sampled after different depuration times (0, 0.6, 1, 3 days). Results demonstrated limited bioaccumulation with a lipid normalized biomagnification factor (BMF, concentration ratio in tissue to that in diet) of <0.1 and rapid subsequent depuration with a tissue elimination half-life of <1 day. The half-life value of <1 day was used to calculate a BCF in fish of <1 L/kg for DIDP.

Executive summary

Di-isodecyl phthalate ester (DIDP) has a low potential to bioaccumulate in the environment based on results from a fish dietary lab study.The elimination rate constant was calculated as 0.83 ug/g day-1. The low water solubility and high Kow of DIDP prevent conducting an aqueous exposure bioconcentration factor (BCF) study.At the end of the exposure period, fish were sampled after different depuration times (0, 0.6, 1, 3 days). Results demonstrated limited bioaccumulation with a lipid normalized biomagnification factor (BMF, concentration ratio in tissue to that in diet) of 0.1 and rapid subsequent depuration with a tissue elimination half-life of 1 day.The half-life value of 1 day was used to calculate a BCF in fish of 1 L/kg for DIDP.

Dissemination Dossier
Bioaccumulation Endpoint.004

Administrative Data

Purpose flag supporting study
Study result type estimated by calculation
Study period Not applicable
Reliability 2 (reliable with restrictions)
Rationale for reliability The reliability rating is 2 because the data are calculated.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Computer model	U.S. Environmental Protection Agency (USEPA)	2000	EPI SuiteTM, Estimation Program Interface Suite, v3.12	USEPA, Washington, DC, USA					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: Computer model	

Principles of method if other than guideline

The bioconcenuration factor (BCF) was calculated by the BCFWIN subroutine (version 2.15) in the EPI SuiteTM (2000) computer model that estimates the BCF based upon chemical structure and log octanol-water partition coefficient.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

SMILES Notation used: O=C(c1ccccc1C(=O)OCC(C)C(C)CC(C)CC)OCCC(C)CC(C)CCC

Study design

Total exposure / uptake duration
d

Results and discussions

Bioaccumulation factor

Conc. in environment / dose	Type	Value	Basis	Time of plateau	Calculation basis	Remarks
	BCF	3.2				

Applicant's summary and conclusion

Validity criteria fulfilled
yes

Conclusions

Di-isooctyl has a low potential to bioconcentrate, based on an estimated BCF value of 3.2.

Executive summary

Di-isodecyl has a low potential to bioconcentrate, based on an estimated BCF value of 3.2.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	4 (not assignable)		
Rationale for reliability	The reliability rating is a 4 because although the study followed a standard guideline, which describes a procedure designed to evaluate this endpoint, the study did not follow GLP, there were limited data on water quality parameters, and the reported exposure concentration was at a level above the test substance water solubility, which prevents calculation of an accurate BCF value.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: publication; handbook	Chemicals Inspection & Testing Institute	1992	Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan	Japan Chemical Industry Ecology-Toxicology & Information Center, Japan					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	OECD Guideline 305 C (Bioaccumulation: Test for the Degree of Bioconcentration in Fish)	

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
no

Radiolabelling

no

Test organisms

Test organisms (species)
Cyprinus carpio

Details on test organisms

Fish weight approximately 30 grams; fish length approximately 10 cm.

Study design

Route of exposure

aqueous

Water media type

freshwater

Total exposure / uptake duration

56 d

Test conditions

Nominal and measured concentrations
1 mg/L nominal concentration

Results and discussions

Lipid content
>= 2 — <= 6 %
Time point
Remarks

Bioaccumulation factor

Conc. in environment / dose	Type	Value	Basis	Time of plateau	Calculation basis	Remarks
	BCF	< 3.6	no data			

Depuration

Elimination	Endpoint	Depuration time (DT)
no		

Details on results

BCF = <3.6; log BCF = <0.56

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

1,2-Benzenedicarboxylic acid, diisodecyl ester, has a low potential to bioconcentrate based on a measured BCF of <3.6 from an exposure concentration of 1 mg/L.

Executive summary

1,2-Benzenedicarboxylic acid, diisodecyl ester, has a low potential to bioconcentrate based on a measured BCF of <3.6. As an analog to DIDP, di-isodecyl phthalate (CAS #68515-49-1), these data suggest that DIDP will also exhibit an equally low potential to bioconcentrate.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	4 (not assignable)		
Rationale for reliability	The reliability rating is a 4 because although the study followed a standard guideline, which describes a procedure designed to evaluate this endpoint, the study did not follow GLP, there were limited data on water quality parameters, and the reported exposure concentration was at a level above the test substance water solubility, which prevents calculation of an accurate BCF value.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: publication; handbook	Chemicals Inspection & Testing Institute	1992	Biodegradation and Bioaccumulation Data of Existing Chemicals Based on the CSCL Japan	Japan Chemical Industry Ecology-Toxicology & Information Center, Japan					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	OECD Guideline 305 C (Bioaccumulation: Test for the Degree of Bioconcentration in Fish)	

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
no

Radiolabelling

no

Test organisms

Test organisms (species)
Cyprinus carpio

Details on test organisms

Fish weight approximately 30 grams; fish length approximately 10 cm.

Study design

Route of exposure

aqueous

Water media type

freshwater

Total exposure / uptake duration

56 d

Test conditions

Nominal and measured concentrations
0.1 mg/L nominal concentration

Results and discussions

Lipid content
>= 2 — <= 6 %
Time point
Remarks

Bioaccumulation factor

Conc. in environment / dose	Type	Value	Basis	Time of plateau	Calculation basis	Remarks
	BCF	< 14.4	no data			

Depuration

Elimination	Endpoint	Depuration time (DT)
no		

Details on results

BCF = <14.4; log BCF = <1.16

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

1,2-Benzenedicarboxylic acid, diisodecyl ester, has a low potential to bioconcentrate based on a measured BCF of <14.4 from an exposure concentration of 0.1 mg/L.

Executive summary

1,2-Benzenedicarboxylic acid, diisodecyl ester, has a low potential to bioconcentrate based on a measured BCF of <14.4. As an analog to DIDP, di-isodecyl phthalate (CAS #68515-49-1), these data suggest that DIDP will also exhibit an equally low potential to bioconcentrate.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	3 (not reliable)		
Rationale for reliability	Test procedure analyses do not accurately measure parent test substance concentrations and the exposure solutions allow for excess test material to interfere with quantifying the amount of test material in the organisms.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Brown D and Thompson R	1982	Phthalates and the aquatic environment: Part II. The bioconcentration and depuration of di-2-ethylhexyl phthalate (DEHP) and di-isodecyl phthalate (DIDP) in mussels (Mytilus edulis)	Chemosphere 11(4): 427-435					

Materials and methods

GLP compliance
no

Test materials

Test material equivalent to submission substance identity
no

Radiolabelling

yes

Details on test material

The 14C samples of di-isodecyl phthalate ester (DIDP) were synthesised from phthalic anhydride, labelled in the benzene ring, and an isodecyl alcohol. The chemical and radiochemical purity was found to be >97.5% as checked by GLC using two different columns. The sample was supplied in acetone solution at specific activity of 4.7 mCi/g. An accurate CAS and EC number cannot be identified because the synthesis is not equivalent to standard manufacturing processes for DIDP.

Details on sampling

Five mussels from each test vessel were sacrificed for analysis at intervals throughout the 28 day bioconcentration phase on days 1, 3, 7, 14, 21, 24, and 28 and on days 29, 31, 35, and 42 during the 14 day deputation phase.

Vehicle

yes

Test organisms

Test organisms (species)
other: Mytilus edulis

Details on test organisms

Mytilus edulis were collected locally, to Devon, England, and 30 randomly selected mussels from those collected had a mean shell length (30 mussels) of 22.6 mm (range 20-28 mm) and 15 randomly selected mussels had a mean wet tissue weight of 472 mg (range 274-772 mg).

Study design

Route of exposure
aqueous

Test type

flow-through

Water media type

saltwater

Total exposure / uptake duration

28 d

Total depuration duration

14 d

Groups of 80 mussels were exposed for 28 days to each of the following nominal concentrations: DIDP at 5 ug/l and 50 ug/l, and a solvent control (0.5 ml acetone/litre). Following this bioconcentration phase, the mussels were maintained in clean seawater for a depuration period of 14 days. The test vessels were glass reinforced plastic tanks with a 35 L capacity, each receiving a continuous supply of filtered (5 pm) seawater at a flow rate of 500 ml/min, and at a temperature controlled to 15 +/- I°C. The mussels were fed by continuous addition of a cultured unicellular alga (Platlnnonas suecica) to the dilution water, to provide approximately 2000 algae/ml in the supply to each vessel. The phthalates were prepared as stock solutions in acetone at 2000 times the required exposure level using the appropriate 14C labelled sample for the 5 g/l levels, and a mixture of 1 part 14C labelled phthalate and 9 parts non-labelled material for the 50 ug/l levels. The stock solutions were delivered by peristaltic pump to a stirred mixing chamber to mix with the seawater immediately prior to delivery to the test vessel. Acetone alone was similarly added to the supply to the solvent control, all vessels having a nominal acetone concentration of 0.5 ml/L.

Reference substance (positive control)

no

Details on estimation of bioconcentration

Calculations were made using total radioactivity.

Results and discussions

Lipid content

Time point

Remarks Not measured

Metabolites

Metabolites were not measured.

Results with reference substance (positive control)

A reference substance was not tested.

Details on results

Estimated plateau levels and bioconcentration factors for DIDP during 28-day uptake phase: Estimated Mean Plateau Concentration Level Bioconcentration Mean Bioconcentration (ug/L) (ug/mg) at Plateau at Plateau 4.4 17.5 3977 3488 41.7 125 2998

Remarks on results including tables and figures

Non-quantitative observations were made at intervals during the study of the deposition of faecal/pseudofaecal material in the test vessels, of byssal thread attachment, and of the general appearance and activity of the mussels. There was no evidence of any adverse effects on the mussels, and all groups appeared to be actively feeding throughout the study. The mussels were also examined daily for mortalities, defined as mussels displaying an abnormal degree of shell opening and subsequent inability to close the shell within 1 minute of removal from the test vessels. Throughout the test period there was 1 death in the solvent control.

The exposure of the mussel, Mytilus edulis, to C14 radiolabelled DIDP led to a plateau level of radioactive residues corresponding to a mean bioconcentration factor (BCF) of approximately 3,500. Additionally, these residues were rapidly lost from the mussels (T1/2 was approximately 31/2 days) and the 28 day exposure period to nominal levels of 5 ug/l and 50 ug/l of DIDP produced no apparent adverse effects. However, the BCF was calculated based on total radioactivity and consequently the reported BCF value is not valid because total activity does not differentiate between the parent test substance and metabolites.

Applicant's summary and conclusion

Validity criteria fulfilled

no The study is not valid due to an inaccurate calculation of BCF.

Conclusions

The exposure of the mussel, Mytilus edulis, to C14 radiolabelled DIDP led to a plateau level of radioactive residues corresponding to a mean bioconcentration factor (BCF) of approximately 3,500. Additionally, these residues were rapidly lost from the mussels (T1/2 was approximately 31/2 days) and the 28 day exposure period to nominal levels of 5 ug/l and 50 ug/l of DIDP produced no apparent adverse effects. However, the BCF was calculated based on total radioactivity and consequently the reported BCF value is not valid

because total activity does not differentiate between the parent test substance and metabolites.

Executive summary

The exposure of the mussel, Mytilus edulis, to C14 radiolabelled DIDP led to a plateau level of radioactive residues corresponding to a mean bioconcentration factor (BCF) of approximately 3,500. Additionally, these residues were rapidly lost from the mussels (T1/2 was approximately 31/2 days) and the 28 day exposure period to nominal levels of 5 ug/l and 50 ug/l of DIDP produced no apparent adverse effects. However, the BCF was calculated based on total radioactivity and consequently the reported BCF value is not valid because total activity does not differentiate between the parent test substance and metabolites.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	April 1996
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study proceedure followed an accepted test guideline and was conducted under GLP. The data are consistent with known toxicological properties of similar high molecular weight phthalate ester substances.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Study report; company data		1996							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: OECD Guideline 207 (Earthworm, Acute Toxicity Test)	no

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity
yes

Radiolabelling

no

Details on test material

Substance type: technical product

Study design

Details on sampling
Test soils dosed with diisodecyl phthalate ester (DIDP) were analyzed at test initiation and termination, days -1 and 14, respectively.

Details on preparation and application of test substrate

Test soil was homogenized prior to use by placing soil into 4L size plastic (HDPE) containers and mixing on a jar mill for approximately 15 minutes. After homogenizing, a sample was removed to determine the moisture fraction. The moisture fraction was measured by placing soil into a crystallizing dish and weighing it (initial wt.). The sample and crystallizing dish were then placed in an oven at 100 degrees C for 23 hours. After drying and cooling in a desiccator, the final weight of the sample and crystallizing dish was measured. Treatments were prepared by adding the appropriate amount of test material to a soil sample. The treatment soils were stirred copiously in stainless steel bowls with stainless steel spoons for 15 to 30 minutes and held overnight at room temperature. On

day 0, each treatment was divided into 5 replicates. The test chambers were one pint glass canning jars containing approximately 200g of a soil control or treatment and the appropriate amount of hydration water to bring the soils up to 75% of their water holding capacity. The worms were then transferred to randomized test chambers, which were capped with a lid containing a 1/8 inch hole in the center.

Test organisms

Test organisms (species)
Eisenia fetida

Details on test organisms

Worms, Eisenia fetida, were obtained from Carolina Biological, Burlington, NC, USA. Species were verified based on: Earthworms of Ontario, J.W. Reynolds, Life Sciences Miscellaneous Publishing, The Royal Ontario Museum, 15 June 1977 Average weight of worms was 0.393g (sd = 0.090), based on a subsample (n=20) of worms. The organism loading rate during the study was 10 worms/~200 g soil.

Total exposure / uptake duration

14 d

Total depuration duration

0 d

Nominal and measured concentrations

Soil samples were dosed with 10,000 mg test substance/kg soil. Soil were analyzed for DIDP concentration at test initiation and termination. The soil analytical results are based on the mean of duplicate samples for each soil sampled: DIDP Conc. Day -1: 7664 mg/kg soil, dry wt. DIDP Conc. Day 14: 7994 mg/kg soil, dry wt. Average Conc.: 7829 mg/kg soil, dry wt.

Test conditions

Test temperature

Test temperature ranged from 18.2 to 20.6 degrees C as measured continuously and recorded by computer for the first 6 days, then measured daily thereafter.

pH

Soil pH was measured at test initiation (day 0) of the study. Ten grams of each treatment were mixed with 20mL of distilled water. The pH value of the slurry was measured using a soil pH probe. Soil pH ranged from 6.9 to 7.2.

Moisture

The water holding capacity of each soil was determined as follows: 25g of the dried sample was placed into a 100mL glass beaker with 25mL of reverse osmosis water and mixed thoroughly. This slurry was added to a pre-weighed, wetted filter paper and funnel (initial weight = wt. of funnel, wetted paper, + 25 g soil). The filter paper (#113 Whatman 150mm) was wetted with 9mL of reverse osmosis water. The glass funnel measured 10cm top diameter with an approximately 30mm stem. The slurry, filter and funnel were covered with aluminum foil and allowed to stand for 3 hours at which time a final weight was measured. The water holding capacity, expressed in mL water/100g of soil, is the difference between the final and initial weights multiplied by 4 to achieve 100g equivalence.

Details on test conditions

Natural soil was obtained from Snyder Research Farm located in Pittstown, NJ, USA, which was managed by Rutgers University. The soil was sieved through a 10 mesh sieve prior to use to remove large particles. Artificial soil was prepared using 70% sand, 20% clay, 10% peat, and CaCO3 to adjust pH.

Results and discussions

Bioconcentration factor

Type	Value	Basis	Time of plateau	Calculation basis	Remarks
BSAF	0.015	whole body w.w.			

Details on results

The biota-soil accumulation factor (BSAF) as measured in a natural soil was 0.015 based on a DIDP concentration in the earthworm of 120 mg/kg (wet weight) and in soil of 7829 mg/kg (dry weight). A BSAF value of <1 indicates a lack of bioaccumulation.

Remarks on results including tables and figures

The biota-soil accumulation factor (BSAF) as measured in a natural soil was 0.015 based on a DIDP concentration in the earthworm of 120 mg/kg (wet weight) and in soil of 7829 mg/kg (dry weight). A BSAF value of <1 indicates a lack of bioaccumulation.

Applicant's summary and conclusion

Conclusions

The biota-soil accumulation factor (BSAF) as measured in a natural soil was 0.015 based on a DIDP concentration in the earthworm of 120 mg/kg (wet weight) and in soil of 7829 mg/kg (dry weight). A BSAF value of <1 indicates a lack of bioaccumulation.

Executive summary

Data to assess the potential for terrestrial bioaccumulation of DIDP were reported in a 14-day earthworm (Eisenia fetida) toxicity study. The biota-soil accumulation factor (BSAF) as measured in a natural soil was 0.015 based on a DIDP concentration in the earthworm of 120 mg/kg (wet weight) and in soil of 7829 mg/kg (dry weight). A BSAF value of <1 indicates a lack of bioaccumulation.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is a 2 because the study followed a U.S. EPA standard guideline, which describes a procedure designed to evaluate this endpoint, and the results were reviewed for reliability and assessed as valid. However, the study was not conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Williams M, Adams W, Parkerton T, Biddinger G and Robillard K	1995	Sediment sorption coefficients for four phthalate esters: Experimental results and model theory.	Environ. Toxicol. Chem. 14: 1477-1486					

Materials and methods

Study type
adsorption

Media

sediment

Type of method

other: radiolabelled method

Test guideline

Qualifier	Guideline	Deviations
according to	EPA OTS 796.2750 (Sediment and Soil Adsorption Isotherm)	

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
yes

Radiolabelling

yes

Details on test material

DIDP was 14C-uniformly ring-labeled with a radiopurity of 92.5%. Analyses showed that the radiolabelled DIDP was equivalent to the commercial substance.

Study design

Test temperature

25 degrees C

Batch equilibrium or other method

Analytical monitoring

yes

Details on sampling

Solid-to-solution ratios were 1:50 and 1:500 for each soil type. The test was conducted in triplicate at six concentrations. Triplicate 1.0 ml aliquots of each test solution at time 0 were analyzed by LSC (liquid scintillation counting) to establish actual concentrations. Test systems were incubated for 7 days after which samples were analyzed by LSC.

Details on matrix

Three sediments were used: U.S. EPA 8 (0.15% organic carbon, pH = 8.32), U.S. EPA 18 (0.66% organic carbon, pH = 7.76), and U.S. EPA 21 (1.88% organic carbon, pH = 7.60).

Details on test conditions

Test systems were incubated on a rotary shaker, in the dark at 25 degrees C.

Results and discussions

Adsorption coefficient Koc
286000

log Koc

5.46

Results: Batch equilibrium or other method

Recovery of test material
Mass balance determinations for DIDP were: EPA Soil 8 - 103% at initiation EPA Soil 18 - 105% at initiation EPA Soil 21 - 106% at initiation

Concentration of test substance at end of adsorption equilibration period

Mass balance determinations for DIDP were: EPA Soil 8 - 103% at termination EPA Soil 18 - 102% at termination EPA Soil 21 - 107% at termination

Transformation products

not measured

Applicant's summary and conclusion

Validity criteria fulfilled
yes

Conclusions

Sediment partition coefficients were measured for the commercial phthalate ester, disodecyl phthalate (DIDP). The Freundlich equation was used to calculate the organic carbon-normalized sediment/water partition coefficient (Koc), which averaged 2.86 E5 for DIDP.

Executive summary

Sediment partition coefficients were measured for the commercial phthalate ester, disodecyl phthalate (DIDP). The experimental procedure was based on the U.S. Environmental Protection Agency (EPA) Test Guideline 796.2750, "Sediment and Soil Adsorption Isotherm." Three sediments were used: EPA 8 (0.15% organic carbon), EPA 18 (0.66% organic carbon), and EPA 21 (1.88% organic carbon). The Freundlich equation was used to calculate the organic carbon-normalized sediment/water partition coefficient (Koc), which averaged 2.86 E5 for DIDP.

Administrative Data

Purpose flag	supporting study		
Study result type	estimated by calculation	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is 2 because the data are calculated.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Computer model	U.S. Environmental Protection Agency (USEPA)	2000	EPI SuiteTM, Estimation Program Interface Suite, v3.12	USEPA, Washington, DC, USA					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: Computer model	

Principles of method if other than guideline

The calculated value was determined using PCKOCWIN version 1.66, a subroutine within the computer program EPI SuiteTM version 3.12.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

yes

Radiolabelling

no

Details on test material

SMILES Notation used: O=C(c1ccccc1C(=O)OCCCCCCCCC(C)C)OCCCCCCCCC(C)C

Study design

Batch equilibrium or other method

Analytical monitoring

no

Computational methods

The calculated value was determined using Soil Adsorption Coefficient Program (PCKOCWIN) version 1.66, a subroutine within the computer program EPI SuiteTM version 3.12. PCKOCWIN estimates the soil adsorption coeffiecient (Koc) of organic compounds. Koc can be defined as "the ratio of the amount of chemical adsorbed per unit weight of organic carbon (oc) in the soil or sediment to the concentration of the chemical in solution at equilibrium" (Lyman, 1990); it is represented by the following equation (Lyman, 1990): Koc = (ug adsorbed/g organic carbon) / (ug/mL solution)

Results and discussions

Adsorption coefficient Koc
1589000

log Koc

6.2

Applicant's summary and conclusion

Validity criteria fulfilled
yes

Conclusions

Estimated di-isodecyl phthalate log Koc is 6.2.

Executive summary

Estimated di-isodecyl phthalate log Koc is 6.2.

Dissemination Dossier
Henry law Endpoint.001

Administrative Data

Purpose flag key study

Study result type estimated by calculation

Study period Not applicable

Reliability 2 (reliable with restrictions)

Rationale for reliability Recommended value from European Commission risk assessment for 1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich, CAS#: 68515-49-1, EINECS#: 271-091-4,and:di-"isodecyl" phthalate (DIDP), CAS#: 26761-40-0, EINECS#: 247-977-1.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		2003							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
no guideline required		

Principles of method if other than guideline

Henry's Law constant is calculated based on vapor pressure and water solubility.

GLP compliance

no not applicable

Test materials

Test material equivalent to submission substance identity

yes

Results and discussions

Henry's Law constant H

H	114 Pa m³/mol
Temp. (°C)	25
Atm. press.	101325 Pa

Applicant's summary and conclusion

Conclusions

Henry's Law constant for DIDP, 114 Pa.m3/mole at 25 degrees C, indicates that volatilization from water is not expected to occur at a rapid rate, but may occur at a significant rate.

Executive summary

Henry's Law constant for DIDP, 114 Pa.m3/mole at 25 degrees C, indicates that volatilization from water is not expected to occur at a rapid rate, but may occur at a significant rate.

Administrative Data

Purpose flag	key study		
Study result type	estimated by calculation	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is 2 because the data are calculated.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Mackay D, DiGuardo A, Paterson S and Cowan C	1996	Evaluating the environmental fate of a variety of types of chemicals using the EQC model	Eviron. Toxicol. Chem. 15: 1627-1637					
other: Mathematical model	Mackay D	1997	Level III Fugacity-Based Environmental Equilibrium Partitioning Model, Version 1.01	Environmental Modelling Centre, Trent University, Ontario, Canada					
publication	Mackay D	2001	Multimedia environmental models:	Second edition, pp. 1-261, Lewis					

The fugacity approach Publisher, Boca Raton, Fl, USA

Materials and methods

Model
Calculation according to Mackay, Level III

Calculation programme

Level III simulation using the Mackay Multimedia Environmental Model, version 2.80, released 2004, available at the Canadian Environmental Modelling Centre, Trent University, Canada.

Release year

2004

Media

air - biota - sediment(s) - soil - water

Test materials

Test material equivalent to submission substance identity
yes

Test substance input data

Parameter Value w/ Units Molecular Weight 446.68 Temperature 25° C Log Kow 8.8 Water Solubility 0.00017 g/m3 Vapor Pressure 0.000051 Pa Melting Point -50°C Emissions rates used in the calculation: Compartment Rate (kg/hr) Air 1000 Water 1000 Soil 1000

Results and discussions

Percent distribution in media

Remarks on results including tables and figures

The potential environmental distribution of di-isodecyl phthalate ester in 4 environmental compartments as calculated using a fugacitymodel, the Mackay Level III, under the default emission scenario (1000 kg/h into each of air water and soil compartments) with 2 differenthalf-life data sets (see above) is shown below:

First Calculation

Relative distribution when released (see half-life values above):

Air 0.3%

Soil 63.5%

Water 4.3%

Sediment 31.9%

Second Calculation

Relative distribution when released (see half-life values above):

Air <0.1%

Soil 99.6%

Water <0.1%Sediment 0.4%

Level III simulation using the Mackay Multimedia Environmental Model (Mackay, 2001). Mass balances are calculated for the four bulk media of air (gas + aerosol), water (solution + suspended sediment + biota), soil, (solids + air + water), and sediment (solids + pore water). Equilibrium exists within, but not between media. Physical-chemical properties are used to quantify a chemical's behavior in an evaluative environment. Three types of chemicals are treated in this

model: chemicals that partition into all media (Type 1), non volatile chemicals (Type 2), and chemicals with zero, or near-zero, solubility (Type 3). The model cannot treat ionizing or speciating substances. The Level III model assumes a simple, evaluative environment with user-defined volumes and densities for the following homogeneous environmental media (or compartments): air, water, soil, sediment, suspended sediment, fish and aerosols.

This model provides a description of a chemical's fate including the important degradation and advection losses and the intermedia transport processes. The distribution of the chemical between media depends on how the chemical enters the system, e.g. to air, to water, or to both. This mode of entry also affects persistence or residence time.

The rates of intermedia transport are controlled by a series of 12 transport velocities. Reaction half-lives are requested for all 7 media. The advective residence time selected for air also applies to aerosols and the residence time for water applies to suspended sediment and fish. The advective residence time of aerosols, suspended sediment and fish cannot be specified independently of the air and water residence times.

Applicant's summary and conclusion

Conclusions

The Mackay Level III equilibrium model estimates that DIDP will partition largely to the soil compartment (approximately 64%), followed by the sediment (approximately 32%), water (approximately 4%), and air (less than 1%) compartments, based on all available measured data and the model's default emission rates. In comparison, the model estimates that DIDP will partition largely to the soil compartment (approximately 99%), based on ECHA generic guidance and the model's default emission rates.

Executive summary

The Mackay Level III equilibrium model estimates that DIDP will partition largely to the soil compartment (approximately 59%), followed by the sediment (approximately 36%), water (approximately 5%), and air (less than 1%) compartments, based on all available measured data and the model's default emission rates. In comparison, the model estimates that DIDP will partition largely to the soil compartment (approximately 99%), based on ECHA generic guidance and the model's default emission rates.

Administrative Data

Purpose flag	key study		
Study result type	estimated by calculation	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability rating is 2 because the data are calculated.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Mackay D, DiGuardo A, Paterson S and Cowan C	1996	Evaluating the environmental fate of a variety of types of chemicals using the EQC model	Eviron. Toxicol. Chem. 15: 1627-1637					
other: Mathematical model	Mackay D, DiGuardo A, Paterson S and Cowan C	1997	EQC Model ver. 1.01	Available from the Environmental Centre, Trent University, Canada.					

publication	Mackay D	2001	Multimedia environmental models: The fugacity approach	Second edition, pp. 1-261, Lewis Publisher, Boca Raton, Fl, USA

Materials and methods

Model
Calculation according to Mackay, Level I

Calculation programme

Level I simulation using the Mackay Multimedia Environmental Model, version 3.0, released 2004, available at the Canadian Environmental Modelling Centre, Trent University, Canada.

Release year

1997

Media

air - biota - sediment(s) - soil - water

Test materials

Test material equivalent to submission substance identity
yes

Test substance input data

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentec0a.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-7fc2fb97-aab4-4477-aefa-6e31db7efc72%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Parameter Value w/ Units Molecular Weight 446.68 Temperature 25° C Log Kow 8.8 Water Solubility 0.00017 g/m3 Vapor Pressure 0.000051 Pa Melting Point -50°C

Results and discussions

Percent distribution in media

Air (%)
0

Water (%)

0

Soil (%)

97.7

Sediment (%)

2.2

Susp. sediment (%)

0.1

Biota (%)

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentec0a.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-7fc2fb97-aab4-4477-aefa-6e31db7efc72%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

0

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions

The Mackay Level I equilibrium model estimates that di-isodecyl phthalate ester will partition largely to the soil compartment (approximately 98%), followed by the sediment (approximately 2%) compartment.

Executive summary

The Mackay Level I equilibrium model estimates that di-isodecyl phthalate ester will partition largely to the soil compartment (approximately 98%), followed by the sediment (approximately 2%) compartment.

Dissemination Dossier
Monitoring Endpoint:001

Administrative Data

Purpose flag supporting study
Study result type no data **Study period** Not applicable
Reliability 4 (not assignable)
Rationale for reliability Brief summary only

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Government report		1990							

Materials and methods

GLP compliance
no

Type of measurement

background concentration

Media

food

Test materials

Test material equivalent to submission substance identity
no

Applicant's summary and conclusion

Executive summary

Food samples including jelly, pickles, and sauces from containers with closure seals containing 25-40% DIDP were analyzed during the late 1980's.DIDP was not detected in any sample at a detection limit of 1 mg/kg (N=10).

Administrative Data

Purpose flag	supporting study		
Study result type	no data	Study period	Not applicable
Reliability	4 (not assignable)		
Rationale for reliability	Brief summary only		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Government Report		1995							

Materials and methods

GLP compliance
no

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument690c.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-9ce03faa-01cb-4d31-8ce6-2eeafd62dc92%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Type of measurement

concentration at contaminated site

Media

sediment

Test materials

Test material equivalent to submission substance identity

no

Applicant's summary and conclusion

Executive summary

Sediment samples were collected downstream from two point source discharges. Mean DIDP concentrations above and below both point sourceswere below detection limits, 0.02 mg/kg dry wt, in all three samples collected at each station. Sediment concentrations at stations upstream of bothpoint sources were also below detection limits.

Administrative Data

Purpose flag	supporting study		
Study result type	no data	Study period	Not applicable
Reliability	4 (not assignable)		
Rationale for reliability	Brief summary only		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Government report		1995							

Materials and methods

GLP compliance
no

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumenta840.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-20a61e1b-2023-4b42-af1b-24b73209682f%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Type of measurement

background concentration

Media

sediment

Test materials

Test material equivalent to submission substance identity

no

Results and discussions

Details on results

Sediment samples were collected downstream from two point source discharges. Mean DIDP concentrations above and below both point sourceswere below detection limits, 0.02 mg/kg dry wt, in all three samples collected at each station. Sediment concentrations at stations upstream of bothpoint sources were also below detection limits.

Remarks on results including tables and figures

Applicant's summary and conclusion

Executive summary

Sediments from 8 lakes in and 10 sample locations in a Swedish river system that provided a gradientof anthropogenic influence were analyzed forDIDP in 1994. A total of 54 sediment analyses wereperformed on samples collected from these locations. DIDP was not detected in any

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumenta840.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-20a61e1b-2023-4b42-af1b-24b73209682f%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

sample(estimateddetection limit was 0.02 mg/kg dry wt).

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a U.S. EPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1983							
publication	Adams W, Biddinger G, Robillard K and Gorsuch J	1995	A summary of the acute toxicity of 14 phthalate esters to representative aquatic organisms	Environ. Toxicol. Chem. 14(9):1569-1574					
publication	Staples C, Adams	1997	Aquatic toxicity of	Environ. Toxicol.					

	W, Parkerton T, Gorsuch J, Biddinger G and Reinert K	eighteen phthalate esters	Chem. 16(5):875-891
publication	2003		

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: USEPA, (660/3-75-009) Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians	

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

Details on sampling

Water quality samples were taken daily. Analytical samples were taken at time zero and on a composite of replicates at study termination.

Vehicle

no

Details on test solutions

Test treatments were prepared by using a proportional diluter modified to enhance mixing of phthalates. The dilution water was Wareham, Mass., USA, town water (untreated and unchlorinated). A concentrated stock solution was prepared and combined with dilution water prior to pumping into the diluter.

Test organisms

Test organisms (species)
Pimephales promelas

Study design

Test type
flow-through

Water media type

freshwater

Limit test

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentac10.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-371dc6f0-52f0-4865-917a-d0cc25c2ffc6%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

no

Total exposure duration

96 h Remarks

Test conditions

Hardness

Range was 25 to 50 mg/L as CaCO3

Test temperature

Range was 21 to 23 degrees C

pH

Range was 7.6 to 7.9

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
96 h	LC50	> 1 mg/L	meas. (not specified)	test mat.	mortality	
96 h	NOEC	1 mg/L	meas. (not specified)	test mat.	mortality	

Details on results

96 hr LC50 >1.0 mg/L. Diisodecyl phthalate ester did not produce acute lethal toxicity at the highest achievable concentration under

the conditions of this test.

Reported statistics and error estimates

Statistical methods applied the following procedures: Moving average angle, Probit, and Bionomial Probability.

Any other information on results incl. tables

It was concluded in the European Risk Assessment Report (2003) for DIDP that no chemical toxic effect could be attributed to the substances tested in any of the valid studies used to assess the aquatic toxicity of DIDP. The report went on to state that "a two-generation test with Oryzias latipes showed that oral intake of 20 mg/kg had no adverse effect upon reproduction and growth. It can therefore be concluded that based on the available data, DIDP has no adverse effects upon fish and that a NOEC cannot be determined."

European Commission (2003). Risk-Assessment Report Vol. 36, 2003 on:1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich, CAS#: 68515-49-1, EINECS#: 271-091-4.and:di-"isodecyl" phthalate (DIDP), CAS#: 26761-40-0, EINECS#: 247-977-1. Publication: EUR 20785 EN.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

The acute fathead minnow (Pimephales promelas) toxicity data reported for di-isodecyl phthalate ester (DIDP) are consistent with the data for several fish species as summarized by Staples et al. (1997). These data clearly show that DIDP does not produce acute toxicity to fish at or below its maximum attainable water solubliity.

Executive summary

The acute toxicity of di-isodecyl phthalate ester (DIDP) as measured by mortality to fathead minnow (*Pimephales promelas*) was evaluated in

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentac10.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-371dc6f0-52f0-4865-917a-d0cc25c2ffc6%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

freshwater. DIDP did not produce acute lethal toxicity to fathead minnow at its maximum water solubility (1.0 mg/L) under the conditions of this study.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a U.S. EPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1983							
publication	Adams W, Biddinger G, Robillard K and Gorsuch J	1995	A summary of the acute toxicity of 14 phthalate esters to representative aquatic organisms	Environ. Toxicol. Chem. 14(9):1569-1574					
publication	Staples C, Adams W, Parkerton T,	1997	Aquatic toxicity of eighteen phthalate esters	Environ. Toxicol. Chem. 16(5):875-					

	Gorsuch J, Biddinger G and Reinert K	891
publication	2003	

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: USEPA, (660/3-75-009) Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians	

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial substance

Analytical monitoring

yes

Details on sampling

Water quality samples were taken daily. Analytical samples were taken at time zero and on a composite of replicates at study termination.

Vehicle

no

Details on test solutions

Test treatments were prepared by using a proportional diluter modified to enhance mixing of phthalates. The dilution water was Wareham, Mass., USA, town water (untreated and unchlorinated). A concentrated stock solution was prepared and combined with dilution water prior to pumping into the diluter.

Test organisms

Test organisms (species)
Oncorhynchus mykiss

Details on test organisms

Mean length = 62 mm Mean wet weight = 2.3 g

Study design

Test type
flow-through

Water media type

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument352c.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f5d8702f-97f0-4849-bcf0-7c5a0cdc8a5a%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934
freshwater

Limit test

no

Total exposure duration

96 h Remarks

Test conditions

Hardness
Range was 20 to 26 mg/L as CaCO3

Test temperature

11 degrees C

pH

Range was 7.1 to 7.4

Dissolved oxygen

Range was 9.5 to 9.6 mg/L

Nominal and measured concentrations

Nominal test concentrations: control, 0.094, 0.19, 0.38, 0.75, and 1.5 ul/L Mean measured test concentrations: <0.021 (control,

minimum level of detection), 0.043, 0.075, 0.14, 0.25, and 0.62 mg/L

Reference substance (positive control)

no

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
96 h	LC50	> 0.62 mg/L	meas. (not specified)	test mat.	mortality	
96 h	NOEC	0.62 mg/L	meas. (not specified)	test mat.	mortality	See other information on results below.

Details on results

96 hr LC50 >0.62 mg/L. Diisodecyl phthalate ester did not produce acute lethal toxicity at the highest achievable concentration under the conditions of this test. Measured values dropped slightly during the exposure period. Droplets of undissolved test material were observed on the surface of all test solutions throughout the exposure period and a film of undissolved test material was observed on the surface of the two high concentrations throughout the test. % Mortality results at 96 hrs per replicate for control and treatment levels: Conc. (mg/L) Rep1/Rep2 Control 0 / 20 0.043 0 / 20 0.075 0 / 10 0.14 0 / 0 0.25 0 / 10 0.62 0 / 0

Reported statistics and error estimates

Statistical methods applied the following procedures: Moving average angle, Probit, and Bionomial Probability.

Any other information on results incl. tables

It was concluded in the European Risk Assessment Report (2003) for DIDP that no chemical toxic effect could be attributed to the substances tested in any of the valid studies used to assess the aquatic toxicity of DIDP. The report went on to state that "a two-generation test with Oryzias latipes showed that oral intake of 20 mg/kg had no adverse effect upon reproduction and growth. It can therefore be concluded that based on the

available data, DIDP has no adverse effects upon fish and that a NOEC cannot be determined."
European Commission (2003). Risk-Assessment Report Vol. 36, 2003 on:1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich, CAS#: 68515-49-1, EINECS#: 271-091-4.and:di-"isodecyl" phthalate (DIDP), CAS#: 26761-40-0, EINECS#: 247-977-1. Publication: EUR 20785 EN.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

The acute rainbow trout (Oncorhynchus mykiss) toxicity data reported for di-isodecyl phthalate ester (DIDP) are consistent with the data for several fish species as summarized by Staples et al. (1997). These data clearly show that DIDP does not produce acute toxicity to fish at or below its maximum attainable water solubliity.

Executive summary

The acute toxicity of di-isodecyl phthalate ester (DIDP) as measured by mortality to rainbow trout (*Oncorhynchus mykiss*) was evaluated in freshwater. DIDP did not produce acute lethal toxicity to*Oncorhynchus mykiss*at its maximum water solubility (0.62 mg/L) under the conditions of this study.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a U.S. EPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1984							
publication	Adams W, Biddinger G, Robillard K and Gorsuch J	1995	A summary of the acute toxicity of 14 phthalate esters to representative aquatic organisms	Environ. Toxicol. Chem. 14(9):1569-1574					
publication	Staples C, Adams W, Parkerton T,	1997	Aquatic toxicity of eighteen phthalate esters	Environ. Toxicol. Chem. 16(5):875-					

	Gorsuch J, Biddinger G and Reinert K	891
publication	2003	

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: USEPA, (660/3-75-009) Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians	

GLP compliance

yes

Test materials

Details on test material

Substance type: commercial product

Analytical monitoring

yes

Details on sampling

Water quality samples were taken daily. Analytical samples were taken at time zero and on a composite of replicates at study termination.

Vehicle

no

Details on test solutions

Test treatments were prepared by using a proportional diluter modified to enhance mixing of phthalates. The dilution water was Wareham, Mass., USA, town water (untreated and unchlorinated). A concentrated stock solution was prepared and combined with dilution water prior to pumping into the diluter.

Test organisms

Test organisms (species)

Cyprinodon variegatus

Study design

Test type

static

Water media type

saltwater

Limit test

no

Total exposure duration

96 h Remarks

Test conditions

Hardness

Range was 25 to 50 mg/L as CaCO3

Test temperature

Range was 21 to 23 degrees C

pH

Range was 7.6 to 7.9

Salinity

19%

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
96 h	LC50	> 0.47 mg/L	meas. (not specified)	test mat.	mortality	
96 h	NOEC	0.47 mg/L	meas. (not specified)	test mat.	mortality	

Details on results

96 hr LC50 >0.47 mg/L. Diisodecyl phthalate ester did not produce acute lethal toxicity at the highest achievable concentration under

the conditions of this test.

Reported statistics and error estimates

Statistical methods applied the following procedures: Moving average angle, Probit, and Bionomial Probability.

Any other information on results incl. tables

It was concluded in the European Risk Assessment Report (2003) for DIDP that no chemical toxic effect could be attributed to the substances tested in any of the valid studies used to assess the aquatic toxicity of DIDP. The report went on to state that "a two-generation test with Oryzias latipes showed that oral intake of 20 mg/kg had no adverse effect upon reproduction and growth. It can therefore be concluded that based on the available data, DIDP has no adverse effects upon fish and that a NOEC cannot be determined."

European Commission (2003). Risk-Assessment Report Vol. 36, 2003 on:1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich, CAS#: 68515-49-1, EINECS#: 271-091-4.and:di-"isodecyl" phthalate (DIDP), CAS#: 26761-40-0, EINECS#: 247-977-1. Publication: EUR 20785 EN.

Applicant's summary and conclusion

Validity criteria fulfilled : yes

Conclusions

The acute sheepshead minnow (Cyprinodon variegatus) toxicity data reported for di-isodecyl phthalate ester (DIDP) are consistent with the data for several fish species as summarized by Staples et al. (1997). These data clearly show that DIDP does not produce acute toxicity to fish at or below its maximum attainable water solublity.

Executive summary

The acute toxicity of di-isodecyl phthalate ester (DIDP) as measured by mortality to sheepshead minnow (*Cyprinodon variegatus*) was evaluated in saltwater. DIDP did not produce acute lethal toxicity to fathead minnow at its maximum water solubility (0.55 mg/L) under the conditions of this study.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a U.S. EPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1983							
publication	Adams W, Biddinger G, Robillard K and Gorsuch J	1995	A summary of the acute toxicity of 14 phthalate esters to representative aquatic organisms	Environ. Toxicol. Chem. 14(9):1569-1574					
publication	Staples C, Adams W, Parkerton T,	1997	Aquatic toxicity of eighteen phthalate esters	Environ. Toxicol. Chem. 16(5):875-					

	Gorsuch J, Biddinger G and Reinert K	891
publication	2003	

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: USEPA, (660/3-75-009) Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians	

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

Details on sampling

Water quality samples were taken daily. Analytical samples were taken at time zero and on a composite of replicates at study termination.

Vehicle

no

Details on test solutions

Test treatments were prepared by using a proportional diluter modified to enhance mixing of phthalates. The dilution water was Wareham, Mass., USA, town water (untreated and unchlorinated). A concentrated stock solution was prepared and combined with dilution water prior to pumping into the diluter.

Test organisms

Test organisms (species)
Pimephales promelas

Study design

Test type
static

Water media type

freshwater

Limit test

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument39ca.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-555752a3-f6bd-4a78-b7e2-6dd41dce014a%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

no

Total exposure duration

96 h Remarks

Test conditions

Hardness

Range was 25 to 50 mg/L as CaCO3

Test temperature

Range was 21 to 23 degrees C

pH

Range was 7.6 to 7.9

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
96 h	LC50	> 0.47 mg/L	meas. (not specified)	test mat.	mortality	
96 h	NOEC	0.47 mg/L	meas. (not specified)	test mat.	mortality	

Details on results

96 hr LC50 >0.47 mg/L. Diisodecyl phthalate ester did not produce acute lethal toxicity at the highest achievable concentration under

the conditions of this test.

Reported statistics and error estimates

Statistical methods applied the following procedures: Moving average angle, Probit, and Bionomial Probability.

Any other information on results incl. tables

It was concluded in the European Risk Assessment Report (2003) for DIDP that no chemical toxic effect could be attributed to the substances tested in any of the valid studies used to assess the aquatic toxicity of DIDP. The report went on to state that "a two-generation test with Oryzias latipes showed that oral intake of 20 mg/kg had no adverse effect upon reproduction and growth. It can therefore be concluded that based on the available data, DIDP has no adverse effects upon fish and that a NOEC cannot be determined."

European Commission (2003). Risk-Assessment Report Vol. 36, 2003 on:1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich, CAS#: 68515-49-1, EINECS#: 271-091-4.and:di-"isodecyl" phthalate (DIDP), CAS#: 26761-40-0, EINECS#: 247-977-1. Publication: EUR 20785 EN.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

The acute fathead minnow (Pimephales promelas) toxicity data reported for di-isodecyl phthalate ester (DIDP) are consistent with the data for several fish species as summarized by Staples et al. (1997). These data clearly show that DIDP does not produce acute toxicity to fish at or below its maximum attainable water solubliity.

Executive summary

The acute toxicity of di-isodecyl phthalate ester (DIDP) as measured by mortality to fathead minnow (*Pimephales promelas*) was evaluated in

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument39ca.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-555752a3-f6bd-4a78-b7e2-6dd41dce014a%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

freshwater. DIDP did not produce acute lethal toxicity to fathead minnow at its maximum water solubility (0.47 mg/L) under the conditions of this study.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a U.S. EPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1983							
publication	Adams W, Biddinger G, Robillard K and Gorsuch J	1995	A summary of the acute toxicity of 14 phthalate esters to representative aquatic organisms	Environ. Toxicol. Chem. 14(9):1569-1574					
publication	Staples C, Adams W, Parkerton T,	1997	Aquatic toxicity of eighteen phthalate esters	Environ. Toxicol. Chem. 16(5):875-					

	Gorsuch J, Biddinger G and Reinert K	891
publication	2003	

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: USEPA, (660/3-75-009) Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians	

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument6d73.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-0d864dec-322a-4011-aaed-12f810335637%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Details on sampling

Water quality samples were taken daily. Analytical samples were taken at time zero and on a composite of replicates at study termination.

Vehicle

no

Details on test solutions

Test treatments were prepared by using a proportional diluter modified to enhance mixing of phthalates. The dilution water was Wareham, Mass., USA, town water (untreated and unchlorinated). A concentrated stock solution was prepared and combined with dilution water prior to pumping into the diluter.

Test organisms

Test organisms (species)
Lepomis macrochirus

Study design

Test type
static

Water media type

freshwater

Limit test

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument6d73.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-0d864dec-322a-4011-aaed-12f810335637%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

no

Total exposure duration

96 h Remarks

Test conditions

Hardness

Range was 25 to 50 mg/L as CaCO3

Test temperature

Range was 21 to 23 degrees C

pH

Range was 7.6 to 7.9

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
96 h	LC50	> 0.37 mg/L	meas. (not specified)	test mat.	mortality	
96 h	NOEC	0.37 mg/L	meas. (not specified)	test mat.	mortality	

Details on results

96 hr LC50 >0.37 mg/L. Diisodecyl phthalate ester did not produce acute lethal toxicity at the highest achievable concentration under

the conditions of this test.

Reported statistics and error estimates

Statistical methods applied the following procedures: Moving average angle, Probit, and Bionomial Probability.

Any other information on results incl. tables

It was concluded in the European Risk Assessment Report (2003) for DIDP that no chemical toxic effect could be attributed to the substances tested in any of the valid studies used to assess the aquatic toxicity of DIDP. The report went on to state that "a two-generation test with Oryzias latipes showed that oral intake of 20 mg/kg had no adverse effect upon reproduction and growth. It can therefore be concluded that based on the available data, DIDP has no adverse effects upon fish and that a NOEC cannot be determined."

European Commission (2003). Risk-Assessment Report Vol. 36, 2003 on:1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich, CAS#: 68515-49-1, EINECS#: 271-091-4.and:di-"isodecyl" phthalate (DIDP), CAS#: 26761-40-0, EINECS#: 247-977-1. Publication: EUR 20785 EN.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

The acute bluegill fish (Lepomis macrochirus) toxicity data reported for di-isodecyl phthalate ester (DIDP) are consistent with the data for several fish species as summarized by Staples et al. (1997). These data clearly show that DIDP does not produce acute toxicity to fish at or below its maximum attainable water solubliity.

Executive summary

The acute toxicity of di-isodecyl phthalate ester (DIDP) as measured by mortality to bluegill fish (*Lepomis macrochirus*) was evaluated in

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument6d73.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-0d864dec-322a-4011-aaed-12f810335637%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

freshwater. DIDP did not produce acute lethal toxicity to bluegill fish at its maximum water solubility (0.37 mg/L) under the conditions of this study.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	2002
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability is rated 2 because the study generally followed an OECD standard guideline, applied valid scientific testing principles, and the results were reviewed for reliability and assessed as valid. However, the study was not conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Study report; company data		2002							

Materials and methods

Test type

other: Two-generation life cycle: reproduction, (sub)lethal effects

Test guideline

Qualifier	Guideline	Deviations
equivalent or similar to	other guideline: OECD Guideline 210 (Fish, Early-Life Stage Toxicity Test) with evaluation of two generations	not applicable

Principles of method if other than guideline

Medaka were used because they are sensitive to estrogen and estrogenic compounds producing ovotestis and other reproductive effects. Medaka reach sexual maturity in 40 to 60 days post-hatch, which allows for a multigeneration study to be completed in one year. The test substance was administered via the diet since this is the major route of exposure to hydrophobic compounds.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

Details on sampling

The test diet was analyzed three times during the study: pre-study, day 136, and day 284.

Vehicle

yes

Details on test solutions

The test substance was administered through the diet.

Test organisms

Test organisms (species)
Oryzias latipes

Study design

Test type
flow-through

Water media type

freshwater

Limit test

yes

Total exposure duration

284 d Remarks

Test conditions

Test temperature
Temperature was measured daily in each replicate chamber and was maintained at 25°C ± 2°C for the duration of the study.

pH

Untreated Acetone Test Control Control Substance pH 6.5-7.6 6.9-7.7 6.8-7.7

Dissolved oxygen

Untreated Acetone Test Control Control Substance Dissolved Oxygen 7.0-8.8 7.1-8.7 6.8-8.8 (mg/l)

Nominal and measured concentrations

A single dietary concentration of the test substance was prepared at a nominal loading of 20 µg/g. The mean measured concentration of the test substance in the test diet ranged from 19.2 ± 0.64 µg/g to 22.7 ± 0.81 µg/g.

Details on test conditions

Diet Preparation: A single dietary concentration was prepared at a nominal loading of 20 µg/g. The exposure concentration represented a reasonable worst-case scenario based on US EPA field measurements and equilibrium partitioning theory predictions for concentrations in prey organisms. The experimental diet was prepared by adding the test substance to Tetramin flake fish food (5% lipid content) with the help of acetone as a solvent in order to evenly distribute the test substance in the fish food. The solvent was allowed to evaporate overnight under ambient laboratory conditions. An acetone solvent control was included with an untreated control group and prepared under similar conditions. The diets were stored at -20°C ± 2°C for the duration of the study to prevent spoilage. The feed was analyzed by GC-MSD for concentration verification purposes prior to, during, and after the study. Methods: A flow-through exposure system was constructed to provide a sufficient volume of water to the exposure chambers. The flow rate (approximately 250 ml/min) was monitored daily and adjusted as necessary in order to maintain optimal water quality for the test

organisms. Five replicate chambers were prepared for each of the three treatment groups (treated, solvent control, untreated control). Test chambers were 19 liter glass aquaria with stainless steel standpipes cut to allow a test volume of 10 liters of water. Embryos collected during the study were hatched in 250 ml glass beakers under continuous aeration. Test water in the hatching chambers was replaced as needed to preserve water quality and maintain embryo health. During overlap between generations, juvenile fish were housed in glass cylinders suspended in the test chambers to prevent losses due to consumption by adult fish. Replicate integrity was maintained throughout the study. For the F0 generation, 50 Medaka larvae per replicate (a total of 250 fish per group) were fed the appropriate diet at a rate of 50% body weight per day. The food ration was periodically adjusted to compensate for growth of the fish during the study. Feeding was also supplemented three times weekly with freshly hatched brine shrimp (Artemia spp.). Observations for mortality were performed and recorded daily. Dead organisms were recorded and removed from the test chambers. Test chambers were also cleaned periodically to remove accumulated organic material. Once adults reached sexual maturity (about 40 to 60 days post-hatch (DPH)), eggs were collected on sponge filters. Egg production was observed for approximately 3 to 4 weeks and recorded before eggs were collected for hatching of the next generation. Eggs for hatching were collected once all replicates were observed producing eggs. During the embryo-rearing stages of the study the rearing chambers were observed daily and all embryos with fungus or an opaque appearance were removed. Eggs from each replicate were hatched to provide 50 larval fish for the next generation. The remaining collected eggs were counted and frozen for chemical analysis. At termination of each generation (140 DPH) there remained at least 25 fish per replicate (125 fish per group). Population, individual, and biochemical test parameters were evaluated at this time. Male and female fish were processed separately. Fish were evaluated for morphometric parameters such as total weight, standard length, gonad weight, and gonadal-somatic index. As with the original population (F0), the F1 fish were allowed to spawn (F2 generation) and fecundity, egg viability, and embryo development were evaluated. Adult F1 fish were also evaluated based on histopathology, morphological characteristics, and biochemical parameters. F1 larvae were evaluated for lesion occurrence, stage development, post-hatch survival and growth. The F2 larvae were allowed to grow out until 42 DPH, at which time they were weighed, measured, sacrificed, and processed for histopathology evaluation.

Reference substance (positive control)

no

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc.	Basis for effect	Remarks (e.g.

284 d	NOEC	>= 19.2 — <= 22.7 ug/g feed	meas. (not specified)	based on test mat.	other: Survival, development, reproduction, carcinogenicity	95% CL)

Details on results

The nominal test substance loading rate was 20 µg/g feed. Mean test concentration of the test diet ranged from 19.2 ± 0.64 ug/g feed to 22.7 ± 0.81 ug/g feed. No significant difference in survival was observed between the treated group and the controls. Mean Percent Mortality Generation F0 F1 F2 Control 11.2 24.6 14.4 Solvent Control 7.6 18.0 14.0 Test Substance 7.6 22.4 12.4 There were no treatment-related gross lesions or disease processes observed in the adult fish. No significant reduction growth or egg production was observed between the treated group and the controls. However, the untreated group produced fewer eggs than both the treated group and the solvent control group in both generations. Sex ratio (male to female) was similar among all groups (approximately 1:1) for the F0, F1 and F2 generations. Phenotypic and histological gender classifications were in agreement for both males and females. There was no statistically significant gonadal-somatic index (GSI) differences among the treated and control groups in either the F0 or the F1 generation. F2 generation juvenile fish were processed on Day 42 post-hatch. The primary organs examined for general developmental conditions and the occurrence of lesions included the brain, digestive system, liver, kidney, gonads, and skeleton. There were no treatment-related histological lesions observed in the fish. The results demonstrate that the test substance did not elicit endocrine-mediated effects such as testis-ova, intersex conditions, or sex reversal in Japanese Medaka. EROD activity of the F1 generation male and female Medaka were not significantly different among the control and treated fish. Activity in male fish ranged from 0.04 to 0.08 pmol/min/mg protein and for female fish ranged from 0.09 to 0.12 pmol/min/mg protein. Significant induction or reduction in EROD activity was considered to be 2-fold different than the solvent control for either male or female hepatic samples. There were also no major metabolic differences among the groups with respect to testosterone hydroxylase activity. Hepatic vitellogenin production was not detectable in Western Blot analysis of F0 and F1 generation male Medaka at 140 DPH. The F0 females showed faint banding at approximately 170 kDa and the F1 females showed a 2 to 3-fold increase in staining when compared to the untreated control group. Positive controls (17ß-estradiol) had a 5 to 6-fold increase in staining in both males and females when compared to the untreated control group. Histological and biochemical endpoints are addressed in a separate peer-reviewed article: Patyna P. et. al. (2006). Hazard evaluation of diisononyl phthalate and diisodecyl phthalate in a Japanese medaka multigenerational assay. Ecotoxicol. Environ. Safety 65(1): 36-47.

Results with reference substance (positive control)

A positive control was not included.

Reported statistics and error estimates

An Analysis of Variance (ANOVA) was used to determine differences in the groups based on survival, growth, and fecundity. The ANOVA was determined using the General Linear Models procedure of SAS.

Remarks on results including tables and figures

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) did not produce significant carcinogenic, teratological, or reproductive effects in the Medaka fish (Oryzias latipes) exposed to DIDP through the diet at a nominal concentration of 20 ug/g feed (measured concentrations ranged from 19.2 to 22.7 ug/g feed).

Executive summary

Specific guidelines for the study were not available. Therefore, the study was performed following procedures outlined in existing chronic fish toxicity test guidelines. The results showed that di-isodecyl phthalate ester (DIDP) did not produce significant carcinogenic, teratological, or reproductive effects in Oryzias latipes in a 284 -day chronic toxicity study. Measured feed concentrations of DIDP through the study ranged from 19.2 to 22.7 ug/g feed.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a U.S. EPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		1998							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test)	no

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

Vehicle

yes

Details on test solutions

Test substance exposure solutions were prepared by adding 1 mg/L of the test substance and 10 mg/L of dispersant (Marlowet 40) to one liter of dilution medium. The dilution medium was Elendt's medium (Elendt and Bias, 1990), which was pH adjusted to 8 and aerated for >2 hours prior to use.

Test organisms

Test organisms (species)

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumente5a3.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-dae8749a-46cd-4aac-ac01-1a61b62778d4%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934
Daphnia magna

Details on test organisms

Organisms were supplied by in-house continuous cultures. Age = <24 hours old. Test organisms were not fed during the study.

Study design

Test type
static

Water media type

freshwater

Limit test

yes

Total exposure duration

48 h
Remarks

Test conditions

Test temperature
19 to 21 degrees C

pH

8

Dissolved oxygen

8 to 9 mg/L

Nominal and measured concentrations

A chronic and acute study were conducted following the same test solution preparation procedures. The nominal test substance loading was 1 mg/L for both tests. The mean measured test substance concentrations for the 21-day period were 1.0 mg/L in new exposure solutions and 1.0 mg/L in old exposure solutions, which represents 100 and 100%, respectively, of the nominally added test substance. However, the analytical results for the acute study were not included in the article. Because test conditions were similar for both the chronic and acute studies, the exposure concentrations in the acute study are likely to have been equivalent to the day 21 results.

Details on test conditions

Test substance exposure solutions were prepared by adding 1 mg/L of the test substance and 10 mg/L of dispersant (Marlowet 40) to one liter of dilution medium. The dilution medium was Elendt's medium (Elendt and Bias, 1990), which was pH adjusted to 8 and aerated for >2 hours prior to use. Two replicate test systems, containing five daphnids each (<24 hours old), were prepared for the single treatment, control and dispersant control. Test chambers were glass beakers with loose fitting lids. Each beaker contained 80 ml of exposure solution with a depth of approximately 5 cm. The study was conducted under static conditions in a temperature controlled room. Lighting = 16 hours light and 8 hours dark with a 15 minute transition period.

Reference substance (positive control)

no

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
48 h	LL50	> 1 mg/L	nominal	test mat.	mortality	
48 h	NOELR	1 mg/L	nominal	test mat.	mortality	
48 h	EC50	> 1 mg/L	meas. (arithm. mean)	test mat.	mobility	Analytical data are from the chronic study conducted after the acute study. Since the solution preparation procedures were similar for the two studies, the analytical results from the chronic study are used to estimate the acute solution concentration.
48 h	NOEC	1 mg/L	meas. (arithm. mean)	test mat.	mobility	Analytical data are from the chronic study conducted after the acute study. Since the solution preparation procedures were similar for the two studies, the analytical results from the chronic study are used to estimate the acute solution concentration.

Details on results

LL50 >1.0 mg/L (with 10 mg/L dispersant), based on nominal loading level of the test substance. LC50 >1.0 mg/L (with 10 mg/L dispersant), based on analytical measurements for chronic study run subsequently with same test substance at same loading level. NOELR = 1.0 mg/L (with 10 mg/L dispersant), based on nominal loading level. NOELR = 1.0 mg/L (with 10 mg/L dispersant), based on analytical measurements for chronic study run subsequently with same test substance at same loading level. No immobilization or flotation effects were observed over the 48-hour test period in either thet treatment or control solutions.

Applicant's summary and conclusion

Validity criteria fulfilled

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumente5a3.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-dae8749a-46cd-4aac-ac01-1a61b62778d4%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) does not produce acute toxicity (immobility) to Daphnia magna, based on the results from a study that evaluated DIDP in the presence of a surfactant and at a loading level above its water solubility.

Executive summary

The acute toxicity of di-isodecyl phthalate ester (DIDP) as measured by immobility to the water flea (Daphnia magna) was evaluated in freshwater.

Di-isodecyl phthalate ester (DIDP) was not acutely toxic to Daphnia and results from this study are consistent with the extant aquatic toxicity database for DIDP. Testing in this study was conducted at a loading rate with a surfactant that exceeds the water solubility of DIDP (1 mg/L) after it was demonstrated that such a procedure was able to satisfactorily disperse the test substance and prevent flotation of the test organisms (a documented problem that can occur when evaluating the toxicity of similar substances).

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a U.S. EPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1984							
publication	Adams W, Biddinger G, Robillard K and Gorsuch J	1995	A summary of the acute toxicity of 14 phthalate esters to representative aquatic organisms	Environ. Toxicol. Chem. 14(9):1569-1574					
publication	Staples C, Adams W, Parkerton T,	1997	Aquatic toxicity of eighteen phthalate esters	Environ. Toxicol. Chem. 16(5):875-					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: USEPA, (660/3-75-009) Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians	no

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

Details on sampling

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument95ee.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-7c066180-f172-44ab-bf0f-878979325bb1%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Analytical samples taken at time zero and on a composite of replicates at termination. Measured values declined during study exposure. The concetration of test substance measured in the high treatment solution is considered the maximum solubility achievable under the conditions of this test.

Vehicle

no

Test organisms

Test organisms (species)
Daphnia magna

Details on test organisms

Daphnia were <24 hours old and obtained from in-house stock.

Study design

Test type
static

Water media type

freshwater

Limit test

yes

Total exposure duration

48 h

Remarks

Test conditions

Hardness

The range of total hardness as CaCO3 of the dilution water was 150 to 170 mg/L.

Test temperature

Test temperature = 20 degree C.

pH

The pH ranged from 7.9 to 8.0 at initiation and was 8.2 on day 2.

Dissolved oxygen

Dissolved oxygen ranged from 7.6 to 8.4 at initiation and 8.4 to 8.5 on day 2.

Nominal and measured concentrations

Nominal test concentrations: control, 0.16, 0.26, 0.43, 0.72, and 1.2 ul/L. Mean measured test concentrations of time 0 and 48 hr values: <0.014, 0.074, 0.12, 0.22, 0.34, and 0.61 mg/L.

Details on test conditions

Test treatments for the initial test were prepared by mixing the test substance and dilution water (fortified well water) in a Polytron

homogenizer for 30 minutes. The stock solution was prepared at the highest treatment concentration. Dilutions of the stock were prepared for each treatment level. Three replicates of five organisms were tested per treatment. Test vessels were 250 ml beakers with 200 ml of test solution. Analytical method was Gas Liquid Chromatography (GLC). Water quality parameters for the first test: Test temperature = 21.5 +/- 0.5 Deg C. The pH was 8.4 at initiation and 8.4 on day 2. Dissolved oxygen ranged from 8.3 to 8.5 at initiation and 8.0 to 8.4 on day 2. The range of total hardness of the dilution water was 150 to 170 mg/L. Daphnia were <24 hours old and obtained from in-house stock. Test treatments for the repeat study were prepared by mixing the test substance and 3 L of dilution water (fortified well water) on a magnetic stirrer for 1 hour at a loading of 9.7 mg/L, with a 50% vortex. After mixing the treatment solution was allowed to stand for 1 hour after which 2.5 L of solution was drained from the bottom of the flask into a glass bottle. The solution was allowed to stand for 24 hours after which 2.0 L was drained from the bottom into the test flasks and samples removed for analysis. Three replicates of five organisms were tested. Test vessels were 250 ml beakers with 200 ml of test solution. Control test vessels were prepared under the same conditions but without test substance. Analytical method was Gas Liquid Chromatography (GLC). Water quality parameters for the second test: Test temperature = 20 Deg C. The pH ranged from 7.9 to 8.0 at initiation and was 8.2 on day 2. Dissolved oxygen ranged from 7.6 to 8.4 at initiation and 8.4 to 8.5 on day 2. The range of total hardness of the dilution water was 150 to 170 mg/L. Daphnia were <24 hours old and obtained from in-house stock.

Reference substance (positive control)

no

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
48 h	LC50	> 0.02 mg/L	meas. (not specified)	test mat.	mobility	
48 h	NOEC	0.02 mg/L	meas. (not specified)	test mat.	mobility	

Details on results

48 hr EC50 >0.18 mg/L (based upon time zero analytical samples; no effects at test substance saturation). Value was recalculated as >0.02 mg/L as per U.S. EPA current practices using mean of measured initiation and termination samples as reported in Staples et al.

(1997). Mean measured values were used in the final EC50 calculation. % Immobility results at 48 hrs per replicate for control and treatment levels in the first test: Conc. (mg/L) Rep1/Rep2/Rep3 Control 0 / 0 / 20 0.074 0 / 0 / 20 0.12 20 / 20 / 40 0.22 40 / 80 / 80 0.34 60 / 100 / 100 0.61 100 / 100 / 100 More than 50% of the organisms were trapped on the surface of all treatment solutions and a film of test material was present in all but the lowest treatment level. Consequently, the study was repeated as a limit test using a saturated treatment solution. % Immobility results at 48 hrs per replicate for control and treatment levels in the second limit test: Conc. (mg/L) Rep1/Rep2/Rep3 Control 0 / 0 / 0 0.02 0 / 0 / 0 Undissolved test substance was avoided in the repeat study. Data from the second test are used to characterize the acute toxicity of the test substance.

Reported statistics and error estimates

Statistical methods applied the following procedures: Moving average angle, Probit, and Bionomial Probability.

Remarks on results including tables and figures

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) does not produce acute toxicity (immobility) to Daphnia magna at its maximum water solubility (0.02 mg/L) under the conditions of this study.

Executive summary

The acute toxicity of di-isodecyl phthalate ester (DIDP) as measured by immobility to the water flea (*Daphnia magna*) was evaluated in freshwater. DIDP did not produce acute toxicity to Daphnia at its maximum water solubility (0.02 mg/L) under the conditions of this study.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a U.S. EPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1984							
publication	Adams W, Biddinger G, Robillard K and Gorsuch J	1995	A summary of the acute toxicity of 14 phthalate esters to representative aquatic organisms	Environ. Toxicol. Chem. 14(9):1569-1574					
publication	Staples C, Adams	1997	Aquatic toxicity of	Environ. Toxicol.					

W, Parkerton T, Gorsuch J, Biddinger G and Reinert K	eighteen phthalate esters	Chem. 16(5):875-891

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: USEPA, (660/3-75-009) Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians	no

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumente16d.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-519e8bcb-c551-42b9-8b4f-7fb0be32a12d%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Vehicle

no

Test organisms

Test organisms (species)
Mysidopsis bahia (new name: Americamysis bahia)

Study design

Test type
static

Water media type

saltwater

Limit test

no

Total exposure duration

96 h
Remarks

Test conditions

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumente16d.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-519e8bcb-c551-42b9-8b4f-7fb0be32a12d%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Reference substance (positive control)

no

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
96 h	LC50	> 0.08 mg/L	meas. (initial)	test mat.	mortality	
96 h	NOEC	0.08 mg/L	meas. (initial)	test mat.	mortality	

Details on results

96 hr LC50 >0.08 mg/L. Di-isodecyl phthalate ester did not produce acute lethal toxicity at the highest achievable concentration under the conditions of this test. Mean measured values were used in the LC50 calculation.

Reported statistics and error estimates

Statistical methods applied the following procedures: Moving average angle, Probit, and Bionomial Probability.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) does not produce acute lethal toxicity to Mysidopsis bahia at its maximum water solubility (0.08 mg/L) under the conditions of this study.

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumente16d.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-519e8bcb-c551-42b9-8b4f-7fb0be32a12d%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Executive summary

The acute toxicity of di-isodecyl phthalate ester (DIDP; CAS #68515-49-1) as measured by lethality to Mysidopsis bahia was evaluated in saltwater. DIDP did not produce acute toxicity to mysids at its maximum water solubility (0.08 mg/L) under the conditions of this study.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability is rated 2 because the study followed an OECD standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, but the study did not followed GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Brown D and Thompson R	1982	Phthalates and the aquatic environment: Part 1. The effect of di-2-ethylhexyl phthalate (DEHP) and di-isodecyl phthalate (DIDP) on the reproduction of Daphnia magna and observations on their bioconcentration	Chemosphere 11(4):417-426					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test)	no

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

no

Details on test material

A C14 Radiolabeled di-isodecyl phthalate ester was tested. Chemical purity = 98%. An acetone carrier was used.

Analytical monitoring

yes

Vehicle

yes

Test organisms

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument90f5.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-acdbcbbb-b2d1-47c9-8cfb-78f4778bfd9d%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Test organisms (species)
Daphnia magna

Study design

Test type
static

Water media type

freshwater

Limit test

no

Total exposure duration

48 h
Remarks

Test conditions

Reference substance (positive control)
no

Results and discussions

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument90f5.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-acdbcbbb-b2d1-47c9-8cfb-78f4778bfd9d%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
48 h	EC50	> 0.32 mg/L	meas. (not specified)	test mat.	mobility	

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) does not produce acute toxicity (immobility) to Daphnia magna at its maximum water solubility (0.32 mg/L) under the conditions of this study.

Executive summary

The acute toxicity of di-isodecyl phthalate ester (DIDP) as measured by immobility to the water flea (Daphnia magna) was evaluated in freshwater. DIDP did not produce acute toxicity to a Daphnia at its maximum water solubility (0.32 mg/L) under the conditions of this study.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a U.S. EPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1984							
publication	Adams W, Biddinger G, Robillard K and Gorsuch J	1995	A summary of the acute toxicity of 14 phthalate esters to representative aquatic organisms	Environ. Toxicol. Chem. 14(9):1569-1574					
publication	Staples C, Adams	1997	Aquatic toxicity of	Environ. Toxicol.					

W, Parkerton T, Gorsuch J, Biddinger G and Reinert K	eighteen phthalate esters	Chem. 16(5):875-891

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: USEPA, (660/3-75-009) Methods for Acute Toxicity Tests with Fish, Macroinvertebrates, and Amphibians	no

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument68c2.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-56309be7-157a-4268-90ff-29e5344f181b%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Vehicle

no

Test organisms

Test organisms (species)
other: Paratanytarsus parthenogenetica

Study design

Test type
static

Water media type

freshwater

Limit test

no

Total exposure duration

96 h
Remarks

Test conditions

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument68c2.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-56309be7-157a-4268-90ff-29e5344f181b%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Reference substance (positive control)
no

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
48 h	LC50	> 0.64 mg/L	meas. (initial)	test mat.	mortality	
48 h	NOEC	0.64 mg/L	meas. (initial)	test mat.	mortality	

Reported statistics and error estimates

Statistical methods applied the following procedures: Moving average angle, Probit, and Bionomial Probability.

Applicant's summary and conclusion

Validity criteria fulfilled
yes

Conclusions

Di-isodecyl phthalate ester (DIDP) does not produce acute toxicity to Paratanytarsus parthenogenetica at its maximum water solubility (0.96 mg/L) under the conditions of this study.

Executive summary

The acute toxicity of di-isodecyl phthalate ester (DIDP) as measured by lethality to a midge (*Paratanytarsus parthenogenetica*) was evaluated in freshwater. DIDP did not produce acute toxicity to a midge at its maximum water solubility (0.96 mg/L) under the conditions of this study.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	May - July 1997
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed an OECD standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Study report; company data		1998							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations

equivalent or similar to	OECD Guideline 211 (Daphnia magna Reproduction Test)	yes : minor temperature deviation; it was not determined if 3 broods per female were produced, however, it is believed that a sufficient number of young per adult were produced in the controls of each study to evaluate the study.

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

Details on sampling

Samples were removed from each treatment and the control ("old" solutions) on transfer days 3 or 2 times a week. Samples were also removed at termination.

Vehicle

no

Test organisms

Test organisms (species)
Daphnia magna

Details on test organisms

Organism age = <24 hours. Organisms used in the study were from an in-house culture.

Study design

Test type
semi-static

Water media type

freshwater

Limit test

yes

Total exposure duration

21 d Remarks

Test conditions

Hardness

Water hardness = 146 to 184 mg/L (as CaCO3) Alkalinity = 51 to 56 mg/L (as CaCO3)

Test temperature

Temperature = 19.5 to 20.9 degree C

pH

pH = 7.0 to 8.1

Dissolved oxygen

Dissolved oxygen = 7.7 to 9.4 mg/L

Details on test conditions

Test chambers were glass cylinders with Nitex mesh over the bottom. The mesh allowed the water accommodated fraction to circulate throughout the test chambers. The test chambers were suspended in the mixing vessels at a sufficient height to produce an approximate replicate volume of 250mL. The mixing vessels were approximately 13L glass battery jars with a glass and Teflon sampling port at the bottom. The test chambers were covered with plexiglass sheets to minimize contamination. Prior to the addition of the test substance, four replicate chambers were suspended into a glass mixing vessel containing 12.0L of dilution water. This was done to prevent the daphnids from becoming trapped by the test substance floating at the surface. The test substance was then added, volumetrically by glass syringe, approximately 24 hours prior to the addition of the test organisms. The mixing vessels were stirred continuously at a low speed (no vortex) on a magnetic stirplate with a Teflon coated stirbar. The test substance was observed floating on the surface of the mixing vessels. Treatments were prepared every 2 to 3 days (Sun, Tues, Thurs), for renewal, approximately 24 hours prior to the addition or transfer of test organisms. After the transfer of adults and the removal of neonates, all glassware was rinsed with dialyzed water to remove food residue. Observations for mortality/immobilization, abnormal behavior and appearance of the daphnids were performed on all replicate chambers at 24-hour intervals (+/- 1 hour). Adults were transferred, via pipette, to "new" solution every 2 to 3 days (Mon, Wed, Fri) at time of observation. Water quality measurements (pH, dissolved oxygen and temperature) were performed in each "new" and "old" treatment on transfer days and at termination. Once neonates were observed they were counted every 2 to 3 days (Mon, Wed, Fri) and then discarded. Daphnia were fed Selenastrum capricornutum (approx. 0.5

mL / replicate / day days 0 to 6 and approx 1.0 mL / replicate / day days 7 to 21) and yeast/salmon starter/cereal leaves mixture (approx 3.0 mL / replicate / day) during testing. Daphnids were fed once per day during study 1 and the same amount of food was split over two feedings during study 2. This was done to increase the availability of the food to the daphnids and appeared to increase reproduction across all the treatments and controls as seen in the neonate production data.

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
21 d	EC50	> 0.0034 mg/L	meas. (arithm. mean)	test mat.	reproduction	
21 d	NOEC	0.0034 mg/L	meas. (arithm. mean)	test mat.	reproduction	

Details on results

Daphnia percent parent (Po) survival and percent reduction in reproduction were evaluated as the biological endpoints. Diisodecyl phthalate ester (DIDP) showed no statistical effect on survival or reproduction at its water solubility limit, achieved from a loading of 2.0 mg/L under the conditions of this test. Day 21 results from study 1: Po % Mortality % Reduction in Reproduction (a) Control 10 na DIDP 10 19 Day 21 results from study 2: Po % Mortality % Reduction in Reproduction (a) Control 18 na DIDP 28 0 (a) - percent reduction relative to control na - not applicable A 19% reduction in neonate production, as compared to the control, was observed at the end of the 21-day test period in study 1. A comparison of mean neonate production per female was performed using a one-tailed t-test (Zar, 1984) with data from the four exposure chambers. Based on the results of the t-test, the 19% reduction was not significantly different since one replicate chamber had greatly reduced neonate production compared to the other three. Daphnids were fed once per day during study 1 and the same amount of food was split over two feedings during study 2. This was done to increase the availability of the food to the daphnids and appeared to increase reproduction across all the treatments and controls as seen in the neonate production data. Neonate production study 1, day 21 Control average = 46.9 (replicates were 44.3, 48.9, 43.7, 50.6) DIDP treatment average = 38.1 (replicates were 38.5, 31.7, 41.7, 41.7) Neonate production study 2, day 21 Control average = 71.8 (replicates were 78.8, 79.7, 62.4, 66.3) DIDP treatment average = 84.9 (replicates were 87.5, 90.1 75.5 86.4)

Reported statistics and error estimates

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentbf51.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-b49038cd-1913-41b2-818c-2ebfec2af21d%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

No significant effect on daphnid reproduction, when compared to the control, was observed for the test substance based on a one-tailed t-test at a 95% confidence level.

Remarks on results including tables and figures

Two trials were performed for the first study. The first trial was terminated on Day 8 due to 23% mortality/immobilization in the control. The guideline requires control mortality not to exceed 20% for the 21-day period. Excessive control mortality/immobilization is not infrequent in*Daphnia magna*and is unrelated to exposure to the test substance.

A 19% reduction in neonate production, as compared to the control, was observed at the end of the 21-day test period in the first study. A comparison of mean neonate production per female was performed using a one-tailed t-test (1). Based on the results of the t-test, the 19% reduction was not considered significantly different since one replicate chamber had greatly reduced neonate production compared to the other three.

Two trials were also performed for the second study. The first trial was terminated on Day 4 due to 90% mortality/immobilization in a single replicate. No other mortality/immobilization was observed in the treatment. The data and results of the second trial were included in the report.

The test substance showed varied results in neonate production between the two studies. However, neither value was statistically significant, based on a one-tailed t-test at a confidence of 95%, when compared to the control.

Zar, Jerrold H., 1984.*Biostatistical Analysis*. Second Edition. Prentice-Hall., Cliffs, . pp 126-131.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) did not affect reproductive capacity in Daphnia magna at the maximum water soluble concentration acheivable under the test conditions, 0.0034 mg/L.

Executive summary

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentbf51.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-b49038cd-1913-41b2-818c-2ebfec2af21d%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

The chronic toxicity of di-isodecyl phthalate ester (DIDP; CAS #68515-49-1) as measured by reproductive success to the water flea (*Daphnia magna*) was evaluated in freshwater. No significant effect was observed at the maximum DIDP water solubility under the conditions of the test, which measured 0.0034 mg/L.

These chronic invertebrate (*Daphnia magna*) toxicity data are consistent with valid data for several high molecular weight phthalate estersas summarized by Staples et al. (1997). These data together with the current study results show that high molecular weight phthalate esters, includingdiisodecyl phthalate ester, do not produce chronic toxicity to*Daphnia magna.*

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed an OECD standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		1998							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
equivalent or similar to	OECD Guideline 211 (Daphnia magna Reproduction Test)	no

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentc336.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-dd4c7b49-b340-47d2-bb57-8c48e4525c07%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Principles of method if other than guideline

The test method followed the Daphnia chronic testing procedure described in OECD guideline 202 (1984) with the use of a dispersant, castor oil 40-ethoxylate (Marlowet 40), in accordance with guideline specifications.

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

Details on sampling

Test substance analyses were performed on new and old exposure solutions.

Vehicle

yes

Test organisms

Test organisms (species)
Daphnia magna

Study design

Test type
semi-static

Water media type

freshwater

Limit test

yes

Total exposure duration

21 d Remarks

Test conditions

Hardness
Water harness = >140 mg/L (as CaCO3) Alkalinity = >100 mg/L (as CaCO3)

Test temperature

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentc336.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-dd4c7b49-b340-47d2-bb57-8c48e4525c07%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Temperature = 20 +/- 1.0 degree C

pH

pH = approximately 8

Dissolved oxygen

Dissolved oxygen = 8-9 mg/L

Nominal and measured concentrations

The mean measured test substance concentrations were 1.0 mg/L in new exposure solutions and 1.0 mg/L in the old exposure solutions, which represents 100 and 100%, respectively, of the nominally added test substance.

Details on test conditions

Test substance exposure solutions were prepared using stock dispersions prepared by adding 100 mg substance and 1000 mg dispersant (castor oil 40-ethoxylate; Marlowet 40), then bringing the test solution to 1 L by adding dilution medium. The dilution medium was Elendt's medium (Elendt and Bias, 1990), which was pH adjusted to 8 and aerated for >2 hours prior to use. Ten replicate test systems with 1 daphnid each (< 24 hours old) were prepared in glass beakers with loose fitting lids. Each beaker contained 80 ml of exposure solution with a depth of approximately 5 cm. The photoperiod was controlled to 16 hours light and 8 hours dark with a 15 minute transition period. The exposure solution was renewed every Monday, Wednesday, and Friday. On each renewal day the parent organism (Po) was transferred to a new exposure solution and neonates (F1) were counted. Water quality measurements including dissolved oxygen concentration and pH were determined at every renewal for the new and old exposure and control solutions. Standard daily feeding rates with the cultured alga, Chlorella vulgaris, was supplemented with microencapsulated food, "Frippak Booster".

Reference substance (positive control)

no

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
21 d	EC50	> 1 mg/L	meas. (arithm. mean)	test mat.	reproduction	
21 d	NOEC	1 mg/L	meas. (arithm. mean)	test mat.	reproduction	

Details on results

Daphnia parent (Po) survival, reproduction (cumulative number of offspring, F1, per live parent), and parent length were evaluated as the biological endpoints. Diisodecyl phthalate ester showed no effect on survival, reproduction, and length at a loading of 1.0 mg/L test substance and 10 mg/L dispersant under the conditions of this test. Po % Mortality Mean F1/Surviving Po Mean Length Po Test Substance 10 105 (sd=7) 4.2 (sd=0.12) Control 0 93 (sd=9) 4.1 (sd=0.17)

Remarks on results including tables and figures

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) did not produce reproductive effects in Daphnia magna at a test concentration in excess of its water solubility (1 mg/L), which was achieved using a dispersant.

Executive summary

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentc336.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-dd4c7b49-b340-47d2-bb57-8c48e4525c07%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

The chronic toxicity of di-isodecyl phthalate ester (DIDP) as measured by reproductive success to the water flea (*Daphnia magna*) was evaluated in freshwater. No significant effect was observed under the conditions of the test, which evaluated DIDP, measured at 1 mg/L, with a surfactant.These chronic invertebrate (*Daphnia magna*) toxicity data are consistent with valid data for several high molecular weight phthalate estersas summarized by Staples et al. (1997). These data together with the current study results show that high molecular weight phthalate esters, includingdi-isodecyl phthalate ester, do not produce chronic toxicity to*Daphnia magna*.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The study is rated 1 because the test procedure followed an accepted test guideline and was conducted under GLP. The data are consistent with known toxicological properties of similar high molecular weight phthalate ester substances. Control chlorophyll or cell counts were not reported.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1984							
publication	Adams W, Biddinger G, Robillard K and Gorsuch J	1995	A summary of the acute toxicity of 14 phthalate esters to representative aquatic organisms	Environ. Toxicol. Chem. 14(9):1569-1574					
publication	Staples C, Adams W, Parkerton T,	1997	Aquatic toxicity of eighteen phthalate esters	Environ. Toxicol. Chem. 16(5):875-					

Gorsuch J,
Biddinger G and
Reinert K 891

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	other guideline: USEPA 600/9-78-018, Printz Algal Assay Bottle Test	yes

Principles of method if other than guideline

Deviation: Control chlorophyll or cell counts were not reported.

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentc87f.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-52fb016d-20cb-4ef6-aa20-b0e0dafba4a2%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934
yes

Test organisms

Test organisms (species)
Selenastrum capricornutum (new name: Pseudokirchnerella subcapitata)

Details on test organisms

Algal culture stock was obtained from University of Texas at Austin, TX, USA.

Study design

Test type
static

Water media type

freshwater

Limit test

yes

Total exposure duration

192 h
Remarks

Test conditions

Test temperature

Test temperature = 22+/-2 Degrees C

pH

pH = 7.5 at test initiation and 8.6 on day 8.

Details on test conditions

Algal Growth Medium was used as the control and diluent. 10 uL of test substance was added to 1.0 L of sterile water to form a saturated phthalate solution. This solution was sonicated for 1 minute and allowed to settle for 4 hours. After settling, the water soluble fraction (WSF) was removed for testing. Initial algal concentration was 2.0 E4 cells/ml. Only one treatment level was evaluated (100% WSF) because earlier phthalate testing suggested that toxic effects were not expected with higher molecular weight phthalate esters with low water solubility. Lighting = 4,700 lux

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
8 d	EC50	> 0.8 mg/L	meas. (not specified)	test mat.	other: biomass and growth rate	
8 d	NOEC	0.8 mg/L	meas. (not specified)	test mat.	other: biomass and growth rate	

Details on results

192 hr (8 day) EC50 >1.3 mg/L (based upon time zero analytical samples). Value was recalculated as >0.8 mg/L as per U.S. EPA current practices using mean of measured initiation and termination samples as reported in Staples et al. (1997). Mean measured values were used in the final EC50 calculation. Nominal test concentration as a percent of a saturated solution: 0 (control) and

100.0%. Mean measured test concentrations of time 0 and 144 hr values: <0.10 and 0.8 mg/L (detection limit was 0.10 mg/L). Analytical samples taken at time zero and on a composite of replicates at termination. In-vivo chlorophyll a, measured until less than 5% change. Both cell number and in-vivo chlorophyll a, were measured at termination. Control chlorophyll a and cell counts were not reported. A stimulatory effect of DIDP as compared with the control for chlorophyll a was measured on all sampling days after day 1. Analytical samples were taken at time zero and on a composite of replicates at termination. Chlorophyll a percent change relative to control on sampling days and cell number on day 8 results: Conc. Chlorophyll a Percent Change From Control (mg/L) Day 1 Day 2 Day 4 Day 6 Day 8 Cell # Day 8 0.8 0 +2 +21 +23 +9 +2

Reported statistics and error estimates

Moving average angle, Probit or Bionomial

Remarks on results including tables and figures

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) does not produce toxicity (growth inhibition) to Selenastrum capricornutum at its maximum water solubility (0.8 mg/L) under the conditions of this study.

Executive summary

The toxicity of di-isodecyl phthalate ester (DIDP) as measured by biomass and growth rate to the green alga (*Selenastrum capricornutum*) was evaluated in freshwater. No significant effect was observed at the maximum DIDP water solubility under the conditions of this study, which measured 0.8 mg/L.

Administrative Data

Purpose flag	supporting study		
Study result type	experimental result	Study period	April 1997
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability is rated 2 because the study proceedure followed an accepted test guideline, but was not conducted under GLP. The data are consistent with known toxicological properties of similar high molecular weight phthalate ester substances.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Study report; company data		1998							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations

according to other guideline: Microtox(tm) Assay no

Principles of method if other than guideline

The assay measures photo-luminescence response of the marine bacterium Photobacterium phophoreum. Adverse effects are measured as a decrease in photo-luminescence.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

Vehicle

yes

Test organisms

Test organisms (species)

Photobacterium phosphoreum

Study design

Test type

static

Water media type

saltwater

Limit test

yes

Total exposure duration

15 min

Remarks

Test conditions

Test temperature

Approximately 22 Degrees C

Details on test conditions

A nominal concentration of 100 mg/l test substance with Tween 20 dispersant was prepared in lab dilution water contained in a glass

vessel that included a teflon stir bar. The vessel was then placed on a stir plate and agitated for 24 hrs. A sample of the water accommodated fraction was then removed from a port at the bottom of this vessel for microtox testing. Serial dilutions representing 100%, 50%, 25%, 12.5% and 6.25% were prepared and assayed with the Microtox assay according to procedures specified by the manufacturer. The 100% test material concentration was analytically verified as 83 mg/L.

Reference substance (positive control)

yes

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
5 min	NOEC	83.3 mg/L	meas. (initial)	test mat.	other: Photo-luminescence	5.9
15 min	NOEC	83.3 mg/L	meas. (initial)	test mat.	other: Photo-luminescence	5.9

Details on results

The study included two exposure intervals, 5 and 15 minutes. The test material did not demonstrate inhibition to photo-luminescence at either exposure interval.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) did not inhibit photo-luminescence in the bacterium, Photobacterium phosphoreum, at a high test

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument9985.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-d466a1f2-a7a5-4958-a78b-aae8c3d6c4e6%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

material loading of 100 mg/L (83.3 mg/L measured). Therefore, the DIDP is not expected to adversely impact microbial activity.

Executive summary

Di-isodecyl phthalate (DIDP) ester did not inhibit photo-luminescence in the bacterium, *Photobacterium phosphoreum*, at a concentration that exceeds its water solubility, 83.3 mg/L. Therefore, the DIDP is not expected to adversely impact microbial activity.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	April 1997
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability is rated 2 because the study proceedure followed an accepted test guideline, but was not conducted under GLP. The data are consistent with known toxicological properties of similar high molecular weight phthalate ester substances.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Study report; company data		1998							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations

according to OECD Guideline 209 (Activated Sludge, Respiration Inhibition Test) no

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

Vehicle

yes

Test organisms

Test organisms (species)
activated sludge of a predominantly domestic sewage

Study design

Test type

static

Water media type

freshwater

Limit test

yes

Test conditions

Test temperature

Approximately 22 Degrees C

Dissolved oxygen

Dissolved oxygen was 7.71, 7.41, and 7.04 in the DIDP test systems at time 0. Dissolved oxygen was 7.63, 7.83, and 7.62 in the control systems at time 0. After a 30-minute contact time, the contents of each test system were poured into a 300 mL BOD bottle and DO was measured at one minute intervals over a 10 minute period, or until the DO level was approximately 2.5 mg /L, which ever occurred first. Control samples were analyzed at the initiation, the mid point, and the termination of the inhibition testing.

Nominal and measured concentrations

Nominal concentration = 100 mg/L. Measured concentration = 83.3 mg/L

Details on test conditions

Diisodecyl phthalate ester (DIDP) was obtained from Exxon Chemical, New Milford, CT. Due to the very low water solubility of this

substance, a surfactant, sorbitan monolaurate 20 ethoxylate (Tween 20), was used. The Tween 20 was obtained from Mallinckrodt (US), and had a purity of 99+%. DIDP was tested at a nominal concentration of approximately 100 mg/L. A positive control, 3,5-dichlorophenol (DCP), was also tested at 5, 15, and 30 mg/L, which is the expected range for the EC50 concentration (OECD test guideline 209). Preliminary testing of Tween 20 at 1000 mg/L (i.e., the concentration of Tween 20 included in the phthalate dispersions tested) indicated neither stimulation or inhibition of respiration rates. Fresh activated sludge, used as the source of microbial inoculum in the respiration inhibition test, was obtained from a domestic wastewater treatment facility operated by the Pike Brook Sewage Treatment Plant in Belle Mead, New Jersey, USA. Soluble organic material was removed by washing the sludge solids with three consecutive tap water rinses and the final volume adjusted to achieve an approximate total suspended solids (TSS) of 4 g/L. The solids concentration of the respiration inhibition test systems were approximately 1.6 g/L after dilution with the remaining components. A synthetic sewage solution containing an excess of biodegradable substrate was used to feed the fresh activated sludge inoculum in order to stimulate a high metabolic rate. The synthetic substrate solution was prepared by combining the following: 16 grams peptone, 11 grams beef extract, 3 grams urea, 0.7 grams sodium chloride, 0.4 grams calcium chloride, 0.2 grams magnesium sulfate heptahydrate, and 2.8 grams potassium hydrogen phosphate. The mixture was diluted to a 1.0 liter final volume with glass distilled water. Respiration inhibition was assessed by monitoring dissolved oxygen concentration (DO mg/L) in each test system using an Orion pH/selective ion meter, model 720A, coupled to an Orion dissolved oxygen probe, model 97-0899. Triplicate test systems were evaluated. Each test system was prepared in a 500 mL beaker. Each 500 mL beaker received the following additions (not in order of actual sequence followed): 200 mL of fresh activated sludge (TSS 4 g/L), 16 mL of synthetic sewage, 50.0 mL of the stock phthalate dispersion solution, and a sufficient amount of water to bring the total volume of the system to 500 mL. Triplicate control systems were also prepared which contained sludge, synthetic sewage, 50.0 mL of a 10,000 mg/L Tween 20 solution and sufficient water to bring the total volume of the system to 500 mL. The DCP test systems were prepared in 500 mL beakers by pipetting 5, 15, and 30 mL of a 500 mg/L stock solution to individual test systems, followed by addition of 50.0 mL of the 10,000 mg/L Tween 20 solution, sludge, synthetic sewage, and water. After a 30-minute contact time, the contents of each test system were poured into a 300 mL BOD bottle and DO was measured at one minute intervals over a 10 minute period, or until the DO level was approximately 2.5 mg /L, which ever occurred first. Control samples were analyzed at the initiation, the mid point, and the termination of the inhibition testing.

Reference substance (positive control)

yes 3,5-dichlorophenol

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
30 min	EC50	> 83.3 mg/L	meas. (initial)	test mat.	respiration rate	5.9
30 min	NOEC	83.3 mg/L	meas. (initial)	test mat.	respiration rate	5.9

Details on results

No appreciable inhibition of respiration was measured at the highest dose tested, 100 mg/L (nominal), which measured 83.3 mg/L. Therefore, an EC50 value was not calculable. Oxygen consumption rate for one test system replicate was slightly lower than the mean of the controls. Since the respiration rate was within ± 15% of the mean control respiration rate, there is no appreciable inhibition at this concentration. The respiration rate of control replicate 1, was slightly greater than the limit recommended by the guideline. The guideline recommends that control respiration rates be within ± 15% of their mean.The respiration rate of control replicate 1 (of 2 replicates) was approximately 19% higher than the mean. The cause of this may have been drift by the probe or the probe may not have been fully saturated for the first replicate reading. However, since the EC50 for the positive control was within the range specified by the guideline, the difference in respiration rate exhibited by one of the controls was not considered to have invalidated the study.

Results with reference substance (positive control)

In order for the test to be considered valid, the OECD Guideline 209 requires that the EC50 for the positive control (3,5-DCP) be in the range of 5-30 mg/L. The EC50 obtained for 3,5-DCP was 12.7 mg/L, which satisfied the guideline requirement.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) was not inhibitory to sludge respiration at a high test material/sludge loading of 100 mg/L (83.3

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mg/L measured). Therefore, DIDP is not expected to adversely impact microbial activity in a wastewater treatment plant.

Executive summary

Di-isodecyl phthalate ester did not inhibit microbial respiration in a sludge sample at a concentration that exceeds its water solubility, 83.3 mg/L. Therefore, DIDP is not expected to adversely impact microbial activity in a wastewater treatment plant.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a USEPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		2001							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according	other guideline: USEPA/600/R-94/024 Methods for measuring the toxicity and bioaccumulation of sediment-	no

to associated contaminants with freshwater invertebrates

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Purity: 99.7% Diisodecyl phthalate ester (DIDP) was obtained from Exxon Chemical, New Milford, CT. Due to the very low water solubility of this substance, a surfactant, sorbitan monolaurate 20 ethoxylate (Tween 20), was used. The Tween 20 was obtained from Mallinckrodt (US), and had a purity of 99+%.

Analytical monitoring

yes

Details on sampling

During mixing, samples of sediment were collected at periodic intervals for analysis of PE concentrations in the bulk sediment and pore water. Homogeneity of mixing was determined from multiple sediment samples usually collected on day 6. The degree to which an equilibrium in pore-water concentrations had been achieved was determined from samples of pore water collected on two occasions, usually days 3 and 6. During the test, samples of bulk sediment, pore water, and overlying water were sampled on days 0 and 10 and at two intermediate times for measurement of test substance concentrations. Overlying water samples (500 ml) were collected with an Eppendorf pipettor approximately 1 to 2 cm above the sediment. Samples were analyzed by high performance liquid chromatography. The overlying water was then siphoned out of the beaker to obtain sediment samples. Sediment cores were collected using a glass tube (13-mm inner diameter). Pore water was defined as the supernatant liquid obtained from centrifuging wet sediment

at 10,000 g for 30 minutes. Following centrifugation, an aliquot of the pore water was pipetted into a vial and a 1:1 mixture of acetonitrile and deionized water added to bring the sample volume to 1 ml. The vial was capped and mixed, after which the contents were centrifuged to remove any precipitate present. The remainder of the pore water was removed from the sample tube and the weight of the bulk sediment was determined. Sediments were extracted by adding 5 ml of acetonitrile to the centrifuged pellet (from the pore-water preparation step), mixing the pellet and acetonitrile with a stainless steel spatula, and sonicating for 15 minutes in a 35 degrees C water bath. Samples were mixed with a clean spatula and then sonicated for an additional 15 minutes. The tube was centrifuged in a bench-top centrifuge for 5 minutes and a sample of the supernatant diluted with a mixture of acetonitrile and water (1:1, v/v). The remaining supernatant was removed from the sediment and the sediment dried overnight at 27 degrees C for dry weight (%) estimates.

Vehicle

yes

Details on sediment and application

Uncontaminated, natural sediment samples for this study were collected from Airport Pond (St. Louis County, MN, USA) and West Bearskin Lake (Cook County, MN, USA). Samples were collected with a Ponar dredge, placed into clean polyethylene containers, and stored at 4 degrees C until used. For the test, the sediments were homogenized in a 119-L stainless steel container using a commercial drill with a stainless steel mortar-mixing paddle. To achieve a desired medium total organic carbon (TOC) sediment level, aliquots from Airport Pond and West Bearskin Lake were blended. A summary of TOC content and particle size distribution for the two blended sediments follows (+/- standard deviation in parentheses): the mean TOC content was 4.8% (0.65) ; sand content was 46.9% (4.09); silt content was 30.2% (3.59); coarse clay content was 2.3% (1.47); and fine clay content was 20.5% (1.86). The test substance was dissolved in acetone and coated onto a 20% aliquot of a wet sediment sample. The sediment aliquot was dried and then placed into a 4-L glass jar, which was rotated in an air stream to evaporate the acetone. Deionized water equal to the volume lost in drying the 20% portion of wet sediment was then added to the dried sediment aliquot, mixed, and added back into the jar containing the remaining 80% wet sediment sample. The jar was sealed with a Teflon-lined cap and rotated on a roller mill in a cold room (approximately 4 degrees C) for approximately 6 days at a speed of approximately 8 rpm.

Test organisms

Test organisms (species)

Chironomus tentans

Study design

Study type

laboratory study

Test duration type

long-term toxicity

Test type

static

Water media type

freshwater

Type of sediment

natural sediment

Limit test

yes

Total exposure duration

10 d

Remarks

Test conditions

Hardness
Measured, but not reported; was likely to have met guideline requirements.

Test temperature

Measured, but not reported; was likely to have met guideline requirements.

pH

Measured, but not reported; was likely to have met guideline requirements.

Dissolved oxygen

Measured, but not reported; was likely to have met guideline requirements.

Ammonia

Measured, but not reported; was likely to have met guideline requirements.

Nominal and measured concentrations

Nominal test substance loading = 3000 mg/kg sediment dry weight Measured test substance concentration = 2630 mg/kg sediment dry weight (range = 2340-3320 mg/kg sediment dry weight)

Details on test conditions

Sediment testing proceeded in two phases. The first phase evaluated the effectiveness of the mixing process in achieving a homogeneous distribution of test substance in bulk sediment, the establishment of equilibrium concentrations of test chemicals in the pore water, and the stability of the test substance in pore water under simulated toxicity test conditions. This phase was used to determine, in part, if meaningful toxicity tests could be performed (i.e., to assess if stable exposure concentrations could be maintained during the test period). The second phase evaluated the toxicity of the test substance in spiked sediments toward the test species. During the mixing process, samples of bulk sediment were collected on days 1, 3, and 6 after test substance amendment and pore water samples were separated by centrifugation. Duplicate bulk sediment samples were analyzed on day 6 to evaluate homogeneity. Mean pore-water concentrations were compared between days 3 and 6 to determine the extent to which equilibrium had been achieved. Approximately 100 ml of test substance-amended wet sediment was then transferred into 300-ml high-form beakers and placed into the toxicity testing system described below. Samples of sediment, overlying water, and pore water were collected at intervals over 9 to 10 days. The PE stability in pore water was evaluated by calculating half-lives, using log-transformed concentrations in simple linear regression analyses with time. Five replicates of a single nominal concentration of 3,000 mg/kg dry sediment and five control replicates were used to enhance statistical resolution. The rationale for a spiking limit of 3,000 mg/kg was based on several factors. First, the application of true water solubility limits for di-n-hexyl phthalate (DHP) and diethylhexyl phthalate (DEHP) of 0.05 and 0.003 mg/L in EqP calculations resulted in sediment spiking limits of approximately 2,400 and 1,700 mg/kg, respectively, for a low TOC sediment. Second, the sediment concentration of 3,000 mg/kg is well in excess of environmental exposures since it exceeds by at least two orders of magnitude recently reported field concentrations of DEHP as well as maxima for any of the other high molecular weight PEs. Third, preliminary experiments at a DEHP spiking level of 30,000 mg/kg appeared to adversely affect the dissolved oxygen concentration. Based on published aquatic toxicity data and water-only toxicity test results (Call et al., 2001b), the target dose of 3,000 mg/kg dry sediment was not anticipated to exhibit acute toxicity. For the second phase (i.e., toxicity testing), 100 ml of test substance-amended test sediment was added to each beaker and allowed to equilibrate in the flow-through test system for approximately 24 hours before test organisms were added. Ten Hyalella azteca (7-14 days old) or ten Chironomus tentans larvae (2nd-3rd instars, 10-12 days old) were then added to each exposure beaker. The daily feeding regimes utilized for the chambers containing H. azteca and C. tentans consisted of 1.0 to 1.5 ml of a yeast-trout chow-Cerophyll mixture and 1.5 ml of a 4 g/L Tetrafint slurry (TetraWerke, Melle, Germany), respectively. Tests were conducted in an intermittent water renewal system, with screened 300-ml high-form beakers as the primary exposure chambers. They were conducted at a nominal temperature of 23 degrees C, with a 16:8 light:dark photoperiod. The beakers contained approximately 100 ml of sediment and 100 to 175 ml of overlying water, dependent on the stage in the siphoning and renewal cycle. Overlying water, was replaced at a rate of four to eight volume additions daily. The water in the tanks holding the primary exposure chambers was aerated throughout the exposure period to ensure that an adequate level of dissolved oxygen was maintained. General observations were made daily, with counts of survivors obtained after the 10-day exposure period. At that time, the sediment was sieved, survivors collected, cleaned of debris, oven-dried for approximately 24 hours at 105 degrees C, and weighed. Weights were determined to 0.01 mg for the pooled survivors from each replicate. Toxicity tests (48 hours) with KCl as a reference toxicant were performed regularly throughout the testing program with the

test species to ensure that organisms used in tests were healthy and that LC50 values were within acceptable limits for performing the toxicity tests. The reference toxicant tests were conducted within one month of the test substance toxicity test. Control animal survival acceptability criteria of 80 and 70% were used for 10-day toxicity tests with H. azteca and C. tentans, respectively. A silica sand performance control also accompanied each toxicity test as a check on the performance of animals in the test system. Tests were performed using documentation consistent with good laboratory practices. Temperature, dissolved oxygen, and pH were recorded in all test chambers on days 0 and 10. Conductivity was measured in all test chambers on days 1 and 9. Hardness, alkalinity, and ammonia were measured on days 1 and 9 in at least one sediment control chamber. On days 2 to 9, temperature, dissolved oxygen, and pH were measured in at least one sediment control chamber and one exposure chamber.

Reference substance (positive control)

no

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
10 d	LC50	> 2630 mg/kg sediment dw	meas. (arithm. mean)	test mat.	other: mortality; growth	
10 d	NOEC	2630 mg/kg sediment dw	meas. (arithm. mean)	test mat.	other: mortality; growth	

Details on results

Chironomus tentans survival and growth were evaluated as the biological endpoints. The test substance showed no effect on survival or growth at a test substance loading of 3000 mg/kg sediment dry weight (measured as 2630 mg/kg sediment dry weight). There were five control and five exposure systems each containing 10 organisms and two sand controls with 10 organisms each. The means (ranges) of test substance concentrations in pore water and bulk sediment, and mean number of survivors (mean orgnaism dry weights) were as follows: Pore water: control mean conc. = <0.004 mg/L (<0.004-0.004), exposure mean conc. = 1.18 mg/L (0.766-1.80) Bulk sediment: control conc. = <1.89 mg/kg sediment dry weight (<1.89-<1.89), exposure mean conc. = 2630 mg/kg sediment dry weight (2340-3320) Control survivors = 47 (1.60 mg dry weight) Exposure survivors = 45 (1.77 mg dry weight) Sand survivors = 18 (0.99 mg dry weight)

Reported statistics and error estimates

Survival data from toxicity tests were summarized using the trimmed Spearman-Karber method. Dry weight data were analyzed by one-way analysis of variance and Dunnett's procedure using a SigmaStatt Program (SPSS, Chicago, IL, USA).

Remarks on results including tables and figures

Although the test substance was not tested for stability, it was assumed from the measured half-live of DHP (di-n-hexylphthalate) and DIDP (diisodecylphthalate, this substance) and the apparent stability of DEHP (diehthylhexylphthalate) that the test substance would be sufficiently stable to conduct toxicity tests (DHP and DEHP were also evaluated in this study). DEHP was recently reported to have a half-life of 15 d in aqueous solution but >70 d in soil. Overall, the results from the stability study indicated that the high molecular weight phthalate esters were sufficiently stable toproceedwith 10-day sediment toxicity tests.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) was not toxic to Chironomus tentans at a high test material/sediment loading of 3000 mg/kg sediment dry weight (measured as 2630 mg/kg sediment dry weight).

Executive summary

The sediment toxicity data for Chironomus tentans reported for di-isodecyl phthalate ester (DIDP) are consistent with the sediment and aqueous exposure toxicity data for several high molecular weight phthalate esters for two freshwater invertebrates as summarized by the authors. These data clearly showed that high molecular weight phthalate esters, including DIDP, did not produce toxicity, as measured by survival rate and growth, to freshwater sediment invertebrates at a sediment loading rate (3000 mg/kg sediment dry weight) that far exceed expected field levels, based on field measurements of similar higher molecular weight phthalate esters.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	Not applicable
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability is rated 2 because the study applied valid scientific testing principles, and the results were reviewed for reliability and assessed as valid. However, the study was not conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1997							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
no guideline available	other guideline: No standard guideline	not applicable

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Principles of method if other than guideline

The study protocol was designed to assess the toxicity of diisodecyl phthalate ester (DIDP), initially added to sediment, to the early life stage of the moor frog (Rana arvalis) in a test system composed of natural sediment over which water was added to create a two-phase test system. A 43-day exposure included a 14-day period during which newly fertilized moor frog eggs were exposed in the test system. Exposure of newly hatched tadpoles continued for 29 days during which the test organisms were observed for mortality and measured for growth.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: technical product Physical state: liquid Purity: 100% commercial substance

Analytical monitoring

yes

Details on sampling

Treatment sediment samples were anayzed at the end of the study.

Vehicle

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument699f.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-fa546954-d12d-49ae-b032-bbf210f5da72%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

yes

Details on sediment and application

Sediment used in the study was field collected from Lake Stensjon in Halisingland, Sweden. Sediment was composed of both coarse and fine particles. Organic carbon content of the sediment (dry) was 9.0 %. The test substance was dissolved in acetone and mixed with an established uncontaminated, homogenized, and air-dried sediment. The solvent was then evaporated at approximately 40 degrees C in an evaporator apparatus. The resulting sediment represented the stock sample, which was then added to uncontaminated sediment at various loading rates to achieve the various exposure concentrations. To facilitate homogeneity and equilibrium, mixed sediment samples were blended using either a roller mill or shaking table. Mixing was performed at low speeds to prevent erosion of the sediment particles. To assess equilibrium, spiked sediment was periodically collected during mixing and analyzed.

Test organisms

Test organisms (species)

other: Rana arvalis

Details on test organisms

Newly fertilized eggs of the moor frog (Rana arvalis) were field collected in Sweden and were determined to be in the morula or blastula development stage. Collected eggs were transported to the lab in a cooling bath with charcoal filtered aeration. Transport temperature was between approximately 8 to 10 degrees C. To avoid rapid development of the eggs once in the lab, the holding temperature was lowered to aproximately 4 degrees C until the start of the study.

Study design

Study type

laboratory study

Test duration type

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument699f.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-fa546954-d12d-49ae-b032-bbf210f5da72%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

long-term toxicity

Test type

static

Water media type

freshwater

Type of sediment

natural sediment

Limit test

no

Total exposure duration

43 d

Remarks

Test conditions

Test temperature

Temperature = 10 degrees C

pH

pH = approximately 5.5 to 7.0

Dissolved oxygen

Dissolved oxygen = approximately 80 to 100%

Nominal and measured concentrations

Measured DIDP concentration in sediment at test termination was 657 mg/kg sediment (dw).

Details on test conditions

After treatment sediments were equilibrated with the test substance, sediments from the different treatments were divided into 5 replicates (400 g) and added to glass beakers (3 liters), and synthetic lake water (approximately 2 L) was added. The beakers were left for 5 days at 2 degrees C to allow the sediment to settle. The beakers were randomly placed in a temperature chamber and temperature was slowly raised to 10 degrees C overnight before the eggs were added. The photoperiod was 12 hours light followed by 12 hours dark. Each beaker received 50 fertilized eggs with intact jellycoat, randomly chosen from the mixed egg clumps collected in the field. The water was not changed during the study. The water volume was adjusted on occasion. Added water was deionized with NaHCO3 added as a buffer to maintain the pH values during the study. The system was continuously aerated with filtered air. Temperature and pH were measured daily. Ammonia and nitrite were measured at least once every week. At test termination, all hatched tadpoles were transferred to glass dishes where they were counted and visually examined for deformities. Unhatched eggs were also transferred to determine age.

Reference substance (positive control)

no

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
14 d	NOEC	657 mg/kg sediment dw	meas. (arithm. mean)	test mat.	other: frog-egg hatching	
29 d	NOEC	657 mg/kg sediment dw	meas. (arithm. mean)	test mat.	other: tadpole survival and growth	

Reported statistics and error estimates

Hatchability data were first log-transformed and compared with a oneway ANOVA for heterogeneity. Each treatment was then compared to the relevant control group with a two-sided Dunnet's test (SPSS). Statistical evaluation of growth, mortality, and deformations were made with log-tranformed data using Student's T-test. The median hatching time was calculated using probit analysis.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester does not effect the egg hatching followed by tadpole survival and growth of the moor frog (Rana arvalis) at a very high test material/soil loading, 657 mg/kg sediment (dw).

Executive summary

The toxicity of di-isodecyl phthalate ester (DIDP) as measured by moor frog (Rana arvalis) egg hatching followed by tadpole survival and growth was evaluated in a natural sediment.No significant effect on frogegg hatching following a 14 -day exposure and tadpole survival and growth following a 29 -day exposurewas demonstrated in the sediments dosed with DIDP at a measured concentration of 657 mg/kg sediment (dw).

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	Not applicable
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a USEPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		2001							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according	other guideline: USEPA/600/R-94/024 Methods for measuring the toxicity and bioaccumulation of sediment-	

to associated contaminants with freshwater invertebrates

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Purity: 99.7% Diisodecyl phthalate ester (DIDP) was obtained from Exxon Chemical, New Milford, CT. Due to the very low water solubility of this substance, a surfactant, sorbitan monolaurate 20 ethoxylate (Tween 20), was used. The Tween 20 was obtained from Mallinckrodt (US), and had a purity of 99+%.

Analytical monitoring

yes

Details on sampling

During mixing, samples of sediment were collected at periodic intervals for analysis of PE concentrations in the bulk sediment and pore water. Homogeneity of mixing was determined from multiple sediment samples usually collected on day 6. The degree to which an equilibrium in pore-water concentrations had been achieved was determined from samples of pore water collected on two occasions, usually days 3 and 6. During the test, samples of bulk sediment, pore water, and overlying water were sampled on days 0 and 10 and at two intermediate times for measurement of test substance concentrations. Overlying water samples (500 ml) were collected with an Eppendorf pipettor approximately 1 to 2 cm above the sediment. Samples were analyzed by high performance liquid chromatography. The overlying water was then siphoned out of the beaker to obtain sediment samples. Sediment cores were collected using a glass tube (13-mm inner diameter). Pore water was defined as the supernatant liquid obtained from centrifuging wet sediment

at 10,000 g for 30 minutes. Following centrifugation, an aliquot of the pore water was pipetted into a vial and a 1:1 mixture of acetonitrile and deionized water added to bring the sample volume to 1 ml. The vial was capped and mixed, after which the contents were centrifuged to remove any precipitate present. The remainder of the pore water was removed from the sample tube and the weight of the bulk sediment was determined. Sediments were extracted by adding 5 ml of acetonitrile to the centrifuged pellet (from the pore-water preparation step), mixing the pellet and acetonitrile with a stainless steel spatula, and sonicating for 15 minutes in a 35 degrees C water bath. Samples were mixed with a clean spatula and then sonicated for an additional 15 minutes. The tube was centrifuged in a bench-top centrifuge for 5 minutes and a sample of the supernatant diluted with a mixture of acetonitrile and water (1:1, v/v). The remaining supernatant was removed from the sediment and the sediment dried overnight at 27 degrees C for dry weight (%) estimates.

Vehicle

yes

Details on sediment and application

Uncontaminated, natural sediment samples for this study were collected from Airport Pond (St. Louis County, MN, USA) and West Bearskin Lake (Cook County, MN, USA). Samples were collected with a Ponar dredge, placed into clean polyethylene containers, and stored at 4 degrees C until used. For the test, the sediments were homogenized in a 119-L stainless steel container using a commercial drill with a stainless steel mortar-mixing paddle. To achieve a desired medium total organic carbon (TOC) sediment level, aliquots from Airport Pond and West Bearskin Lake were blended. A summary of TOC content and particle size distribution for the two blended sediments follows (+/- standard deviation in parentheses): the mean TOC content was 4.8% (0.65) ; sand content was 46.9% (4.09); silt content was 30.2% (3.59); coarse clay content was 2.3% (1.47); and fine clay content was 20.5% (1.86). The test substance was dissolved in acetone and coated onto a 20% aliquot of a wet sediment sample. The sediment aliquot was dried and then placed into a 4-L glass jar, which was rotated in an air stream to evaporate the acetone. Deionized water equal to the volume lost in drying the 20% portion of wet sediment was then added to the dried sediment aliquot, mixed, and added back into the jar containing the remaining 80% wet sediment sample. The jar was sealed with a Teflon-lined cap and rotated on a roller mill in a cold room (approximately 4 degrees C) for approximately 6 days at a speed of approximately 8 rpm.

Test organisms

Test organisms (species)

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Hyalella azteca

Study design

Study type

laboratory study

Test duration type

long-term toxicity

Test type

static

Water media type

freshwater

Type of sediment

natural sediment

Limit test

yes

Total exposure duration

10 d

Remarks

Test conditions

Hardness
Measured, but not reported; was likely to have met guideline requirements.

Test temperature

Measured, but not reported; was likely to have met guideline requirements.

pH

Measured, but not reported; was likely to have met guideline requirements.

Dissolved oxygen

Measured, but not reported; was likely to have met guideline requirements.

Ammonia

Measured, but not reported; was likely to have met guideline requirements.

Nominal and measured concentrations

Nominal test substance loading = 3000 mg/kg sediment dry weight Measured test substance concentration = 2090 mg/kg sediment dry weight (range = 1550-2630 mg/kg sediment dry weight)

Details on test conditions

Sediment testing proceeded in two phases. The first phase evaluated the effectiveness of the mixing process in achieving a homogeneous distribution of test substance in bulk sediment, the establishment of equilibrium concentrations of test chemicals in the pore water, and the stability of the test substance in pore water under simulated toxicity test conditions. This phase was used to determine, in part, if meaningful toxicity tests could be performed (i.e., to assess if stable exposure concentrations could be maintained during the test period). The second phase evaluated the toxicity of the test substance in spiked sediments toward the test species. During the mixing process, samples of bulk sediment were collected on days 1, 3, and 6 after test substance amendment and pore water samples were separated by centrifugation. Duplicate bulk sediment samples were analyzed on day 6 to evaluate homogeneity. Mean pore-water concentrations were compared between days 3 and 6 to determine the extent to which equilibrium had been achieved. Approximately 100 ml of test substance-amended wet sediment was then transferred into 300-ml high-form beakers and placed into the toxicity testing system described below. Samples of sediment, overlying water, and pore water were collected at intervals over 9 to 10 days. The PE stability in pore water was evaluated by calculating half-lives, using log-transformed concentrations in simple linear regression analyses with time. Five replicates of a single nominal concentration of 3,000 mg/kg dry sediment and five control replicates were used to enhance statistical resolution. The rationale for a spiking limit of 3,000 mg/kg was based on several factors. First, the application of true water solubility limits for di-n-hexyl phthalate (DHP) and diethylhexyl phthalate (DEHP) of 0.05 and 0.003 mg/L in EqP calculations resulted in sediment spiking limits of approximately 2,400 and 1,700 mg/kg, respectively, for a low TOC sediment. Second, the sediment concentration of 3,000 mg/kg is well in excess of environmental exposures since it exceeds by at least two orders of magnitude recently reported field concentrations of DEHP as well as maxima for any of the other high molecular weight PEs. Third, preliminary experiments at a DEHP spiking level of 30,000 mg/kg appeared to adversely affect the dissolved oxygen concentration. Based on published aquatic toxicity data and water-only toxicity test results (Call et al., 2001b), the target dose of 3,000 mg/kg dry sediment was not anticipated to exhibit acute toxicity. For the second phase (i.e., toxicity testing), 100 ml of test substance-amended test sediment was added to each beaker and allowed to equilibrate in the flow-through test system for approximately 24 hours before test organisms were added. Ten Hyalella azteca (7-14 days old) or ten Chironomus tentans larvae (2nd-3rd instars, 10-12 days old) were then added to each exposure beaker. The daily feeding regimes utilized for the chambers containing H. azteca and C. tentans consisted of 1.0 to 1.5 ml of a yeast-trout chow-Cerophyll mixture and 1.5 ml of a 4 g/L Tetrafint slurry (TetraWerke, Melle, Germany), respectively. Tests were conducted in an intermittent water renewal system, with screened 300-ml high-form beakers as the primary exposure chambers. They were conducted at a nominal temperature of 23 degrees C, with a 16:8 light:dark photoperiod. The beakers contained approximately 100 ml of sediment and 100 to 175 ml of overlying water, dependent on the stage in the siphoning and renewal cycle. Overlying water, was replaced at a rate of four to eight volume additions daily. The water in the tanks holding the primary exposure chambers was aerated throughout the exposure period to ensure that an adequate level of dissolved oxygen was maintained. General observations were made daily, with counts of survivors obtained after the 10-day exposure period. At that time, the sediment was sieved, survivors collected, cleaned of debris, oven-dried for approximately 24 hours at 105 degrees C, and weighed. Weights were determined to 0.01 mg for the pooled survivors from each replicate. Toxicity tests (48 hours) with KCl as a reference toxicant were performed regularly throughout the testing program with the

test species to ensure that organisms used in tests were healthy and that LC50 values were within acceptable limits for performing the toxicity tests. The reference toxicant tests were conducted within one month of the test substance toxicity test. Control animal survival acceptability criteria of 80 and 70% were used for 10-day toxicity tests with H. azteca and C. tentans, respectively. A silica sand performance control also accompanied each toxicity test as a check on the performance of animals in the test system. Tests were performed using documentation consistent with good laboratory practices. Temperature, dissolved oxygen, and pH were recorded in all test chambers on days 0 and 10. Conductivity was measured in all test chambers on days 1 and 9. Hardness, alkalinity, and ammonia were measured on days 1 and 9 in at least one sediment control chamber. On days 2 to 9, temperature, dissolved oxygen, and pH were measured in at least one sediment control chamber and one exposure chamber.

Reference substance (positive control)

yes 3,5-dichlorophenol

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
10 d	LC50	> 2090 mg/kg sediment dw	meas. (arithm. mean)	test mat.	other: mortality; growth	
10 d	NOEC	2090 mg/kg sediment dw	meas. (arithm. mean)	test mat.	other: mortality; growth	

Details on results

Hyalella azteca survival and growth were evaluated as the biological endpoints. The test substance showed no effect on survival or growth at a test substance loading of 3000 mg/kg sediment dry weight (measured as 2090 mg/kg sediment dry weight). There were five control and five exposure systems each containing 10 organisms and two sand controls with 10 organisms each. The means (ranges) of test substance concentrations in pore water and bulk sediment, and mean number of survivors (mean organism dry weights) were as follows: Pore water: control mean conc. = <0.047 mg/L (<0.004-0.110), exposure mean conc. = 0.931 mg/L (0.376-2.00) Bulk sediment: control conc. = <1.89 mg/kg sediment dry weight (<1.89-<1.89), exposure mean conc. = 2090 mg/kg sediment dry weight (1550-2630) Control survivors = 49 (0.15 mg dry weight) Exposure survivors = 50 (0.16 mg dry weight) Sand survivors = 20 (0.12 mg dry weight)

Reported statistics and error estimates

Survival data from toxicity tests were summarized using the trimmed Spearman-Karber method. Dry weight data were analyzed by one-way analysis of variance and Dunnett's procedure using a SigmaStatt Program (SPSS, Chicago, IL, USA).

Remarks on results including tables and figures

Although the test substance was not tested for stability, it was assumed from the measured half-lives of DHP (di-n-hexyl phthalate) and DIDP (diisononyl phthalate, this substance) and the apparent stability of DEHP (diehthylhexyl phthalate) that the test substance would be sufficiently stable to conduct toxicity tests (DHP and DEHP were also evaluated in this study). DEHP was recently reported to have a half-life of 15 d in aqueous solution but >70 d in soil. Overall, the results from the stability study indicated that the high molecular weight phthalate esters were sufficiently stable to proceed with 10-day sediment toxicity tests.

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester (DIDP) was not toxic to Hyalella azteca at a high test material/sediment loading of 3000 mg/kg sediment dry weight (measured as 2090 mg/kg sediment dry weight).

Executive summary

The sediment toxicity data for Hyalella azteca reported for di-isodecyl phthalate ester (DIDP) are consistent with the sediment and aqueous exposure toxicity data data for several high molecular weight phthalate esters for two freshwater invertebrates as summarized by the authors.These data clearly showed that high molecular weight phthalate esters, including DIDP, did not produce toxicity, as measured by survival rate and growth, to freshwater sediment invertebrates at a sediment loading rate (3000 mg/kg sediment dry weight) that far exceed expected field levels, based on field measurements of similar higher molecular weight phthalate esters.

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	April 1996
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study proceedure followed an accepted test guideline and was conducted under GLP. The data are consistent with known toxicological properties of similar high molecular weight phthalate ester substances.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Study report; company data		1996							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations

according to OECD Guideline 207 (Earthworm, Acute Toxicity Tests) no

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

Details on sampling

Test soils dosed with diisodecyl phthalate ester (DIDP) were analyzed at test initiation and termination, days -1 and 14, respectively.

Vehicle

no

Details on preparation and application of test substrate

Test soil was homogenized prior to use by placing soil into 4L size plastic (HDPE) containers and mixing on a jar mill for

approximately 15 minutes. After homogenizing, a sample was removed to determine the moisture fraction. The moisture fraction was measured by placing soil into a crystallizing dish and weighing it (initial wt.). The sample and crystallizing dish were then placed in an oven at 100 degrees C for 23 hours. After drying and cooling in a desiccator, the final weight of the sample and crystallizing dish was measured. Treatments were prepared by adding the appropriate amount of test material to a soil sample. The treatment soils were stirred copiously in stainless steel bowls with stainless steel spoons for 15 to 30 minutes and held overnight at room temperature. On day 0, each treatment was divided into 5 replicates. The test chambers were one pint glass canning jars containing approximately 200g of a soil control or treatment and the appropriate amount of hydration water to bring the soils up to 75% of their water holding capacity. The worms were then transferred to randomized test chambers, which were capped with a lid containing a 1/8 inch hole in the center.

Test organisms

Test organisms (species)
Eisenia fetida

Animal group

annelids

Details on test organisms

Worms, Eisenia fetida, were obtained from Carolina Biological, Burlington, NC, USA. Species were verified based on: Earthworms of Ontario, J.W. Reynolds, Life Sciences Miscellaneous Publishing, The Royal Ontario Museum, 15 June 1977 Average weight of worms was 0.393g (sd = 0.090), based on a subsample (n=20) of worms. The organism loading rate during the study was 10 worms/~200 g soil.

Study design

Study type
laboratory study

Test duration type

short-term toxicity

Substrate type

other: Two soils were tested: natural soil and artificial soil

Limit test

yes

Total exposure duration

14 d

Remarks

Test conditions

Test temperature

Temperature = 18.2 to 20.6 degrees C

pH

pH = 6.9 to 7.2

Moisture

Control and test soils were hydrated with the appropriate amount of reverse osmosis water to achieve 75% of the water holding capacity of the soil.

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Nominal and measured concentrations

Soil samples were dosed with 10,000 mg test substance/kg soil. Soil were analyzed for DIDP concentration at test initiation and termination. The soil analytical results are based on the mean of duplicate samples for each soil sampled: DIDP Conc. Day -1 DIDP Conc. Day 14 Soil Sample (mg/kg soil, dry wt.) (mg/kg soil, dry wt.) Snyder Soil 7664 7994 Artificial Soil 8435 9180 Snyder soil was a natural soil.

Details on test conditions

Two soils were tested, a natural soil and an artificial soil. Natural soil was obtained from Snyder Research Farm located in Pittstown, NJ, USA, which was managed by Rutgers University. The soil was sieved through a 10 mesh sieve prior to use to remove large particles. Artificial soil was prepared using 70% sand, 20% clay, 10% peat, and CaCO3 to adjust pH. The water holding capacity of each soil was determined as follows: 25g of the dried sample was placed into a 100mL glass beaker with 25mL of reverse osmosis water and mixed thoroughly. This slurry was added to a pre-weighed, wetted filter paper and funnel (initial weight = wt. of funnel, wetted paper, + 25 g soil). The filter paper (#113 Whatman 150mm) was wetted with 9mL of reverse osmosis water. The glass funnel measured 10cm top diameter with an approximately 30mm stem. The slurry, filter and funnel were covered with aluminum foil and allowed to stand for 3 hours at which time a final weight was measured. The water holding capacity, expressed in mL water/100g of soil, is the difference between the final and initial weights multiplied by 4 to achieve 100g equivalence. Test temperature ranged from 18.2 to 20.6 degrees C as measured continuously and recorded by computer for the first 6 days, then measured daily thereafter. Light intensity ranged from 721 to 1185 Lux. Lighting was measured continuously and recorded by computer for the first 6 days, then measured daily thereafter. Soil pH was measured at test initiation (day 0) of the study. Ten grams of each treatment were mixed with 20mL of distilled water. The pH value of the slurry was measured using a soil pH probe. Soil pH ranged from 6.9 to 7.2. Observations for worm mortality were performed on all replicate chambers on day 7 and 14. Worms not found were assumed to have died and decomposed.

Reference substance (positive control)

no

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
14 d	LC50	> 7664 mg/kg natural soil dw	meas. (initial)	test mat.	mortality	
14 d	NOEC	7664 mg/kg natural soil dw	meas. (initial)	test mat.	mortality	
14 d	LC50	> 8435 mg/kg artificial soil dw	meas. (initial)	test mat.	mortality	
14 d	NOEC	8435 mg/kg artificial soil dw	meas. (initial)	test mat.	mortality	

Details on results

Diisodecyl phthalate ester (DIDP) demonstrated no effect on survival in the two soils tested at a soil loading rate of 10,000 mg/kg soil (dry wt.) (7664 mg/kg natural soil (dry wt.) and 8435 mg/kg artificial soil (dry wt.); measured concentrations reflect initial measured concentrations). The following are the survival results: Earthworm Mean % Soil Sample Survival* Survival Snyder Soil Control 10,10,10,10,10 100 Artificial Soil Control 10,10,10,10,10 100 Snyder Soil + DIDP 10,10,10,10,10 100 Artificial Soil + DIDP 10,9,10,10,10 98 *10 earthworms were added per replicate. There were five replicates per control and treatment.

Reported statistics and error estimates

None reported.

Remarks on results including tables and figures

Applicant's summary and conclusion

Validity criteria fulfilled

yes

Conclusions

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Di-isodecyl phthalate ester (DIDP) does not effect earthworm (Eisenia fetida) survival in soil, based on 14-day limit studies at very high concentrations, 7664 mg/kg natural soil (dw) and 8435 mg/kg artifical soil (dw).

Executive summary

The toxicity of di-isodecyl phthalate ester (DIDP) as measured by mortality to the earthworm (Eisenia fetida) was evaluated in 14 -day studies using natural and artificial soils. No significant mortality was observed in the soils dosed with DIDP at a nominal loading rate of 10,000 mg/kg soil (dw), which measured 7664 mg/kg natural soil (dw) and 8435 mg/kg artificial soil (dw) (concentrations are from analyses of soils at test initiation).

Administrative Data

Purpose flag	key study		
Study result type	read-across from supporting substance (structural analogue or surrogate)	Study period	2008
Reliability	2 (reliable with restrictions)		
Rationale for reliability	The reliability is rated 2 because the study procedure followed an accepted test guideline, but was not conducted under GLP. A guideline deviation not beleved to have impacted the outcome of the study was also recorded. However, the data are consistent with known toxicological properties of similar high molecular weight phthalate ester substances.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
company data		2008							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations

according to	OECD Guideline 222 (Earthworm Reproduction Test (Eisenia fetida/Eisenia andrei))	yes A guideline criterium for the controls requires >/=30 juveniles/10 worm replicate with a </=30% CV. Closed test systems to control volatile loss may have led to the slightly lower control result. It is not considered to have invalidated the study due to

GLP compliance

no Study was not conducted under GLP, however, a standard OECD guideline was used with no deviations from the protocol. The laboratory has auditable recieving records, quality assurance coordination, and all data are documented in the raw data set.

Test materials

Test material equivalent to submission substance identity

no

Details on test material

Substance type: commercial product

Details on properties of test surrogate or analogue material

Biological data from the extant database for di-isodecyl phthalate ester (DIDP) and di-isononyl phthalate ester (DINP) show that the two substances behave the same. They are structurally similar, with the alkyl groups in DINP having on average one less carbon, and they share similar physicochemical characteristics.

Analytical monitoring

yes

Details on sampling

A sample from each of the 4 replicate test systems were analyzed on days 0, 28, and 56. The positive and negative controls were not analyzed.

Vehicle

no

Details on preparation and application of test substrate

Artificial soil was prepared according to guideline. The test substance loading was 1000 mg/kg soil in each of 4 test substance systems, which were analytically verified with concentrations of: 925.2 mg/kg, 1052mg/kg, 971.2mg/kg, and 981.2mg/kg on Day 0. The control treatment consisted of 6 replicates with no test substance. The soil was artificial and composed of a mixture of 70% sand (sieved), 20% kaolin clay, and 10% peat moss (sieved with no visible plant material). The artificial soil was transferred to a 1 gallon glass jar with Teflon covered lid. The test substance was spiked into the soil in 4 aliquots and mixed on a mill for 20 minutes after the addition of each aliquot. 500 grams of spiked soil was mixed with 175 mls of moderately hard recon water using a mixer to equally distribute the water within the artificial soil. The hydrated soil was transferred to a quart glass jar and sealed with a Teflon coated lid and weighed. The 4 systems were allowed to equilibrate for several days.

Test organisms

Test organisms (species)

Eisenia fetida

Animal group

annelids

Study design

Study type

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laboratory study

Test duration type

long-term toxicity

Substrate type

artificial soil

Limit test

yes

Total exposure duration

56 d
Remarks

Post exposure observation period

None

Test conditions

Test temperature
22 degrees C

pH

6.5 and 7.0 for test substance and negative and positive control systems at initiation and termination, respectively.

Moisture

34.3 to 37.3% at test initiation.

Nominal and measured concentrations

Nominal positive control loading was 3 mg/kg soil. Nominal test substance loading was 1000 mg/kg soil. Negative and positive control test systems were not analyzed. Measured test substance concentrations were: On day 0 concentrations in 4 replicates ranged from 925.2 to 1052 mg/kg soil with an average of 982.4 mg/kg soil. On day 28 concentrations in 4 replicates ranged from 651.4 to 795.8 mg/kg soil with an average of 739.5 mg/kg soil. On day 56 concentrations in 4 replicates ranged from 428.0 to 477.1 mg/kg soil with an average of 441.1 mg/kg soil.

Details on test conditions

Four replicates were prepared containing 10 worms each (one of the control replicates contained 11 worms and another contained 9 worms). Organism supplier was Carolina Biological Supply Co., Burlington, NC 27215-3398. The test chambers were kept at room temperature which ranged from 17.9-23.7 with a light cycle of 16 hours on, 8 hours off. Every 7 days, the chambers were weighed to monitor moisture loss. The worms were fed 1 gram of Magic Worm food and water was added based on moisture loss for the first 28 days. On Day 28, worms were removed and counted and depurated on wetted filter paper overnight. A sample of soil was removed for concentration verification. The systems were resealed and monitored every 7 days for moisture loss until day 56.

Reference substance (positive control)

yes Carbendazim

Results and discussions

Effect concentrations

Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
56 d	NOEC	> 982.4 mg/kg soil dw	meas. (initial)	test mat.	reproduction	

Details on results

On Day 0, the test substance loading concentrations were: 925.2 mg/kg, 1052mg/kg, 971.2mg/kg, and 981.2mg/kg. On Day 28, the soil concentrations were measured at: 762.2mg/kg, 748.6 mg/kg, 795.8 mg/kg and 651.4mg/kg. On Day 56, the soil concentrations were measured at 469.7mg/kg, 477.1mg/kg, 428mg/kg, 389.6 mg/kg. On Day 56 the juveniles were counted: 92 juveniles were counted from replicate 1, 77 from replicate 2, 149 from replicate 3, and 42 from replicate 4. Test substance concentration average was 982.4 mg/kg soil (dw) at test initiation. 10 worms were added to each of 4 replicates. Weight of 10 worms per replicate at test initiation: Rep 1 - 5.25 g Rep 2 - 4.58 g Rep 3 - 5.12 g Rep 4 - 4.91 g Number of alive worms per replicate on day 28 (cocoons were observed in each replicate): Rep 1 - 10 Rep 2 - 10 Rep 3 - 10 Rep 4 - 10 Weight of worms per replicate on day 56: Rep 1 - 5.23 g Rep 2 - 4.42 g Rep 3 - 5.12 g Rep 4 - 6.02 g Number of juveniles per replicate on day 56: Rep 1 - 92 juveniles Rep 2 - 77 juveniles Rep 3 - 149 juveniles Rep 4 - 42 juveniles Control test systems had 10 worms added to each of 6 replicates. Weight of 10 worms per replicate at test initiation: Rep 1 - 5.35 g Rep 2 - 4.75 g Rep 3 - 6.03 g Rep 4 - 4.75 g Rep 5 - 4.95 g Rep 6 - 4.94 g Number of alive worms per replicate on day 28 (cocoons were observed in each replicate): Rep 1 - 10 Rep 2 - 10 Rep 3 - 11 (replicate 3 included 1 additional worm that was to have been added to replicate 4) Rep 4 - 9 Rep 5 - 10 Rep 6 - 10 Weight of worms per replicate on day 56: Rep 1 - 4.82 g Rep 2 - 4.78 g Rep 3 - 5.74 g Rep 4 - 3.91 g Rep 5 - 4.11 g Rep 6 - 4.38 g Number of juveniles per replicate on day 56: Rep 1 - 18 juveniles Rep 2 - 75 juveniles Rep 3 - 48 juveniles Rep 4 - 29 juveniles Rep 5 - 35 juveniles Rep 6 - 29 juveniles

Results with reference substance (positive control)

Positive control was Carbendazim at a concentration of 3 mg/kg soil (dw). 10 worms were added to each of 2 replicates. Weight of 10 worms per replicate at test initiation: Rep 1 - 3.73 g Rep 2 - 4.12 g Number of alive worms per replicate on day 28 (no cocoons were observed): Rep 1 - 9 Rep 2 - 10 Weight of worms per replicate at test termination: Rep 1 - 4.32 g Rep 2 - 4.80 g Number of juveniles per replicate on day 56: Rep 1 - 11 juveniles Rep 2 - 13 juveniles

Remarks on results including tables and figures

Applicant's summary and conclusion

Validity criteria fulfilled

yes The test is considered acceptable since the mean control survival must be at least 90% over the initial four weeks. However not all replicates of the control produced >30 juveniles but the average of six replicates exceeded 30 juveniles.

Conclusions

Di-isononyl phthalate ester (DINP) does not effect earthworm (Eisenia fetida) reproduction, based on a 56-day limit study in artificial soil at a very high concentration, 982.4 mg/kg soil (dw).

Executive summary

Di-isononyl phthalate ester (DINP) does not effect earthworm (*Eisenia fetida*) reproduction, based on a 56-day limit study in artificail soil at a very high concentration, 982.4 mg/kg soil (dw).

Because DINP is a structural analog to di-isodecyl phthalate ester (DIDP), the earthworm chronic toxicity data for DINP can be used to characterize the potential for DIDP to effect earthworm reproduction. Based on the data for DINP, DIDP is also not expected to cause chronic toxicity to earthworms at high soil loading rates.

Dissemination Dossier

Honeybeestox Endpoint.001

Administrative Data

Data waiving study scientifically unjustified

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	April 1996
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a USEPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP. Additionally, seed germination (mean % germinated) in the controls met guideline requirements, which validates the test results.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Study report; company data		1996							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations

according to	other guideline: U.S. EPA-600/3-88/029 Protocols for Short Term Toxicity Screening of Hazardous Waste Sites (NTIS / PB88-235510/AS)	no

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Substance type: commercial product

Analytical monitoring

yes

Details on sampling

Soil samples dosed with 10,000 mg test substance/kg soil were analyzed for test substance at test initiation.

Vehicle

no

Details on test substrate

Two soils were tested, a natural soil and an artificial soil. Natural soil was obtained from Snyder Research Farm located in Pittstown, NJ, USA, which was managed by Rutgers University. The soil was sieved through a 10 mesh sieve prior to use to remove large particles. Artificial soil was prepared using 70% sand, 20% clay, and 10% peat.

Test organisms

Test organisms

Species	Lactuca sativa
Plant group	Dicotyledonae (dicots)
Details on test organisms	Seeds were obtained from Carolina Biological Supply Co., Burlington, NC, USA.

Study design

Study type

laboratory study

Test duration type

short-term toxicity

Test type

seedling emergence toxicity test

Substrate type

other: Two soils were tested: natural soil and artificial soil

Limit test

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yes

Total exposure duration

5 d

Remarks

Test conditions

Test temperature

Test temperature = 24.5 degrees C (sd = 0.3 degrees C)

pH

pH = 6.4 to 7.0

Moisture

Soil moisture was adjusted by adding the appropriate amount of reverse osmosis water to achieve 85% of the water holding capacity of the soil.

Nominal and measured concentrations

Soil samples were dosed with 10,000 mg test substance/kg soil. The soil analytical results are based on the mean of duplicate samples for each soil sampled: DIDP Conc. Day -1 Soil Sample (mg/kg soil, dry wt.) Snyder Soil 8630 Artificial Soil 8551 Snyder soil was a natural soil.

Details on test conditions

Seeds were inspected and sized. Lettuce (Lactuca sativa) seeds selected for the test passed through a 1/6 x 1/30 inch screen. Test soils

were homogenized prior to use by placing soil into 4L size plastic (HDPE) containers and mixing on a jar mill for approximately 15 minutes. After homogenizing, a sample was removed to determine the moisture fraction. The moisture fraction was measured by placing soil into a crystallizing dish and weighing it (initial wt.). The sample and crystallizing dish were then placed in an oven at 100C for 23 hours. After drying and cooling in a desiccator, the final weight of the sample and crystallizing dish was measured. The water holding capacity of each soil was determined as follows: 25g of the dried sample was placed into a 100mL glass beaker with 25mL of reverse osmosis water and mixed thoroughly. This slurry was added to a pre-weighed, wetted filter paper and funnel (initial weight = wt. of funnel, wetted paper, + 25 g soil). The filter paper (#113 Whatman 150mm) was wetted with 9mL of reverse osmosis water. The glass funnel measured 10cm top diameter with an approximately 30mm stem. The slurry, filter and funnel were covered with aluminum foil and allowed to stand for 3 hours at which time a final weight was measured. The water holding capacity, expressed in mL water/100g of soil, is the difference between the final and initial weights multiplied by 4 to achieve 100g equivalence. The test chambers were bottom halves of 150mm (diameter) x 15mm (high) plastic petri dishes placed in approximately 11" x 11" Ziploc bags. Each dish contained approximately 190g of test soil including the cover soil. Soil treatments included: control (no test material) and a nominal 10,000 mg test substance per kg soil (dry wt.). Soil was hydrated at 85% of water holding capacity. Five replicates each of the two soils were tested, each with a control soil. Prior to seed distribution, all treatment replicates were randomly positioned, then 40 seeds were distributed to each chamber. The seeds were distributed about the surface, but not closer than approximately 0.5 inches from the edge of the test chamber. Approximately 90g of cover soil was then evenly distributed on top of each hydrated treatment and control soils. Each chamber was placed directly into a resealable polypropylene (Ziploc) bag, centered over the bottom of the bag. The sides were raised to a vertical position over the chamber and the plastic covers were removed. The bags were then sealed leaving headspace. Test temperature: 24.5C (sd = 0.3C), as measured continuously and recorded by computer. Test photoperiod was as follows: Initial 48 hours dark, followed by 16 hours of light and 8 hours of dark until termination of the test. Light intensity ranged from 4300+/- 430 Lux during daylight periods, which was measured daily. Soil pH was measured at test initiation (day 0) of the study. Ten grams of each treatment were mixed with 20mL of distilled water. The pH value of the slurry was measured using a soil pH probe. Soil pH ranged from 6.4 to 7.0. At test termination, after 5 days of exposure, the number of germinated seeds in each dish was determined by counting each seedling that protruded above the surface of the soil.

Reference substance (positive control)

no

Results and discussions

Effect concentrations

Species	Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
Lactuca sativa	5 d	EC50	> 8630 mg/kg natural soil (d.w.)	meas. (initial)	test mat.	germination	
Lactuca sativa	5 d	NOEC	8630 mg/kg natural soil (d.w.)	meas. (initial)	test mat.	germination	
Lactuca sativa	5 d	EC50	> 8551 mg/kg artificial soil (d.w.)	meas. (initial)	test mat.	germination	
Lactuca sativa	5 d	NOEC	8551 mg/kg artificial soil (d.w.)	meas. (initial)	test mat.	germination	

Details on results

At test termination, after 5 days of exposure, the number of germinated seeds was determined by counting each seedling that protruded above the surface of the soil. Diisodecyl phthalate ester (DIDP) demonstrated no effect on germination of lettuce (Lactuca sativa) in the two soils tested. The following are the germination results: Number Seeds Mean % Soil Sample Germinated* Germinated Snyder Soil Control Lettuce 39,36,39,38,35 94 Artificial Soil Control Lettuce 39,40,40,40,35 97 Snyder Soil + DIDP Lettuce 33,40,31,32,35 86 Artificial Soil + DIDP Lettuce 40,37,40,37,39 97 *40 seeds were added per replicate. There were five replicates per control and treatment.

Reported statistics and error estimates

The germination results were evaluated using Dunnett's procedure (one tailed T test, α=0.05) of SAS [SAS/STAT® User's Guide. Version 6, Fourth Edition, Volumes 1 and 2. 1989. SAS Institute, Inc., Cary, NC, USA].

Remarks on results including tables and figures

Applicant's summary and conclusion

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument2086.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-cc846f2e-6489-4e86-9956-f0c698df63bb%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester does not effect the germination of lettuce (Lactuca sativa) seeds at very high test material/soil concentrations, 8630 mg/kg natural soil (dw) and 8551 mg/kg artificial soil (dw).

Executive summary

The toxicity of di-isodecyl phthalate ester (DIDP) as measured by the germination of lettuce (Lactuca sativa) seeds was evaluated in natural and artificial soils. Germination in the control soils ranged from 94 to 97%. Germination in soils dosed with DIDP ranged from 86 to 97%.No significant effect on germination was demonstrated in the soils dosed with DIDP at a nominal loading rate of 10,000 mg/kg soil (dw) (measured at 8630 mg/kg natural soil (dw) and 8551 mg/kg artificial soil (dw).

Administrative Data

Purpose flag	key study		
Study result type	experimental result	Study period	April 1996
Reliability	1 (reliable without restriction)		
Rationale for reliability	The reliability is rated 1 because the study followed a USEPA standard guideline, which describes a procedure designed to evaluate this endpoint, the results were reviewed for reliability and assessed as valid, and the study was conducted under GLP. Additionally, seed germination (mean % germinated) in the controls met guideline requirements, which validates the test results.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
other: Study report; company data		1996							

Materials and methods

Test guideline

Qualifier	Guideline	Deviations

according to	other guideline: U.S. EPA-600/3-88/029 Protocols for Short Term Toxicity Screening of Hazardous Waste Sites (NTIS / PB88-235510/AS)	no

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

Substance type: technical product Physical state: liquid Purity: 100% commercial substance

Analytical monitoring

yes

Details on sampling

Soil samples dosed with 10,000 mg test substance/kg soil were analyzed for test substance at test initiation.

Vehicle

no

Details on test substrate

Two soils were tested, a natural soil and an artificial soil. Natural soil was obtained from Snyder Research Farm located in Pittstown, NJ, USA, which was managed by Rutgers University. The soil was sieved through a 10 mesh sieve prior to use to remove large particles. Artificial soil was prepared using 70% sand, 20% clay, and 10% peat.

Test organisms

Test organisms

Species	other: Lolium species
Plant group	Monocotyledonae (monocots)
Details on test organisms	Seeds were obtained from Carolina Biological Supply Co., Burlington, NC, USA.

Study design

Study type

laboratory study

Test duration type

short-term toxicity

Test type

seedling emergence toxicity test

Substrate type

other: Two soils were tested: natural soil and artificial soil

Limit test

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument01e2.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-b2d2a212-1d87-4857-90dd-f594fd6f0ef4%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

yes

Total exposure duration

5 d

Remarks

Test conditions

Test temperature

Test temperature = 24.5 degrees C (sd = 0.3 degrees C)

pH

pH = 6.4 to 7.0

Moisture

Soil moisture was adjusted by adding the appropriate amount of reverse osmosis water to achieve 85% of the water holding capacity of the soil.

Nominal and measured concentrations

Soil samples were dosed with 10,000 mg test substance/kg soil. The soil analytical results are based on the mean of duplicate samples for each soil sampled: DIDP Conc. Day -1 Soil Sample (mg/kg soil, dry wt.) Snyder Soil 8630 Artificial Soil 8551 Snyder soil was a natural soil.

Details on test conditions

Seeds were inspected and sized. Ryegrass (Lolium species) seeds selected for the test passed through a 1/6 x 1/28 inch screen. Test

soils were homogenized prior to use by placing soil into 4L size plastic (HDPE) containers and mixing on a jar mill for approximately 15 minutes. After homogenizing, a sample was removed to determine the moisture fraction. The moisture fraction was measured by placing soil into a crystallizing dish and weighing it (initial wt.). The sample and crystallizing dish were then placed in an oven at 100C for 23 hours. After drying and cooling in a desiccator, the final weight of the sample and crystallizing dish was measured. The water holding capacity of each soil was determined as follows: 25g of the dried sample were placed into a 100mL glass beaker with 25mL of reverse osmosis water and mixed thoroughly. This slurry was added to a pre-weighed, wetted filter paper and funnel (initial weight = wt. of funnel, wetted paper, + 25 g soil). The filter paper (#113 Whatman 150mm) was wetted with 9mL of reverse osmosis water. The glass funnel measured 10cm top diameter with an approximately 30mm stem. The slurry, filter and funnel were covered with aluminum foil and allowed to stand for 3 hours at which time a final weight was measured. The water holding capacity, expressed in mL water/100g of soil, is the difference between the final and initial weights multiplied by 4 to achieve 100g equivalence. The test chambers were bottom halves of 150mm (diameter) x 15mm (high) plastic petri dishes placed in approximately 11" x 11" Ziploc bags. Each dish contained approximately 190g of test soil including the cover soil. Soil treatments included: control (no test material) and a nominal 10,000 mg test substance per kg soil (dry wt.). Soil was hydrated at 85% of water holding capacity. Five replicates each of the two soils were tested, each with a control soil. Prior to seed distribution, all treatment replicates were randomly positioned, then 40 seeds were distributed to each chamber. The seeds were distributed about the surface, but not closer than approximately 0.5 inches from the edge of the test chamber. Approximately 90g of cover soil was then evenly distributed on top of each hydrated treatment and control soils. Each chamber was placed directly into a resealable polypropylene (Ziploc) bag, centered over the bottom of the bag. The sides were raised to a vertical position over the chamber and the plastic covers were removed. The bags were then sealed leaving headspace. Test temperature: 24.5C (sd = 0.3C), as measured continuously and recorded by computer. Test photoperiod was as follows: Initial 48 hours dark, followed by 16 hours of light and 8 hours of dark until termination of the test. Light intensity ranged from 4300+/- 430 Lux during daylight periods, which was measured daily. Soil pH was measured at test initiation (day 0) of the study. Ten grams of each treatment were mixed with 20mL of distilled water. The pH value of the slurry was measured using a soil pH probe. Soil pH ranged from 6.4 to 7.0. At test termination, after 5 days of exposure, the number of germinated seeds in each dish was determined by counting each seedling that protruded above the surface of the soil.

Reference substance (positive control)

no

Results and discussions

Effect concentrations

Species	Duration	Endpoint	Effect conc.	Nominal/Measured	Conc. based on	Basis for effect	Remarks (e.g. 95% CL)
other: Lolium species	5 d	EC50	> 8630 mg/kg natural soil (d.w.)	meas. (initial)	test mat.	germination	
other: Lolium species	5 d	NOEC	8630 mg/kg natural soil (d.w.)	meas. (initial)	test mat.	germination	
other: Lolium species	5 d	EC50	> 8551 mg/kg artificial soil (d.w.)	meas. (initial)	test mat.	germination	
other: Lolium species	5 d	NOEC	8551 mg/kg artificial soil (d.w.)	meas. (initial)	test mat.	germination	

Details on results

At test termination, after 5 days of exposure, the number of germinated seeds was determined by counting each seedling that protruded above the surface of the soil. Diisodecyl phthalate ester (DIDP) demonstrated no effect on germination of ryegrass (Lolium species) in the two soils tested. The following are the germination results: Number Seeds Mean % Soil Sample Germinated* Germinated Snyder Soil Control Ryegrass 34,40,34,33,40 91 Artificial Soil Control Ryegrass 38,38,38,38,35 94 Snyder Soil + DIDP Ryegrass 40,39,38,37,40 97 Artificial Soil + DIDP Ryegrass 38,38,38,37,38 95 *40 seeds were added per replicate. There were five replicates per control and treatment.

Reported statistics and error estimates

The germination results were evaluated using Dunnett's procedure (one tailed T test, α=0.05) of SAS [SAS/STAT® User's Guide. Version 6, Fourth Edition, Volumes 1 and 2. 1989. SAS Institute, Inc., Cary, NC, USA].

Remarks on results including tables and figures

Applicant's summary and conclusion

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument01e2.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-b2d2a212-1d87-4857-90dd-f594fd6f0ef4%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Validity criteria fulfilled

yes

Conclusions

Di-isodecyl phthalate ester does not effect the germination of ryegrass (Lolium species) seeds at very high test material/soil concentrations, 8630 mg/kg natural soil (dw) and 8551 mg/kg artificial soil (dw).

Executive summary

The toxicity of di-isodecyl phthalate ester (DIDP) as measured by the germination of ryegrass (Lolium species) seeds was evaluated in natural and artificial soils. Germination in the control soils ranged from 91 to 94%. Germination in soils dosed with DIDP ranged from 95 to 97%. No significant effect on germination was demonstrated in the soils dosed with DIDP at a nominal loading rate of 10,000 mg/kg soil (dw) (measured at 8630 mg/kg natural soil (dw) and 8551 mg/kg artificial soil (dw).

Dissemination Dossier
Planttox Endpoint.003

Administrative Data

Data waiving study scientifically unjustified

Dissemination Dossier
Soil micro tox Endpoint.001

Administrative Data

Data waiving study scientifically unjustified

Dissemination Dossier
Bird tox Endpoint.001

Administrative Data

Data waiving study scientifically unjustified

Dissemination Dossier
Data tox Summary

Administrative Data

Results and discussions

Workers

Acute / short-term exposure - systemic effects

Dermal DN(M)EL in mg/kg bw/day not quantifiable Assessment factor Dose descriptor starting point Most sensitive endpoint
Inhalation DN(M)EL in mg/m³ not quantifiable Assessment factor Dose descriptor starting point Most sensitive endpoint

Acute / short-term exposure - local effects

Dermal DN(M)EL in mg/cm² not quantifiable Assessment factor Dose descriptor starting point Most sensitive endpoint
Inhalation DN(M)EL in mg/m³ not quantifiable Assessment factor Dose descriptor starting point Most sensitive endpoint

Long-term exposure - systemic effects

Dermal DN(M)EL in mg/kg bw/day DNEL 41.67 Assessment factor Dose descriptor starting point Most sensitive endpoint
Inhalation DN(M)EL in mg/m³ DNEL 5.29 Assessment factor Dose descriptor starting point Most sensitive endpoint

Long-term exposure - local effects

Dermal DN(M)EL in mg/cm² not quantifiable Assessment factor Dose descriptor starting point Most sensitive endpoint
Inhalation DN(M)EL in mg/m³ not quantifiable Assessment factor Dose descriptor starting point Most sensitive endpoint

General population

Acute / short-term exposure - systemic effects

Dermal DN(M)EL in mg/kg bw/day not quantifiable Assessment factor Dose descriptor starting point Most sensitive endpoint
Inhalation DN(M)EL in mg/m³ not quantifiable Assessment factor Dose descriptor starting point Most sensitive endpoint
Oral DN(M)EL in mg/kg bw/day not quantifiable Assessment factor Dose descriptor starting point Most sensitive endpoint

Acute / short-term exposure - local effects

Dermal DN(M)EL in mg/cm²	not quantifiable	Assessment factor	Dose descriptor starting point	Most sensitive endpoint
Inhalation DN(M)EL in mg/m³	not quantifiable	Assessment factor	Dose descriptor starting point	Most sensitive endpoint

Long-term exposure - systemic effects

Dermal DN(M)EL in mg/kg bw/day	DNEL 20.83	Assessment factor	Dose descriptor starting point	Most sensitive endpoint
Inhalation DN(M)EL in mg/m³	DNEL 1.3	Assessment factor	Dose descriptor starting point	Most sensitive endpoint
Oral DN(M)EL in mg/kg bw/day	DNEL 0.75	Assessment factor	Dose descriptor starting point	Most sensitive endpoint

Long-term exposure - local effects

Dermal DN(M)EL in mg/cm²	DMEL	Assessment factor	Dose descriptor starting point	Most sensitive endpoint
Inhalation DN(M)EL in mg/m³	not quantifiable	Assessment factor	Dose descriptor starting point	Most sensitive endpoint

Administrative Data

Purpose flag	key study
Reliability	2 (reliable with restrictions)
Rationale for reliability	The study is rated a "2" because appropriate testing methods were used; however, the study does not follow and accepted guideline or indicate compliance with GLP.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1981							

Materials and methods

Type of method

in vivo

Objective of study

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentd279.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-47d4d775-3d9e-455b-862e-d89f2a081678%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

metabolism

GLP compliance

no data

Test material equivalent to submission substance identity

yes

Radiolabelling

yes 14C-DIDP

Test materials

Details on test material
Unspecified DIDP; CAS No not provided

Test animals

Species
rat

Strain

Sprague-Dawley

Sex

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentd279.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-47d4d775-3d9e-455b-862e-d89f2a081678%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

male

Details on test animals and environmental conditions

TEST ANIMALS - Age at study initiation: adult - Weight at study initiation: 200g - Housing: individually - Individual metabolism cages: yes - Diet: ad libitum - Water: ad libitum - Acclimation period: 2 days

Administration / exposure

Route of administration

inhalation: aerosol

Vehicle

unchanged (no vehicle)

Details on exposure

TYPE OF INHALATION EXPOSURE: head only GENERATION OF TEST ATMOSPHERE / CHAMPER DESCRIPTION As described in Pegg (1979). Toxicity and biologic fate of di-2-ethylhexyl phthalate following inhalation exposure in rats. GM Research Report. RI-135

Duration and frequency of treatment / exposure

The day of the experiment the rats were exposed to 14C DIDP aerosol atmosphere (nominal concentration 100 mg/m3) for 6 hours.

Doses / concentrations

100 mg/m3

No. of animals per sex per dose

6 rats/dose

Control animals

yes, concurrent no treatment

Details on study design

Immdiately following the exposure, three animals were sacrificed and tissues frozen for analysis. The other three animals were transferred directly to th eRoth-type cages and collections begun. Airflow in the cages was maintained at 500 ml/min. Feces was collected for 24 hour intervals at room temperature. Urine receptacles were maintained in dry ice and changed at 12 hour intervals. All samples were stored at -10 deg C for analysis. Seventy-two hours after the exposure, at termination of the collection period, the animals were sacrificed. Carcasses were skinned and lungs, liver, heart, spleen, kidneys, brain, testes, thymus, and samples of retroperitoneal fat were weighed and frozen. The frozen organ tissues were pulverized and samples taken for analysis. Carcas and feces were homogenized in distilled water. Radioactivity in organ tissues, skin, and feces and carcass homogenates was assayed at 14CO2 evolved from combustion in an RJ Harvey biological materials oxidizer and quanified by liquid scintillation spectromtery. Radioactivity in urine was determined by direct addition of 0.1 ml to 20 ml Aquasol liquid scintillation cocktail. Data were expressed as umole equivalents. DIDP.

Statistics

Data were analyzed using the Student's t test and random complete block analysis of variance. Regression and linearity of interval excretion data were tested by analysis of variance. The 0.05 level of probability was used as the criterion of significance.

Results and discussions

Pharmacokinetic studies

Absorption

Total body burden following the exposure was 6.75 umole equivalents or ~3.0 mg. The excretion of radioactivity was distributed equally between urinary and fecal routes through the 72 hour sampling period, comprising 45.3 and 41.3% respectively of the total body burden. The remaining radioactivity was recovered in carcas (9.4%), skin (2.4%) and in acetone:water (50:50) rinses of the metabolism cage surfaces (1.6%).

Distribution in tissues

The distribution of radioactivity in rat tissues immediately following the 6 hour 14C-DIDP inhalation exposure and after 72 hours was measured. The highest concentration of radioactivity was detected in lung immediately after exposure, followed by gastrointestinal tract, liver and kidney. The remaining tissues, brain, thymus, heart, spleen, fat and testes contained far lesser amounts. After 72 hours the concentration was decreased in all tissues. The highest levels of radioactivity were still found in lung, which contained 27% of the content of 14C present immediately following exposure. The pulmonary content of radioactivity decreased to a lesser extent than all other tissues except fat, which did not appear to change. Radioactivity was below detection limits in brain, spleen, and testes. Heart tissue in only 1 of 3 animals contained detectable quantities of radioactivity.

Excretion

The excretion of radioactivity in urine during the 72 hour collection period following inhalation exposure was best described using first order kinetics. Based on 12 hour interval excretion data the hal-life of elimination was 16 hours with an elimination rate constant, Ke, or 0.042 hr-1. Though the analysis was limited with only 3 data points, when tested for regression it was found the points did not represent a straight line. Using total recovered radioactivity to represent body content or body burden of 14C immediately following exposure, and given urinary and fecal interval excretion data, an estimate of the disappearance of radioactivity from the whole body with time can be obtained. The decline in body burden is linear and apparent first order with a half life of 26 hours and an elimination rate constant, Ke, of 0.027 hr-1.

Applicant's summary and conclusion

Conclusions

The data indicate that inhaled DIDP is metabolized and excreted rapidly exhibiting a low order of toxicity.

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Executive summary

The fate of DIDP was evaluated in 6 male Sprague Dawley rats (mean body weight 200 g) receiving head only exposure to 14C-DIDP aerosol atmosphere nominal concentration: 100 mg/m^{3}for 6 hours (General Motors Research Laboratories, 1981). The mass median aerodynamic diameter of DIDP aerosol was 0.98 μm. Three animals were sacrificed immediately following exposure, the remaining animals at the end of the 72-hour collection period. Feces were collected at 24-hour intervals and urine was collected at 12-hour intervals for 72 hours. The radioactivity was determined by liquid scintillation spectrometry.

Absorption: Total body burden following the exposure was 6.75 μmole equivalents or approximately 3 mg. Radioactivity derived from 14C -DIDP was excreted in urine and feces during the 72-hour post-exposure collection period: 45.3% and 41%, respectively, of the total body burden. At the end of the collection period following exposure, 9.4% of the absorbed dose of radioactivity was recovered from carcass and tissues, 2.4% from skin and 1.6% from cage wash.
Distribution: The distribution of radioactivity in rat tissues immediately following exposure, indicated the highest concentration of radioactivity was in lung followed by GIT, liver and kidney. The remaining tissues contained far lesser amounts. Radioactivity was below detection limit in brain, spleen and testes.
Elimination: After 72 hours the concentration was decreased in all tissues. The highest level of radioactivity was still found in lung which contained 27% of the content of radioactivity present immediately following exposure. The pulmonary load decreased to a lesser extent than all the tissues except fat which did not appear to change. Radioactivity derived from 14C -DIDP was excreted in urine and feces during the 72-hour post-exposure collection period: 45.3% and 41%, respectively, of the total body burden. The excretion of radioactivity in urine during the 72-hour collection period following inhalation exposure was best described using first order kinetics. Based on 12-hour interval excretion data, the half-life (T½) of elimination was 16 hours with an elimination rate constant Ke of 0.042/hour. Radioactivity derived from 14C -DIDP was excreted in urine (45.3%) and feces (41.3%) during the 72-hour post-exposure collection period. An additional 1.6% was recovered in washings of the metabolic cage collection surfaces and was derived from urine and fecal contamination. From these data 88% of the total absorbed dose of the radioactivity was excreted from the body, and the carcass retention data imply that a small fraction of DIDP or metabolites was retained in the body for a longer period of time. Using total recovered radioactivity to represent body content or body burden of ^{14}C immediately following exposure, and given urinary and fecal interval excretion data, an estimate of the disappearance of radioactivity from the whole body with time can be obtained. The decline in body burden was linear with an apparent first order with T½ of 26 hours and an elimination rate constant Ke of 0.027/h.

Administrative Data

Purpose flag	supporting study
Reliability	2 (reliable with restrictions)
Rationale for reliability	The study is rated a "2" because appropriate testing methods were used; however, the study does not follow and accepted guideline or indicate compliance with GLP.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1983							

Materials and methods

Type of method
in vivo

Objective of study

metabolism

GLP compliance

no data

Test material equivalent to submission substance identity

yes

Radiolabelling

yes carboxyl-14C

Test animals

Species

rat

Strain

Sprague-Dawley

Sex

male

Details on test animals and environmental conditions

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumenta1f5.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-4b5f5dbc-b949-4e68-a532-176e0af5f80d%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

TEST ANIMALS - Weight at study initiation: 200 g - Fasting period before study: 12 hours - Housing: Individual, Roth-type all-glass metabolism cages - Individual metabolism cages: yes - Diet: ad libitum - Water : ad libitum - Acclimation period: 2 days

Administration / exposure

Route of administration

oral: gavage

Vehicle

corn oil

Duration and frequency of treatment / exposure

Single exposure

Doses / concentrations

0.1, 11.2, 1000 mg/kg Specific concentrations of radioactivity were 10.9, 16.3, and 10.6 u Ci/ml, respectively to the low, middle, and high doses. Dosing volumes were 1 ml/kg in animals receiving 0.1 or 11.2 mg/kg DIDP and 2 ml/kg, to accommodate the larger volume of DIDP, in animals administered 1000 mg/kg.

No. of animals per sex per dose

3 males/dose

Control animals

no data

Details on dosing and sampling

METABOLITE CHARACTERISATION STUDIES - Tissues and body fluids sampled (delete / add / specify): urine, faeces, bile, homogenates of the carcass and feces, organ tissues (skin, brain, lungs, heart, thymus, liver, spleen, kidneys, adrenals, testes, fat, and the entire GI tract) - Time and frequency of sampling:Feces collected over 24 hour periods; urine collected over 12 hour periods; 72 hours after exposure at sacrifice, all tissues were collected - From how many animals: (samples pooled or not) - Method type(s) for identification: HPLC, Liquid scintillation counting, NMR, MS Experimental: Seventy-two hours after exposure, at termination of the collection periods, the animals wre sacrificed. Radioactivity in organ tissues, skin and feces, and carcass homogenates was assayed as 14CO2 evolved from combustion in a biological materials oxidizer and quantified by liquid scintillation spectrometry. Radioactivity in urine was determined by direct addition of 0.1 ml into 20ml Aquasol liquid scintillation cocktail. Data were expressed as umole equivalents DIDP or as percent of administered dose. Bile: Radioactivity in bile was determined using a modificaiton of the method reported by Enderlin and Honohan. Rats were fasted for 12 hours prior to surgery. Following anesthesia using sodium pentobarbital the common bile duct was exposed through a midline incision and carefully stripped of pancreatic tissue. The duct was cannulated and ligated distally, being cautious not to obstruct the pancreatic duct. The cannula was routed under the skin to the nape of the neck and exteriorized. Following recovery from anestheis, once adequate biole flow was established, teh animals were gavaged with 14CDIDP and placed in their individual cages. Bile was drained into a pre-weighed vial. Metabolism: DIDP and metabolites in tissues, bile and excreta were separated uisng HPLC. NMR and MS were used to confirm the monoester compound. Urine and bile from treated animals were filtered and applied directly to the column for analysis. Liver and feces were extracted using methanol at 50 deg C. Essentially 100% of fecal radioactivity was extracted but only 75-85% could be recovered for radioactivity.

Statistics

Data were analyzed using the Student's t-test and random complete block analysis of variance. Regression and linearity of interval excretion data were tested by analysis of variance. The 0.05 level of provability was used as the criterion of significance.

Results and discussions

Pharmacokinetic studies

Excretion

The primary route of excretion of radioactivity was in feces accounting for 57.5, 65.6 and 91.7% of the total body burden after 0.1,

11.2 and 1000 mg/kg, respectively. Elimination in urine and feces together represented greater than 99% of the administered dose. Only 0.5, 0.8, and 0.2% of the administered radioactivity was detected in the carcass of high, middle, and low dose animals. The percentage of total administered dose excreted in urine during the 72 hr collection interval was decreased with increasing dose from 41.3 to 32.1 and 12.6% after low, middle, and high doses. Radioactivity was detected only in the liver, kidney and the GI tract of animals 72 hours after treatment. The content of tissues in u mole equivalents of DIDP was increased with increasing dose. When expressed as a percentage of the total administered dose the values decreased slightly as dosage was increased. In bile, the percentage of total administered dose recovered within 72 hours was significantly decreased at the highest dose, from 14.3 and 13.8% after 0.1 and 11.2 mg/kg, respectively, to 4.7% after 1000 mg/kg.

Metabolite characterisation studies

Metabolites identified

yes

Details on metabolites

Phthalic acid and the oxidized monoester derivative were detected in urine from animals administered 14C DIDP. The monoester derivative was the major metabolite in urine accounting for as much as 72% after 1000 mg/kg. Concurrently, the proportion of radioactivity associated with phthalic acid was observed to decrease from 38 to 18% after 0.1 and 1000 mg/kg doses. MIDP or DIDP were not detected in urine after any of the doses. In feces, the monoester derivative, MIDP and DIDP were detected. When bile samples taken from 0-24 hours following dosing or liver and kidney samples taken 72 hours following dosing were assayed, DIDP was not detected in extracts.

Applicant's summary and conclusion

Conclusions

The disposition of DIDP administered perorally by gavage was dose dependent. It was observed that with increasing dose the percent total administered radioactivity in feces was increased while the percent in urine was decreased. These data suggest that absorption of DIDP or its metabolites was limited and that with dose, increasing amounts of unabsorbed compound were being eliminated.

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumenta1f5.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-4b5f5dbc-b949-4e68-a532-176e0af5f80d%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Executive summary

Dose-related alterations in disposition were investigated for DIDP. Sprague Dawley rats were administered (carboxyl-^{14}C)DIDP perorally in corn oil at 0.1, 11.2 and 1000 mg/kg. At each treatment level, 99% of administered ^{14}C was recovered in excreta within 72 hours. The percent of total administered ^{14}C revocered in feces increased with increasing dose (58, 66, 82%) and in extracts analyzed by HPLC, 30% of ^{14}C at the low dose and 60% at the high dose were identified as DIDP, the remainder as metabolites. Excretion in urine was biphasic and there was not an apparent dose effect on the rates of elimination. Metabolites in urine included phthalic acid (PA) and a group of mono-isodecyl phthalate derivatives. The proportions of PA in urine were 38 and 40% after 0.1 and 11.2 mg/kg respectively and decreased to 18% after 1000 mg/kg. In major organ tissues, the percent of the dose retained after 72 hours was not dose dependent. Therefore, gastrointestinal absorption is limited with increasing dose and distribution to tissue is proportional. There is evidence suggesting partial saturation or inhibition of metabolism but it was not an apparent factor in clearance capacity.

Dissemination Dossier
Dermal absorption Endpoint:091

Administrative Data

Purpose flag supporting study

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Elsisi AE, Carter DE, Sipes IG.	1989	Dermal absorption of phthalate diesters in rats.	Fundam Appl Toxicol. 1989 Jan;12(1):70-7.					

Dissemination Dossier
Acute oral Endpoint.001

Administrative Data

Purpose flag key study

Study result type experimental result

Reliability 4 (not assignable)

Rationale for reliability Study is rated a "4" because the study predates GLP and limited details are provided.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Smyth HF, Jr, et al	1962	Range-Finding Toxicity Data: List VI	Am Ind Hyg Assoc J 23:95-107					

Materials and methods

Principles of method if other than guideline

Method: other: Smyth H.F. et al. Am. Ind. Hyg. Assoc. J. 23:95-107

GLP compliance

no

Test materials

Details on test material

IUCLID4 Test substance: other TS: unspecified DIDP isomer

Test animals

Species

rat

Strain

Wistar

Sex

male

Details on test animals and environmental conditions

TEST ANIMALS
- Age at study initiation: 4-5 wks of age
- Weight at study initiation: 90-120 g
- Diet (e.g. ad libitum): Rockland rat diet, complete

Administration / exposure

Route of administration

oral: gavage

Details on oral exposure

14 day observation period following single dose administration

No. of animals per sex per dose

5

Results and discussions

Effect levels

Sex	Endpoint	Effect level	95% CL	Remarks
male	LD50	> 60000 mg/kg bw		

Remarks on results including tables and figures

Applicant's summary and conclusion

Interpretation of results

practically nontoxic

Conclusions

The test substance is assumed to have a low order of acute toxicity by the oral route.

Executive summary

The LD50 of DIDP in rats is greater than 62,080 mg/kg (Smyth et al., 1962).

Dissemination Dossier
Acute oral Endpoint.002

Administrative Data

Purpose flag supporting study

Reliability 4 (not assignable)

Rationale for reliability Study is rated a "4" because the study predates GLP and limited details are provided.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Shibko SI and Blumenthal H	1973	Toxicology of Phthalic Acid Esters Used in Food-Packaging Material	Env Health Perspec 3:131-137					

Materials and methods

Principles of method if other than guideline

Method: other: not specified

GLP compliance

no data

Test materials

Details on test material

IUCLID4 Test substance: other TS: unspecified DIDP

Test animals

Species

rat

Results and discussions

Effect levels

Sex	Endpoint	Effect level	95% CL	Remarks
	LD50	64000 mg/kg bw		

Dissemination Dossier
Acute oral Endpoint.003

Administrative Data

Purpose flag supporting study

Study result type experimental result

Reliability 4 (not assignable)

Rationale for reliability The study is rated a "4" because it predates GLP and limited details are provided.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Krauskopf, LG	1973	Studies on the toxicity of phthalates via ingestion	Environmental Health Perspectives, p 61-72					

Materials and methods

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

yes

Test animals

Species

other: rat and rabbit

Administration / exposure

Route of administration

oral: unspecified

Doses

single dose

Results and discussions

Effect levels

Sex	Endpoint	Effect level	95% CL	Remarks

no data	LD50	29100 mg/kg bw	rat
no data	LD50	29100 mg/kg bw	rabbit

Mortality

non-lethal

Applicant's summary and conclusion

Interpretation of results

practically nontoxic

Criteria used for interpretation of results

not specified

Conclusions

The test substance is assumed to have a low order of acute toxicity by the oral route. The LD50 was reported to be 29,100 mg/kg in rats and in rabbits, a minimum lethal dose of 21,825-29,100 mg/kg has been calculated

Administrative Data

Purpose flag	key study
Study result type	experimental result
Reliability	2 (reliable with restrictions)
Rationale for reliability	The study is rated a "2" because appropriate testing methods were used; however, the study predates GLP.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1975							

Materials and methods

Principles of method if other than guideline
Method: other: not specified

GLP compliance

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentb9d6.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-21832e04-749b-4b28-bca5-bfa5d98cd2f7%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

no data

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

IUCLID4 Test substance: as prescribed by 1.1 - 1.4

Test animals

Species

other: albino rats, mice and guinea pigs

Strain

other: other

Sex

male/female

Administration / exposure

Route of administration

inhalation: vapour

Type of inhalation exposure

whole body

Details on inhalation exposure

A stream of clean, dry air (-40 deg dewpoint) was passed through the undiluted test material and into the exposure chamber.

Duration of exposure

6 h Remarks

Concentrations

0.13 mg/l air

No. of animals per sex per dose

Test groups: 5 animals/species/sex/dose. A total of 30 animals were used, 10 rats, 10 mice, 10 guinea pigs, 5 of each sex. Control Groups: A total of 15 animals were used, 5 rats, 5 mice, 5 guinea pigs. For each species, 3 were males and 2 were females.

Control animals

yes

Results and discussions

Effect levels

Sex	Endpoint	Effect level	95% CL	Exp. duration	Remarks

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentb9d6.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-21832e04-749b-4b28-bca5-bfa5d98cd2f7%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

male/female	LC50	> 0.13 mg/L air	6 h

Mortality

No animals died during the study.

Body weight

The average 2 week body weight gains were within the normal limits except for 1 male guinea pig that lost 175 g. The remaining 4 guinea pigs weights were averaged.

Gross pathology

Necropsy, performed on all animals at the end of the observation period, revealed no gross pathologic alterations.

Applicant's summary and conclusion

Interpretation of results
practically nontoxic

Conclusions

The test substance is expected to have a low order of acute toxicity by the inhalation route, due to its very low vapor pressure and the results obtained.

Executive summary

A 6-hour exposure inhalation study was conducted in rats, mice and Guinea pigs (5 males and 5 females) at 0.13 mg/l (nominal concentration). DIDP is indicated to be administered as a vapour, but regarding the test conditions the substance was probably administered as an aerosol. No death occurred, no adverse reactions were noticed following the 14-day observation period, no gross

tissue changes attributable to effects of the test material were observed in any of the animals examined.

Dissemination Dossier
Acute inhal Endpoint.002

Administrative Data

Purpose flag supporting study

Study result type experimental result

Reliability 4 (not assignable)

Rationale for reliability The study is rated a "4" because it predates GLP and limited details are provided.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Smyth HR Jr et al.	1962	Range finding toxicity data: List VI	Am Ind Hyg Assoc J 23:95-107					

Materials and methods

Test type

other:

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

Unspecified DIDP isomer

Test animals

Species

rat

Strain

Wistar

Sex

male/female

Details on test animals and environmental conditions

TEST ANIMALS
- Age at study initiation: 4-5 wks of age
- Weight at study initiation: 90-120 g
- Diet (e.g. ad libitum): Rockland rat diet, complete

Administration / exposure

Route of administration

inhalation: vapour

Type of inhalation exposure

no data

Duration of exposure

8 h **Remarks**

No. of animals per sex per dose

6 male and 6 female rats/dose

Control animals

no data

Results and discussions

Mortality

non-lethal

Applicant's summary and conclusion

Interpretation of results

practically nontoxic

Criteria used for interpretation of results

not specified

Conclusions

LC50 not determined. Doses were not specified although the exposure was not lethal to rats.

Administrative Data

Purpose flag	key study
Study result type	experimental result
Reliability	2 (reliable with restrictions)
Rationale for reliability	The study is rated a "2" because it applied appropriate testing methods; however, the study predates GLP.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1975							

Materials and methods

Test type

standard acute method

Principles of method if other than guideline

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument4870.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-264e2181-19a4-47b8-87b6-b6663c1deb9d%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934
Method: other: not specified

GLP compliance

no data

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

IUCLID4 Test substance: as prescribed by 1.1 - 1.4

Test animals

Species
rabbit

Strain

other: Albino

Sex

male/female

Administration / exposure

Details on dermal exposure

The test skin site of all rabbits was abraded.

Doses

200 and 3,160 mg/kg

No. of animals per sex per dose

4

Results and discussions

Effect levels

Sex	Endpoint	Effect level	95% CL	Remarks
male/female	LD50	> 3160 mg/kg bw		

Mortality

No animals died during the course of the study.

Gross pathology

Necropsy examination did not reveal any gross pathologic alterations except for local skin changes as described.

Other findings

The test material was midly irritating to the skin of the albino rabbits from both dose levels. Skin changes at 24 hours were characterized by pale red to red, well-defined erythema. Slight desquamation was observed at 7 and 14 days.

Applicant's summary and conclusion

Interpretation of results

practically nontoxic

Conclusions

The LD50 > 3,160 mg/kg/day.

Executive summary

In a rabbit occlusive study, two groups of 2 males and 2 females were exposed cutaneously for 24 hours to 200 and 3,160 mg/kg. During the observation period of 14 days, no death occurred, no systemic toxicity was noted, skin changes at 24 hours were characterised by a well-defined erythema and slight desquamation at 7 and 14 days. Necropsy examination did not reveal any gross pathologic alterations except for the local skin changes previously described. The conclusion was that the LD50 was greater than 3,160 mg/kg.

Administrative Data

Purpose flag	key study
Study result type	experimental result
Reliability	2 (reliable with restrictions)
Rationale for reliability	The study is rated a "2" because it applied appropriate testing methods; however, the study predates GLP.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1978							1978-08-14

Materials and methods

Test type

standard acute method

Test guideline

Qualifier	Guideline	Deviations
equivalent or similar to	OECD Guideline 402 (Acute Dermal Toxicity)	not applicable

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

- Name of test material (as cited in study report): MRD-78-44

Test animals

Species
rabbit

Strain

New Zealand White

Sex

no data

Details on test animals and environmental conditions

TEST ANIMALS - Source: Bunnyville Farms, Littlestown, Pennsylvania - Housing: indivial in metal cages - Diet: Rabbit ration (Purina Rabbit Chow Checkers) ad libitum - Water: ad libitum

Administration / exposure

Type of coverage

occlusive

Duration of exposure

24 hours

Doses

3160 mg/kg bw

No. of animals per sex per dose

4

Control animals

no

Details on study design

- Duration of observation period following administration: 14 days - Frequency of observations and weighing: All rabbits were observed daily for mortality, and signs of toxic and pharmacologic effects. All rabbits were weighed initially, and at termination

(Day14). - Necropsy of survivors performed: yes

Results and discussions

Effect levels

Sex	Endpoint	Effect level	95% CL	Remarks
no data	LD50	> 3160 mg/kg bw		

Mortality

All 4 rabbits survived the 14 day test period at the 3160 mg/kg dose level.

Clinical signs

Clinical observation included slight to marked anorexia, and slight to moderate depression in all four rabbits. At termination, all 4 rabbits appeared normal.

Body weight

All 4 rabbits showed body weight gain. Statistics were not used to determine significance of body weight gain.

Gross pathology

Gross pathology finding noted in teh animals sacrificed on day 14 included dark red lungs in 3 rabbits and white, raised areas on all lobes of the lungs in the 4th rabbit.

Other findings

Slight to well-defined erythema was noted in two rabbits at 24 hours. Very slight erythema was noted in these two rabbits at day 3.

The remaining two rabbits exhibited very slight erythema at 24 hours. Erythema in these rabbits reversed itself by day 3. No edema was noted in any of the rabbits treated.

Applicant's summary and conclusion

Conclusions

The LD50 > 3,160 mg/kg bw/day.

Dissemination Dossier
Acute dermal Endpoint.003

Administrative Data

Purpose flag supporting study
Study result type experimental result
Reliability 4 (not assignable)
Rationale for reliability Study is rated a "4" because the study predates GLP and limited details are provided.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Smyth HF, Jr, et al	1962	Range-Finding Toxicity Data: List VI	Am Ind Hyg Assoc J 23:95-107					

Materials and methods

Principles of method if other than guideline
Method: other: Smyth H.F. et al. Am. Ind. Hyg. Assoc. J. 23:95-107

GLP compliance

no

Test materials

Details on test material
IUCLID4 Test substance: other TS: unspecified DIDP

Test animals

Species
rabbit

Sex

male

Results and discussions

Effect levels

Sex	Endpoint	Effect level	95% CL	Remarks
male	LD50	16000 mg/kg bw		

Applicant's summary and conclusion

Executive summary

In a briefly reported study, 4 male rabbits were exposed to 10 ml DIDP (purity unknown) cutaneously for 24 hours, clinical signs and mortality were not reported and the conclusion was that the LD50 was greater than 10 ml/kg (9,700 mg/kg).

Administrative Data

Purpose flag	supporting study
Study result type	experimental result
Reliability	4 (not assignable)
Rationale for reliability	Study is rated a "4" because the study predates GLP and limited details are provided.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Lawrence WH, et al	1975	A Toxicological Investigation of some Acute, Short-Term, and Chronic Effects of Administering Di-2-ethylhexyl Phthalate (DEHP) and Other Phthalate Esters	Environ Res 9:1-11					

Materials and methods

Principles of method if other than guideline

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumente6c1.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-dd8f5ab2-da4c-4482-9ebe-4c17aeee4013%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

other : not specified

GLP compliance

no data

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

IUCLID4 Test substance: other TS: DIDP with different CAS#

Test animals

Species

mouse

Strain

ICR

Sex

male

Administration / exposure

Route of administration

intraperitoneal

Results and discussions

Effect levels

Sex	Endpoint	Effect level	95% CL	Remarks
male	LD50	> 100 g/kg		

Applicant's summary and conclusion

Conclusions

The test substance has a low order of acute toxicity by the i.p route of exposure. The LD50 > 100 g/kg.

Administrative Data

Purpose flag	supporting study
Study result type	experimental result
Reliability	4 (not assignable)
Rationale for reliability	Study is rated a "4" because the study predates GLP and limited details are provided.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
	Lawrence WH, et al	1975	A Toxicological Investigation of some Acute, Short-Term, and Chronic Effects of Administering Di-2-ethylhexyl Phthalate (DEHP) and Other Phthalate Esters	Environ Res 9:1-11					

Materials and methods

Principles of method if other than guideline

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument076a.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-505c7dbd-10c9-42ed-89c7-f0491a362944%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934
Method: other: single intradermal injection

GLP compliance

no data

Test materials

Details on test material
IUCLID4 Test substance: other TS: DIDP with different CAS#

Test animals

Species
mouse

Test system

Vehicle
other: cottonseed oil

Amount/concentration applied

undiluted

Number of animals

10

Control animals

yes

Results and discussions

Irritation / corrosion results

Irritation parameter	Basis	Time point	Score	Max. score	Reversibility	Remarks
other: TIC-4 value: 10 responses for each concentration were obtained, scored, and converted to an 8-point scale for graphic determination by the method of Luduena and Hoppe, 1952.			> 100			The TIC-4 value provokes a mild but distinct irritant reaction. When the undiluted phthalate failed to produce a degree of irritation equivalent to that for TIC-4, it is recorded as > 100%

Applicant's summary and conclusion

Interpretation of results

not irritating

Conclusions

Under the conditions of this study, the test substance is not an irritant.

Dissemination Dossier
Skin irritation Endpoint.002

Administrative Data

Purpose flag supporting study

Study result type experimental result

Reliability 4 (not assignable)

Rationale for reliability Study is rated a "4" becausethe study predates GLP and limited details are provided.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
	Smyth HF, Jr, et al	1962	Range-Finding Toxicity Data: List Vi	Am Ind Hyg Assoc J 23:95-107					

Materials and methods

Principles of method if other than guideline

Method: other: 24 hr exposure

GLP compliance

no

Test materials

Details on test material

IUCLID4 Test substance: other TS: unspecified DIDP

Test animals

Species

rabbit

Strain

other: Albino

Test system

Amount/concentration applied

0.01 ml of undiluted sample

Duration of treatment / exposure

24 hours

Number of animals

5

Control animals

yes

Applicant's summary and conclusion

Interpretation of results

not irritating

Conclusions

Undiluted test substance produced no sign of irritation via the intraperitoneal route and is therefore not considered an irritant.

Administrative Data

Purpose flag	key study
Study result type	experimental result
Reliability	1 (reliable without restriction)
Rationale for reliability	This study is rated a "1" because it applied GLP, used appropriate testing procedures, and followed an accepted test guideline.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1996							

Materials and methods

Type of method

in vivo

Test guideline

Qualifier	Guideline	Deviations
according to	OECD Guideline 404 (Acute Dermal Irritation / Corrosion)	

GLP compliance

yes

Test material equivalent to submission substance identity

yes

Test materials

Details on test material
IUCLID4 Test substance: as prescribed by 1.1 - 1.4

Test animals

Species
rabbit

Strain

New Zealand White

Details on test animals and environmental conditions

TEST ANIMALS - Source: HRP Inc., Denver, PA - Age at study initiation: 13-14 weeks - Weight at study initiation: 2.17-2.42 kg - Housing: single housed - Diet: certified Rabbit Diet 5322. Animals received new feed each day. - Water: ad libitum - Acclimation

period: 10 days ENVIRONMENTAL CONDITIONS - Temperature (°C): 65-70 - Humidity (%): 40-60 - Photoperiod (hrs dark / hrs light): 12 hours light/ 12 hours dark IN-LIFE DATES: From: 1995-12-21 To:1995-12-26

Test system

Type of coverage

semiocclusive

Preparation of test site

other: closely clipped with electric clipper

Vehicle

unchanged (no vehicle)

Amount/concentration applied

TEST MATERIAL - Amount(s) applied (volume or weight with unit): 0.5ml

Duration of treatment / exposure

4 hours

Observation period

Dermal responses were evaluated 60 minutes, 24, 48, and 72 hours following patch removal.

Number of animals

Details on study design

TEST SITE - Area of exposure: 1 inch x 1 inch REMOVAL OF TEST SUBSTANCE - Washing (if done): Test site was wiped using peanut oil and paper towels to remove any residual material without altering the existing response or integrity of the epidermis. - Time after start of exposure: 4 hours SCORING SYSTEM: All scoring was made according to the modified Draize method of scoring (Draize, 1959). Mean erythema and edema scores were calculated (Snedecor and Cochran, 1989).

Results and discussions

Irritation / corrosion results

Irritation parameter	Basis	Time point	Score	Max. score	Reversibility	Remarks
primary dermal irritation index (PDII)	mean	24-72 hour	0		fully reversible	

Irritant/corrosive response data

Topical application of the test substance elicited very slight erythema in one animal at the 60 minute time point. All animals were free of erythema, edema, or other supplemental dermal findings during the remainder of the study. Consequently, the study was terminated following the 72 hour observation period.

Other effects

Clinical signs were not observed in any animal during the test period. All animals survived to study termination.

Remarks on results including tables and figures

The mean erythema and edema scores for each time interval were as follows:

ERYTHEMA:

60 min: 0.17

24 hr: 0.00

48 hr: 0.00

72 hr: 0.00

EDEMA:

60 min: 0.00

24 hr: 0.00

48 hr: 0.00

72 hr: 0.00

Mean erythema and edema for 24, 48, and 72 hours were as follows:

Erythema : 0.00

Edema: 0.00

Applicant's summary and conclusion

Interpretation of results
not irritating

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument8fe6.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f6231a0e-fe77-434a-a531-3b8147f78452%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Conclusions

Based on the findings of this study and a primary irritation index of 0.00, the test substance is considered a non-irritant to rabbit skin.

Executive summary

Six male rabbits were exposed to 0.5 ml of the test material during 4 hours, the patch held in contact with the skin by means of a semi-occlusive dressing. Only very slight erythema in one animal was noted at 60 minutes after removal of the patch, no other signs of irritation at 24, 48 and 72 hours were observed. This study was performed according to GLP procedures.

Administrative Data

Purpose flag	supporting study
Study result type	experimental result
Reliability	1 (reliable without restriction)
Rationale for reliability	This study is rated a "1" because it applied GLP and used appropriate testing procedures.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Medeiros MA, Devlin JD and Keller LH	1999	Evaluation of skin sensitization response of dialkyl (C6-C13) phthalate esters	Contact Dermatitis 41:287-289					
study report		1995							

Materials and methods

Type of method

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument9f29.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f73d7f3e-4aa2-43ad-9fbc-aeeca7951b26%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934
in vivo

Principles of method if other than guideline

Method: other: single 24 hr application

GLP compliance

yes

Test material equivalent to submission substance identity

yes

Test materials

Details on test material
IUCLID4 Test substance: as prescribed by 1.1 - 1.4

Test animals

Species
human

Test system

Type of coverage
occlusive

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument9f29.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f73d7f3e-4aa2-43ad-9fbc-aeeca7951b26%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Vehicle

unchanged (no vehicle)

Amount/concentration applied

Concentration: 100 %

Duration of treatment / exposure

24 hour(s)

Observation period

30 minutes and 24 hours following patch removal

Number of animals

15

Details on study design

Fifteen subjects (14 female and 1 male) entered and completed the study. Undiluted test materials were applied to a nonwoven cotton pad, covered by and held securely onto the skin on all sides with an occlusive, hypoallergenic tape. Two evaluations were conducted, the 1st at 30 min after patch removal, and the 2nd at 24 hours post-patch removal.

Results and discussions

Irritation / corrosion results

Irritation parameter	Basis	Time point	Score	Max. score	Reversibility	Remarks

primary dermal irritation index (PDII) 0

Applicant's summary and conclusion

Interpretation of results

not irritating

Conclusions

There was no significant irritation when undiluted phthalate esters were applied to the skin for 24 hours. Therefore the test substance is considered non irritating.

Administrative Data

Purpose flag	supporting study
Study result type	experimental result
Reliability	4 (not assignable)
Rationale for reliability	Study is rated a "4" because the study predates GLP and limited details are provided.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
	Lawrence WH, et al	1975	A Toxicological Investigation of some Acute, Short-Term, and Chronic Effects of Administering Di-2-ethylhexyl Phthalate (DEHP) and Other Phthalate Esters	Environ Res 9:1-11					

Materials and methods

Type of method

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument3dd1.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-bd1f3dee-ef53-4ef5-9d55-e07c40c94622%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

in vivo

Principles of method if other than guideline

Method: other: Lawrence W.H. et al. (1971) J. Pharm. Sci. 60:568-571.

GLP compliance

no data

Test materials

Details on test material

IUCLID4 Test substance: other TS: DIDP with different CAS#

Test animals

Species

rabbit

Test system

Amount/concentration applied

undiluted

Observation period

Signs of irritation were noted at 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 24.0 or 48 hours after instillation of the undiluted test substance.

Number of animals

10

Applicant's summary and conclusion

Interpretation of results

not irritating

Conclusions

Under the conditions of this study, the test substance was not irritating to the eye.

Administrative Data

Purpose flag	key study
Study result type	experimental result
Reliability	2 (reliable with restrictions)
Rationale for reliability	The study is rated a "2" because appropriate testing methods were used; however, the study predates GLP.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1975							1975-09-17

Materials and methods

Type of method
in vivo

Test guideline

Qualifier	Guideline	Deviations
according to	OECD Guideline 405 (Acute Eye Irritation / Corrosion)	

GLP compliance

no

Test material equivalent to submission substance identity

yes

Test animals

Species
rabbit

Strain

other: Albino

Test system

Vehicle
unchanged (no vehicle)

Amount/concentration applied

Concentration: 0.1 undiluted Amount applied: 0.1 ml

Duration of treatment / exposure

single exposure

Observation period

4 days

Number of animals

6

Results and discussions

Overall irritation / corrosion results

Irritation parameter	Basis	Time point	Max. score	Reversibility	Remarks
cornea score	mean	24-48 hours	0	fully reversible	
conjunctivae score	mean	24-48 h	0	fully reversible	

Applicant's summary and conclusion

Interpretation of results

slightly irritating

Conclusions

Under the conditions of this study, the test substance was considered minimally irritating.

Executive summary

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument03ab.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-536c5928-6eab-4dbc-94dc-9087fa096152%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

In a study conducted in 6 rabbits, undiluted DIDP produced only slight signs of irritation in the conjunctiva at 1, 4 and 24-hour observation time (redness score 1 or 2 and discharge at 1 hour, redness score 1 at 4 hours and redness score 1 in 1 animal at 24 hours). All the eyes were normal at 48, 72 and 96 hours.

Administrative Data

Purpose flag	supporting study
Study result type	experimental result
Reliability	1 (reliable without restriction)
Rationale for reliability	This study is rated a "1" because it applied GLP, used appropriate testing procedures, and followed an accepted test guideline.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1992							1992-10-08

Materials and methods

Type of study

Buehler test

Test guideline

Qualifier	Guideline	Deviations
according to	OECD Guideline 406 (Skin Sensitisation)	

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

IUCLID4 Test substance: as prescribed by 1.1 - 1.4

Test animals

Species
guinea pig

Strain

Hartley

Sex

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentf14c.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-fc104f45-aba8-4e86-9034-1a93dab10c06%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

female

Details on test animals and environmental conditions

TEST ANIMALS - Source: Hazelton Research Products, Inc. Denver, PA - Age at study initiation: ~6 weeks - Weight at study initiation: 328-432 g - Housing: single housed in suspended stainless steel and wire mesh with absorbent paper below cages. - Diet: Agway PROLAB certified guinea pig diet, ad libitum - Water: ad libitum - Acclimation period:16 days ENVIRONMENTAL CONDITIONS - Temperature (°C): 65-71 - Humidity (%): 40-70 - Photoperiod (hrs dark / hrs light): 12 hours light/12 hours dark

Test system

Traditional sensitisation test

Route of induction exposure

epicutaneous, occlusive

Route of challenge exposure

epicutaneous, occlusive

Vehicle

peanut oil

Concentration

100%

No. of animals per dose

20 animals/dose

Details on study design (Traditional tests)

1st application: Induction undiluted occlusive epicutaneous 2nd application: Challenge 5 % occlusive epicutaneous 3rd application: Challenge 1 % occlusive epicutaneous MAIN STUDY A. INDUCTION EXPOSURE - No. of exposures: 3 - Exposure period: 6hrs - Test groups: 1 - Control group: 1 - Site: scapular region B. CHALLENGE EXPOSURE - No. of exposures: 1 - Day(s) of challenge: 1 - Exposure period: 6 hours - Test groups: 1 - Control group: 1 (10 animals only) - Site: right flank in the abdominal region - Concentrations: 5.0% w/w in carrier - Evaluation (hr after challenge): 24 and 48 hours C. RECHALLENGE - No. of exposures: 1 - Day(s) of challenge: 1 - Exposure period: 6 hours - Test groups: 1 (all 20 animals) - Control group: 10 animals only - Site: left flank in the abdominal region - Concentrations: 1.0% w/w in carrier - Evaluation (hr after rechallenge): 24 and 48 hours

Positive control substance(s)

yes DNCB

Results and discussion

Positive control results

Topical application of DNCB (0.1%) to the positive control group animals elicited slight to well-defined erythema and slight edema during the induction phase. Following the challenge phase, signs of sensitization were observed in 9/10 positive control animals.

Traditional sensitisation test

Results of test (except LLNA)

Reading	Hours after challenge	Group	Dose level	No. with + reactions	Total no. in group	Clinical observations
1st reading	24	negative control				Very slight erythema was observed in 4/10 irritation control animals and well-defined erythema was noted in one irritation control animal

				at the Day 29 interval. Very slight edema was observed in 1 irritation control animal.
2nd reading	48	negative control		Erythema scores diminished in incidence and severity following 48hrs after challenge when 3 irritation control animals exhibited very slight erythema.
1st reading	24	test group	5.0%	Following challenge, very slight erythema was observed in 16/20 treated animals and well-defined erythema was observed in 3/20 treated animals. Very slight edema was observed in 2/20 treated animals.
2nd reading	48	test group	5.0%	Very slight erythema was observed in 8/20 treated animals.
rechallenge	48	negative control		One irritation control animal was noted with very slight erythema following rechallenge.
rechallenge	24	test group	1.0%	Rechallenge produced dermal irritation in 15/20 treated group animals. Eight treated animals were observed with very sligh erythema and 7 treated animals were observed with well-defined erythema.
rechallenge	48	test group	1.0%	One animal's erythema increased to moderate/severe. 9/20 were considered very slight and 7/20 were considered well-defined. Very slight edema was observed in 1 treated animal.

Applicant's summary and conclusion

Interpretation of results
ambiguous

Conclusions

The response seen at the 48 hour observation after rechallenge exhibited the sign of sensitization. The scores of the majority of the animals remained the same or increased from the 24 hour scores. Edema was noted in one animal at the 48 hour observation. This

response was not noted at the 24 hour observation and the edema was noted in the animal with moderate/severe erythema. Based on this response the test substance may have a mild to moderate sensitization potential.

Executive summary

In a modified Buehler test 40 Guinea-pigs (20 treated females and 20 controls) were used for the assessment of dermal sensitisation. Induction phase was performed on days 0, 7 and 14 by occlusive topical application with undiluted DIDP. DNCB (0.1%) was used as a positive control. Signs of irritation were observed on 18/20 during induction phase. Challenge was performed on day 28 with 5% DIDP in peanut oil. Due to the reactions of irritation noted in the irritation control group, a rechallenge was conducted on day 35 at a lower concentration (1%). Following challenge and rechallenge, one treated animal did not react. Following rechallenge (1%), 4 of 20 treated animals did not react, 8 of 20 were observed with very slight erythema (score 1), 7 of 20 were observed with well-defined erythema (score 2) and very slight oedema was observed in one treated animal (score 1). On day 37, erythema of one treated animal was increased from slight to moderate/severe erythema (score 3). Irritation was noted in one control animal with very slight erythema following rechallenge.

Administrative Data

Purpose flag	supporting study
Study result type	experimental result
Reliability	1 (reliable without restriction)
Rationale for reliability	This study is rated a "1" because it applied GLP and used appropriate testing procedures.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		1999							
study report		1995							

Materials and methods

Type of study

Patch-Test

Principles of method if other than guideline

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument8883.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-717c73de-0d25-41c2-b78b-aa98b3b7c195%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Method: other: Modified Draize Patch Test

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

IUCLID4 Test substance: as prescribed by 1.1 - 1.4

Test animals

Species

human

Sex

male/female

Test system

Traditional sensitisation test

Route of induction exposure

epicutaneous, occlusive

Route of challenge exposure

epicutaneous, occlusive

Vehicle

unchanged (no vehicle)

Concentration

undiluted at 100% concentration

No. of animals per dose

104

Details on study design (Traditional tests)

1st application: Induction 100 % occlusive epicutaneous 2nd application: Challenge 100 % occlusive epicutaneous

Results and discussion

Traditional sensitisation test

Results of test (except LLNA)

Reading	Hours after challenge	Group	Dose level	No. with + reactions	Total no. in group	Clinical observations

1st reading	48	test group	undiluted, 100% concentration	0	104
2nd reading	96	test group	Undiluted, 100% concentration	0	104

LLNA

Remarks on results including tables and figures

RS-Freetext:
Of the 128 panelist enrolled in the HRIPT, 104 completed the study; the remainder did not complete the study for reasons unrelated to the test materials. During both induction and challenge phases of the study, there was no evidence of dermal irritation.

Applicant's summary and conclusion

Interpretation of results

not sensitising

Conclusions

CL-Freetext: Under the conditions of the HRIPT, there was no evidence of skin irritation or sensitization in any of the 104 panelists completing the study. These HRIPT data provided evidence for the lack of skin sensitization potential for diisodecyl phthalate in humans. Classification: not sensitizing

Executive summary

A repeated insult patch test (modified Draize procedure) has been performed on 128 volunteers, 104 completed the study. All exposures were by 24 ± 1 hour contact under occluded patches with undiluted DIDP. Induction applications were made three times per week for three successive weeks. Following a 10 to 17-day rest period, a challenge application of the test article was made to a naive site located away from the original application site. Simultaneous application to a pre-exposed site (i.e. the original site used for

induction application) was made concurrently with the challenge at a naive site. Reactions were scored 48 or 72 hours after each induction application (24 or 48 hours after patch removal) and 48 and 96 hours after challenge (24 and 72 hours after patch removal). In induction and challenge phases, no responses were observed to the test article throughout the pilot and main phase of the study. Under the conditions of the study, no evidence of clinical sensitisation or irritation was observed in any of the 104 subjects completing the pilot and the main phase of the study.

Administrative Data

Purpose flag	key study
Study result type	experimental result
Reliability	1 (reliable without restriction)
Rationale for reliability	This study is rated a "1" because it applied GLP, used appropriate testing procedures, and followed an accepted test guideline.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1994							1994-09-20

Materials and methods

Type of method

in vivo

Type of study

Buehler test

Principles of method if other than guideline

Method: other: Directive 92/69/EEC, B.6

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

IUCLID4 Test substance: as prescribed by 1.1 - 1.4

Test animals

Species
guinea pig

Strain

Dunkin-Hartley

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentf863.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-67302cc6-3181-4ef4-a265-dfbfc365fafa%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Sex

female

Details on test animals and environmental conditions

TEST ANIMALS - Source: D Hall, Newchurch, Staffordshire, England - Age at study initiation: 6-7 weeks - Weight at study initiation: 283-343 g - Housing: groups of 5 in suspended metal cages with wire mesh floors - Diet (e.g. ad libitum): vitamin C enriched guinea-pig diet FD1 ad libitum. Hay was given weekly - Water: ad libitum - Acclimation period: 11 days ENVIRONMENTAL CONDITIONS - Temperature (°C): 21 - Humidity (%): 30-70 - Air changes (per hr): 15/hour - Photoperiod (hrs dark / hrs light): 12 hours light/12 hours dark IN-LIFE DATES: From: 13-07-1994 To: 18-08-1994

Test system

Traditional sensitisation test

Route of induction exposure

epicutaneous, occlusive

Vehicle

other: Alembicol D

Concentration

As supplied

No. of animals per dose

20 animals/dose

Details on study design (Traditional tests)

1st application: Induction undiluted 2nd application: Challenge undiluted RANGE FINDING TESTS: A topical irritancy of a range of dilutions of the test substance was investigated to identify where possible (a) concentrations that would produce irritation suitable for the induction phase of the main study and (b) a maximum non-irritant concentration for the challenge phase. Concentrations tested included 100, 80, 60, 40% v/v. The concentration of test substance was based on the results of the preliminary investigations. This was the maximum practical concentration and did not give rise to irritating effects. MAIN STUDY A. INDUCTION EXPOSURE - No. of exposures: 3 - Exposure period: 6hrs each - Test groups: 1 - Control group: 1 - Site: skin of the left shoulder region, clipped free of hair - Frequency of applications: once per exposure - Concentrations: as supplied - Evaluation (hr after removal of patches): 30 minutes, and 24 hours B. CHALLENGE EXPOSURE - No. of exposures: 1 - Day(s) of challenge: challenge occurred 2 weeks following the final induction application - Exposure period: 6hrs - Test groups: 1 - Control group: 1 - Site: skin of the left shoulder region, clipped free of hair - Concentrations: as supplied - Evaluation (hr after challenge): 24, 48, and 72 hours

Positive control substance(s)

yes formalin

Results and discussion

Positive control results

Positive control results were used from Huntingdon's historical data. In a study Huntingdon conducted in 1993, 10/10 test animals were positive following 3 inductions with formalin at concentrations of 25 or 30% (aqueous dilutions) and challenge at a concentration of 15%.

Traditional sensitisation test

Results of test (except LLNA)

Reading	Hours after challenge	Group	Dose level	No. with + reactions	Total no. in group	Clinical observations
1st reading	24	test group	neat	0	20	
2nd reading	48	test group	neat	0	20	

other: 3rd reading	72	test group	neat	0	20
1st reading	24	negative control	0	0	20
2nd reading	48	negative control	0	0	20
other: 3rd reading	72	negative control	0	0	20

Applicant's summary and conclusion

Interpretation of results
not sensitising

Conclusions

There were no dermal reactions observed in control or test animals following induction or challenge application. Therefore, the test substance did not produce evidence of skin sensitization (delayed contact hypersensitivity) in any animals.

Executive summary

In a Buehler test conducted with Jayflex DIDP (composition not available to the laboratory) in 40 Guinea pigs (20 treated and 20 controls), undiluted substance was applied during induction phases (day 1, 8 and 15) and challenge (day 28), no sign of sensitisation was reported. No sign of irritation was reported during the induction period. This study was conducted in compliance with Method B6 of directive 92/69/EEC and performed according to GLP procedures.

Administrative Data

Purpose flag	supporting study
Study result type	experimental result
Reliability	2 (reliable with restrictions)
Rationale for reliability	The study is rated a "2" because it used appropriate test methods but was conducted prior to the development of test guidlines and GLP.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1968							1968-10-16

Materials and methods

Test type

subchronic

Limit test

no

Principles of method if other than guideline

Method: other: not specified

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

IUCLID4 Test substance: other TS: unspecified DIDP

Test animals

Species
rat

Strain

other: Charles River Caesarean-derived

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument6e2d.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f8fcf3d3-f5c1-44bd-adc4-240630daf70e%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Sex

male/female

Details on test animals and environmental conditions

TEST ANIMALS - Age at study initiation: no data - Weight at study initiation: male, 250-310 g; females 175-218 g - Fasting period before study: no data - Housing: Individually housed in elevated wire mesh cages - Diet (e.g. ad libitum): Purina Laboratory Chow, ad libitum - Water (e.g. ad libitum): ad libitum - Acclimation period: no data

Administration / exposure

Route of administration

oral: feed

Vehicle

unchanged (no vehicle)

Details on oral exposure

DIET PREPARATION: Diet was prepared fresh weekly by mixing DIDP into the basal feed (w/w) using a Patterson-Kelley twin-shell blender. No data are available concerning homogeneity, stability, or concentration of DIDP in the treated feed. VEHICLE: None

Analytical verification of doses or concentrations

no data

Duration of treatment / exposure

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument6e2d.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f8fcf3d3-f5c1-44bd-adc4-240630daf70e%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

13 weeks

Frequency of treatment

daily

Doses/concentrations

0.05, 0.3, 1% (approx. 25, 150 and 500 mg/kg/day)
Basis nominal in diet

No. of animals per sex per dose

10 rats/sex/dose

Control animals

yes, concurrent no treatment

Details on study design

Post-exposure period: none

Positive control

None

Examinations

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument6e2d.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f8fcf3d3-f5c1-44bd-adc4-240630daf70e%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Observations and examinations performed and frequency

CAGE SIDE OBSERVATIONS: Yes - Time schedule: Daily for mortality and weekly for physical appearance and behavior DETAILED CLINICAL OBSERVATIONS: Yes / No / No data - Time schedule: BODY WEIGHT: Yes - Time schedule for examinations: Weekly FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study): - Food consumption for each animal determined and mean daily diet consumption calculated as g food/kg body weight/day: Yes OPHTHALMOSCOPIC EXAMINATION: Yes - Time schedule for examinations: At study initiation and termination - Dose groups that were examined: All animals HAEMATOLOGY: Yes - Time schedule for collection of blood: Following 1 and 3 months of treatment - Anaesthetic used for blood collection: No data - Animals fasted: No data - How many animals: All animals - Parameters examined: Hematocrit, hemoglobin, leukocyte count, erythrocyte count, leukocyte differential count CLINICAL CHEMISTRY: Yes - Time schedule for collection of blood: Following 1 and 3 months of treatment - Animals fasted: No data - How many animals: All animals - Parameters examined: Calcium, chloride, potassium, sodium, alkaline phosphatase, serum alanine aminotransferase, serum aspartate aminotransferase, albumin, blood urea nitrogen, glucose, total bilirubin, total serum protein, serum protein electrophoresis, carbon dioxide URINALYSIS: Yes - Time schedule for collection of urine: Following 1 and 3 months of treatment - Metabolism cages used for collection of urine: No data - Animals fasted: No data - Parameters examined: Specific gravity, pH, sediment (microscopic), protein, glucose, ketones, bilirubin NEUROBEHAVIOURAL EXAMINATION: No

Sacrifice and pathology

No animals died on study. Animals sacrificed on schedule were subjected to gross pathological examination and the following tissues were collected for histological examination: stomach, small intestine, large intestine, liver, pancreas, lung, heart, bone marrow, lymph nodes, spleen, kidneys, urinary bladder, testes, epididymides, seminal vesicle, ovaries, uterus, brain, peripheral nerve, spinal cord, pituitary, eyes, adrenal gland, thyroids, bone and skin. Eight organs including the liver, heart, spleen, kidneys, testes, epidiymides, adrenal gland, and thyroids were weighed.

Statistics

Data were analyzed by ANOVA or F-tests at the 5% level using the methods of Rao, Bartlett, Scheffe, and Sachs, and by the modified t-test of Fisher-Behrens.

Results and discussions

Effect levels

Endpoint	Effect level	Sex	Basis for effect level / Remarks
NOAEL	ca. 150 mg/kg bw/day (nominal)	male/female	
LOEL	ca. 500 mg/kg bw/day (nominal)	male/female	Based on increased absolute liver weights in male and female rats at this dose level.

Observations

Clinical signs and mortality

no effects

Body weight and weight gain

yes

Food consumption and compound intake (if feeding study)

no effects

Food efficiency

no data

Water consumption and compound intake (if drinking water study)

not examined

Ophthalmoscopic examination

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument6e2d.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-f8fcf3d3-f5c1-44bd-adc4-240630daf70e%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

no effects

Haematology

no effects

Clinical chemistry

no effects

Urinalysis

no effects

Neurobehaviour

not examined

Organ weights

yes

Gross pathology

no effects

Histopathology: non-neoplastic

no effects

Histopathology: neoplastic

no effects

Details on results

CLINICAL SIGNS AND MORTALITY No animals died during the treatment period. No treatment-related appearance or behavioral abnormalities were noted during the study. All clinical signs of toxicity occurred randomly and sporadically in all treatment groups. BODY WEIGHT AND WEIGHT GAIN The test substance had no statistically significant effects on the body weights and body weight gains of rats during 13 weeks of treatment. Concentration-related downward trends in body weights and body weight gains were observed in male rats; male rats in the 10,000 ppm treatment group gained 13% less weight than the controls during the treatment period. A similar weight gain depression was not observed in females. FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study) Food consumption by the treated and control group rats was similar. Average weekly food consumption during the 13 week study ranged from 162-169 g for males, and from 111-155 g for females. Compound intake was not determined by the study author. OPHTHALMOSCOPIC EXAMINATION No treatment-related ocular changes were observed during the study. HAEMATOLOGY No treatment-related differences were observed between hematology parameters of rats in the treated and control groups. All parameters remained within expected ranges. CLINICAL CHEMISTRY No treatment-related differences were observed between the clinical blood chemistry of rats in the treated and control groups. All parameters remained within expected ranges. URINALYSIS No treatment-related differences were observed between the urine parameters of rats in the treated and control groups. All parameters remained within expected ranges. ORGAN WEIGHTS Absolute and relative liver weights of the 500, 3000, and 10,000 ppm male, and the 3000, and 10,000 ppm female rats were increased as compared to the controls at the termination of the study; however, only values for the 10,000 ppm groups were of statistical significance ($p<0.05$). Absolute liver weights for males and females in the 10,000 ppm treatment groups were 42 and 35% higher, respectively, than the controls (Table 1). The study author reported that "mean liver weights obtained for control groups from a number of recent subacute studies conducted with rats of the same strain averaged 17-18 g for males and 9-10 g for females." In addition, absolute and relative kidney weights of male rats in the 3000 and 10,000 ppm treatment groups were higher than the controls; only the relative kidney weights were of statistical significance (Table 1). GROSS PATHOLOGY No treatment-related gross postmortem differences were observed between rats in the treated and the control groups. All abnormalities appeared to occur randomly and sporadically in all study groups. HISTOPATHOLOGY: NON-NEOPLASTIC No conclusive treatment-realted microscopic differences were observed between rats in the treated and control groups. All abnormalities were typical of the species and appeared to occur randomly and sporadically in all study groups. The level of thyroid activity in the 10,000 ppm animals was thought to be "slightly increased" relative to the controls based on the presence of "more uniform and smaller" follicles "with a lighter colloid along with a tall cuboidal or columnar epithelium" in animals receiving the

higher dose; however, there were no biochemical differences that supported this conclusion. HISTOPATHOLOGY: NEOPLASTIC (if applicable) No neoplastic tissue was observed in rats in the treatment and control groups. HISTORICAL CONTROL DATA (if applicable) OTHER FINDINGS

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions

Absolute liver weights for males and females in the 10,000 ppm treatment groups were increased 42 and 35%, respectively, as compared to the controls. The trend towards increasing absolute liver weights with increasing dose is clear. Therefore, the NOEL for the study is 3000 ppm(150 mg/kg bw/day).

Executive summary

In a subchronic toxicity study, the test substance was administered to 10 rats/sex/dose in the diet at dose levels of 0, 500, 3000, or 10,000 ppm (approximately 25, 150, or 500 mg/kg/day) for 90 days.

Absolute liver weights for males and females in the 10,000 ppm treatment group were increased 42 and 35%, respectively, as compared to the controls; there were no accompanying histological changes. No other significant differences were observed between rats in the treated groups and the controls. No animals died during the treatment period. There were no treatment-related appearance or behavioral abnormalities. The test substance had no statistically significant effect on the body weights and body weight gains of rats during 13 weeks of treatment, although males in the 10,000 ppm treatment group gained 13% less weight than the controls. Feed consumption by rats in the treated and control groups was similar. There were no treatment-related effects on ophthalmology, hematology, clinical blood chemistry, or urine parameters. No treatment-related grosss or microscopic postmortem differences were observed between rats in the treated and the control groups, and no neoplastic tissues were observed. The LOEL for this study is 10,000 ppm (~500 mg/kg/day) based on increased absolute liver weights in male and female rats at this dose level. The NOEL is 3000 ppm (~150 mg/kg/day).

Administrative Data

Purpose flag	supporting study
Study result type	experimental result
Reliability	3 (not reliable)
Rationale for reliability	The study is rated a "3" because it was conducted prior to the development of test guidlines and GLP, used only 3 animals per sex per dose and no statistical evaluation was conducted.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1968							1968-09-24

Materials and methods

Test type

subchronic

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument2654.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-c0517c13-92a9-444c-9293-79aea1fccd7f%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Limit test

no

Principles of method if other than guideline

Method: other: not specified

GLP compliance

no Study predates GLP

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

IUCLID4 Test substance: other TS: unspecified DIDP

Test animals

Species
dog

Strain

Beagle

Sex

male/female

Details on test animals and environmental conditions

TEST ANIMALS - Age at study initiation: "yong adult" dogs, age not reported - Weight at study initiation: Males: 7.2-13.4 kg and Females 6.0-10.2 kg - Housing: Individually in metal cages - Diet (e.g. ad libitum): Ground Wayne Dog Mean, ad libitum - Water: ad libitum - Acclimation period: Not reported IN-LIFE DATES: From: 28-3-1968 To: 27-6-1968

Administration / exposure

Route of administration

oral: feed

Details on oral exposure

PREPARATION OF DOSING SOLUTIONS: DIET PREPARATION - Rate of preparation of diet (frequency): Diet was prepared fresh weekly by mixing the test substance into the basal feed (w/w) using a twin-shell blender.

Duration of treatment / exposure

13 weeks

Frequency of treatment

daily

Doses/concentrations

0.05, 0.3, 1% (approx. 15, 75 and 300 mg/kg/day)

Basis

No. of animals per sex per dose

3 dogs/sex/dose

Control animals

yes, concurrent no treatment

Details on study design

Post-exposure period: none

Examinations

Observations and examinations performed and frequency

CAGE SIDE OBSERVATIONS: Yes - Time schedule: Daily - Cage side observations included appearance, behavior, elimination, and signs of toxicity. DETAILED CLINICAL OBSERVATIONS: Yes / No / No data - Time schedule: BODY WEIGHT: Yes - Time schedule for examinations: Prior to study initiation and weekly during the study. FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study): - Food consumption for each animal determined and mean daily diet consumption calculated as g food/kg body weight/day: Yes - Compound intake calculated as time-weighted averages from the consumption and body weight gain data: Yes FOOD EFFICIENCY: - Body weight gain in kg/food consumption in kg per unit time X 100 calculated as time-weighted averages from the consumption and body weight gain data: No data OPHTHALMOSCOPIC EXAMINATION: Yes - Time schedule for examinations: At study initiation and termination - Dose groups that were examined: All animals HAEMATOLOGY: Yes - Time schedule for collection of blood: - Anaesthetic used for blood collection: No data - Animals fasted: No data - How many animals: All animals - Parameters examined: Hematocrit, hemoglobin, leukocyte count, erythrocyte count, leukocyte differential count CLINICAL CHEMISTRY: Yes - Time schedule for collection of blood: Prior to study initiation and after 1 and 3 months of treatment - Animals fasted: No data - How many animals: All animals - Parameters examined: calcium, chloride, potassium, sodium, alkaline phasphatase,

serum alanine aminotransferase, serum aspartate aminotransferase, albumin, blood urea nitrogen, bromosulphalein liver function, carbon dioxide, glucose, total bilirubin, total serum protein, triglycerides, serum protein electrophoresis URINALYSIS: Yes - Time schedule for collection of urine: Prior to study initiation and after 1 and 3 months of treatment - Metabolism cages used for collection of urine: No data - Animals fasted: No data - Parameters examined: Appearance, apecific gravity, pH, sediment, protein, glucose, ketones, bilirubin NEUROBEHAVIOURAL EXAMINATION: No OTHER:

Sacrifice and pathology

All animals were sacrificed on schedule and subjected to gross pathological examinations. The following tissues were collected for histological examinations: stomach, duodenum, jejunum, ileum, colon, liver, gall bladder, pancreas, lung, heart, bone marrow, lymph nodes, spleen, kidneys, urinary bladder, testes, epididymides, prostate, ovaries, uterus, brain, spinal cord, pituitary, eyes, adrenal gland, thyroids, bone, skeletal muscle, skin, all gross lesions and masses, nerve with muscle. In addition, the following organs were weighed: liver, heart, spleen, kidneys, testes, epididymides, brain, adrenal gland, thyroids

Statistics

It did not appear that statistical analyses were performed on the data.

Results and discussions

Effect levels

Endpoint	Effect level	Sex	Basis for effect level / Remarks
NOAEL	ca. 75 mg/kg bw/day (nominal)	male/female	
LOAEL	ca. 265 mg/kg bw/day (nominal)	male/female	Based on increased absolute and relative liver weights and the presence of swollen vacuolated hepatocytes from the high dose male and female dogs.

Observations

Clinical signs and mortality

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument2654.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-c0517c13-92a9-444c-9293-79aea1fccd7f%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

no effects

Body weight and weight gain

no effects

Food consumption and compound intake (if feeding study)

no effects

Food efficiency

not examined

Water consumption and compound intake (if drinking water study)

not examined

Ophthalmoscopic examination

no effects

Haematology

no effects

Clinical chemistry

no effects

Urinalysis

no effects

Neurobehaviour

not examined

Organ weights

yes

Gross pathology

no effects

Histopathology: non-neoplastic

yes

Histopathology: neoplastic

no effects

Details on results

CLINICAL SIGNS AND MORTALITY No animals died during the treatment period. No differences in appearance, behavior, appetite or elimination were observed between the treated and control dogs. BODY WEIGHT AND WEIGHT GAIN There were no treatment-related differences in body weights and body weight gains between the treatment and control groups. For all test groups, mean body weights generally exhibited little variation during the 13 week study. FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study) No treatment related differences in food consumption values were observed for any of the treatment

groups. During the study, male and female dogs ingested 93.7%-152.0% of the nominal dose of DIDP. OPHTHALMOSCOPIC EXAMINATION No treatment-related ophthalmological abnormalities were observed in any of the treatment groups. HAEMATOLOGY No treatment-related hematological effects were observed in any of the treatment groups. White blood cell counts in one male and one female dog treated at the 10,000ppm level were elevated at 1 month, but were within normal limits at 3 months. CLINICAL CHEMISTRY No treatment-related effects in clinical blood chemistry parameters were observed in any of the treatment groups. Serum alanine aminotransferase in one 10,000 ppm level male was elevated at 1 month, but was within normal limits at 3 months. URINALYSIS No treatment-related effects were observed between urine parameters of dogs in any of the treatment groups. ORGAN WEIGHTS Increased absolute and relative liver weights were observed in the 10,000 ppm level male and female dogs compared to the controls. Absolute and relative liver weights for the males were 25 and 37% higher, respectively, than the respective control weights. Absolute and relative liver weights for the females were 51 and 44% higher, respectively, than the corresponding control weights. No other differences in organ weights appeared to be treatment-related for any of the treatment groups. See Table 1 GROSS PATHOLOGY No treatment-related differences in gross pathology were observed between dogs in the treated and control groups. All abnormalities noted were considered to be "incidental in nature". HISTOPATHOLOGY: NON-NEOPLASTIC In the 10,000 ppm treatment groups, the livers from 1 of 2 males (liver from 3rd male not examined) and 3 of 3 females showed swollen, vacuolated hepatocytes. The liver from 1 of 2 males and 1 of 3 females in the 10,000 ppm treatment groups showed minimal to slight pericholangitis and slight bile duct proliferation. No other treatment related changes were observed. HISTOPATHOLOGY: NEOPLASTIC (if applicable) No neoplastic tissue was observed in dogs in the treatment or control groups.

Remarks on results including tables and figures

All treated groups and controls appeared normal with respect to appearance, behavior and elimination. Three dogs in the highest diet level showed slight to moderate body weight losses, these findings did not appear to be related to decreased food consumption except for one animal. All clinical laboratory values were generally within acceptable limits and comparable between all groups. Gross necropsy examinations did not reveal any consistent compound-related alterations.
At the high dose a SLIGHTLY ELEVATED LIVER/BODY WEIGHT RATIO was noted in all males and 2/3 of females. Pathological examination revealed SWOLLEN AND VACUOLATED HEPATOCYTES in the livers of these animals. No other histological changes were observed.

Applicant's summary and conclusion

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument2654.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-c0517c13-92a9-444c-9293-79aea1fccd7f%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Conclusions

Male and female beagle dogs fed the test substance in teh diet at a level of 10,000 ppm for 13 weeks had slightly elevated relative liver weights. In the 10,000 ppm treatment groups, the livers from 1 of 2 males and 3 of 3 females showed swollen, vacuolated hepatocytes. Minimal to slight pericholangitis and slight bile duct proliferation were noted in the livers of 1 of 2 male and 1 of 3 female dogs in this dose group. No treatment-related effects were observed in dogs treated at 500 or 3,000 ppm for 13 weeks. Therefore, the NOAEL for this study is 3,000 ppm (75 mg/kg bw/day).

Executive summary

In a subchronic toxicity study, the test substance was administered in the diet to three beagle dogs/sex/dose at dose levels of 500, 3000, or 10,000 ppm for 13 weeks. Actual average doses were approximately 13, 70, and 263 mg/kg/day for males and 14, 72, and 280 mg/kg/day for females.

Absolute and relative liver weights for the 10,000 ppm males were 25 and 37% higher, respectively, and for females were 51 and 44% higher, respectively, than the corresponding control weights. In the 10,000 ppm treatment groups, the livers from 1 of 2 males and 3 of 3 females showed swollen, vacuolated hepatocytes, and the livers from 1 of 2 males and 1 of 3 females showed minimal to slight pericholangitis and slight bile duct proliferation (the liver from the 3rd male was not examined). No dogs died during the study. No treatment-related differences in clinical appearance, body weights, body weight changes, food consumption, ophthalmology, hematology, clinical blood chemistry or urinalysis parameters or gross pathology were observed between dogs in the treated and control groups. The LOEL for this study is 10,000 ppm (~265 mg/kg bw/day), based on increased absolute and relative liver weights and the presence of swollen vacuolated hepatocytes from the high dose male and female dogs. The NOEL is 3,000 ppm (~75 mg/kg bw/day).

Administrative Data

Purpose flag	supporting study
Study result type	experimental result
Reliability	1 (reliable without restriction)
Rationale for reliability	This study is rated a "1" because it applied GLP, used appropriate testing procedures.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Lake BG, et al	1991	Dose-response relationships for induction of hepatic peroxisome proliferation and testicular atrophy by phthalate esters in the rat	Human Experimental Toxicology 10:67-68					
study report		1990							1990-03-30

Materials and methods

Test type

subchronic

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

The test material was supplied as a composite sample from ICI, Exxon and BASF by ICI Chemicals and Polymers Ltd. The sample was made up of equal parts by weight of Hexplas DIDP (ICI), Jaflex DIDP (Exxon) and Palatinol Z (BASF). Analysis of the sample follows: Acid value:0.03 mg KOH/g; Alcohol content: 0.04 % w/w; water content: 0.04 % w/w; ester content: 99.9% w/w and density (20 deg C): 0.967.

Test animals

Species

rat

Strain

Fischer 344

Sex

male

Details on test animals and environmental conditions

TEST ANIMALS - Source: Harlan-Olac Ltd, Bicester, Oxon, UK - Age at study initiation: 6 wks - Weight at study initiation: -

Fasting period before study: no - Housing: groups of five in polypropylene and stainless steel grid-floored cages, suspended over paper. - Diet: ad libitum - Water: ad libitum - Acclimation period: 14 days ENVIRONMENTAL CONDITIONS - Temperature (°C): 19-24 - Humidity (%): 45-70 - Air changes (per hr): approximately 15/hr no circulation with high efficiency filters - Photoperiod (hrs dark / hrs light): 12 hours light/ 12 hours dark

Administration / exposure

Route of administration

oral: feed

Details on oral exposure

PREPARATION OF DOSING SOLUTIONS: DIET PREPARATION - Rate of preparation of diet (frequency): Diets were prepared 4 times, once every seven days - Mixing appropriate amounts with (Type of food): nutritionally adequate diet (RM1(E)SQC, FG) supplied by Special Diet Services Ltd. - Storage temperature of food: 2-6 deg C

Analytical verification of doses or concentrations

yes

Details on analytical verification of doses or concentrations

Samples of diet were extracted by shaking with hexane and an internal standard (DEHP, 5ml). Samples were centrifuged and injected onto the glc (pye 104 gas chromatograph). The ratio of the peak heights for DID and DEHP were calculated using Spectra-Physics SP4270 integrator. The amount of DIDP present in the diet samples was calculated by comparison with prepared standard concentrations.

Duration of treatment / exposure

28 days

Frequency of treatment

daily

Doses/concentrations

0, 0.02, 0.05, 0.1, 0.3, 1.0% (0, 25, 57, 116, 353, 1287 mg/kg/day)
Basis

No. of animals per sex per dose

5 male rats/dose

Control animals

yes, concurrent no treatment

Details on study design

- Rationale for animal assignment (if not random): random

Positive control

DEHP administered at 1.0% in the diet

Examinations

Observations and examinations performed and frequency
CAGE SIDE OBSERVATIONS: Yes - Time schedule: Daily - Cage side observations included variation in behavior or condition.

DETAILED CLINICAL OBSERVATIONS: Yes - Time schedule: Once weekly a more detailed examination was made at the time of weighing. BODY WEIGHT: Yes - Time schedule for examinations: twice weekly FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study): - Food consumption for each animal determined and mean daily diet consumption calculated as g food/kg body weight/day: Yes

Sacrifice and pathology

On day 27, the rats were fasted overnight with water available. On day 28, the rats were weighed and sacrificed by exsanguination from the dorsal aorta under diethyl ether anaesthesia. Serum was separated from the blood and stored. Any abnormalities of the external condition and of the thoracic or abdominal viscera were noted. The weight of the testes (left and right separately) and of the liver were recorded.

Other examinations

Whole liver homogenates were analyzed for protein concentration and cyanide insensitive palmitoyl-CoA oxidation.

Statistics

The continuous variable data from the control and DIDP groups were compared using analysis of variance followed by the least significant difference test. The continuous data from the control and DEHP groups were compared using a two sample Student's t-test with Satterthwaite's correction. A probability of less than 0.05 was taken to indicate a statistically significant difference between groups.

Results and discussions

Effect levels

Endpoint	Effect level	Sex	Basis for effect level / Remarks
NOEL	ca. 0.05 — ca. 57 mg/kg bw/day (nominal)	male	Based on induction of palmitoyl-CoA oxidation (as an index of hepatic peroxisome proliferation)
NOEL	ca. 1 — 1287 mg/kg bw/day	male	Testicular atrophy was not observed in this study and the no-effect level was

(nominal) therefore 1%

Observations

Food consumption and compound intake (if feeding study)

yes

Organ weights

yes

Histopathology: non-neoplastic

yes

Details on results

CLINICAL SIGNS AND MORTALITY No animals died during the study. Animals in the control and treated groups showed no changes in behavior or condition which could be attributed to treatment. BODY WEIGHT AND WEIGHT GAIN Over the course of the study, bodyweights of animals fed the test substance at all levels in the diet were not significantly different when compared to controls. FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study) Examination of the food intake data shows that rats fed the test substance at all levels in the diet consumed similar amounts of food when compared to controls. CLINICAL CHEMISTRY The administration of 0.02-1.0% treatment had no significant effect on whole homogenate protein content. The activity of cyanide-insensitive palmitoyl-CoA oxidation was determined as a specific measure of peroxisomal fatty acid B-oxidation cycle. The administration of 0.1-1.0% test substance in the diet produced significant dose-related increases in rat hepatic palmitoyl-CoA oxidation activity. At the highest dose level, enzyme activity (expressed per unit of homogenate protein, per g of liver and per 100 g of body weight) was increased to 1086, 1116, and 2199% of control; however, when expressed either per unit of homogenate protein or per g of liver, 0.02, 0.05 and 0.1% diets had no significant effect on palmitoyl-CoA oxidation activity. When enzyme activity was expressed as activity per 100 g bodyweight no significant increase was observed at the 0.02 and 0.05% dose levels. ORGAN WEIGHTS Both liver weight and relative liver weight increased in a dose-related manner in animals fed the test substance. The liver weights were statistically significantly increased at 0.3 and 1.0% dietary levels while the relative liver weight was statistically

significantly increased at 0.1, 0.3, and 1.0% dietary levels. There were no statistically significant differences in these parameters in any of the treated groups when compared to controls. HISTOPATHOLOGY: NON-NEOPLASTIC In the livers from rats fed the test substance at a level of 1%, the cytoplasm of hepatocytes was statistically significantly more eosinophilic than that of control animals. At lower concentrations in the diet no apparent histological effects on the liver were observed. Treatment at levels from 0.02 to 1.0% had no apparent histopathological effect on the testes.

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions

The NOEL observed in this study for the induction of palmitoyl-CoA oxidation (as an index of hepatic peroxisome proliferation) was 0.05% (57 mg/kg/day) while testicular atrophy was not observed at any dose indicating a NOEL of 1% (1287 mg/kg/day) for this effect.

Executive summary

In this study the dose-response relationship for induction of hepatic peroxisome proliferation by DEHP and DIDP was assessed in 42-day-old male Fischer 344 rats. Groups of 5 rats were fed with 1% DEHP (control) and 0.02-0.05-0.1-0.3 and 1% (approximately 25-57-116- 353- 1,287 mg/kg/d) DIDP diet. The sample of DIDP used was made up of equal part by weight of Hexaplas (ICI), Jayflex DIDP (Exxon) and Palatinol Z (BASF). Food consumption and body weight were checked twice weekly, hepatic peroxisome proliferation was assessed by measurement of cyanide-insensitive palmitoyl-CoA oxidation activity. Testicular atrophy was also checked (organ weight and histological changes). This study was performed according to GLP procedures. Over the course of the study, body weight of animals fed DIDP, at all levels in the diet was not significantly different compared to controls. The two phthalates esters produced dose-related liver enlargement. At 0.1% and higher, there was a statistically significant increase in relative liver weight (3.3158 g/100 g bodyweight vs. 3.0488 g/100 g bodyweight in controls). At 0.3% and higher, this statistically significant increase was also noticed for absolute liver weight (6.6812 g vs. 5.5830g in controls). Biochemical examination of the livers revealed no effect on the whole homogenate of protein content, but an induction of the enzymes of the peroxisomal fatty acid beta-oxidation cycle. In this way palmitoyl-CoA oxidation activity was statistically dose-related increase from 0.1% expressed as µmol/min/liver weight/100g bodyweight (4.52 vs. 3.71 in controls), and from 0.3% expressed either as nmol/min/mg protein or as µmol/min/g liver

(respectively 11.82 vs. 5.60 and 2.67 vs. 1.22). These slight increases at 0.1% (increase of relative liver weight and of palmitoyl-CoA activity) could be considered as the trend for peroxisome proliferation effects, clearly confirmed at 0.3% (increase of absolute liver weights and increased enzyme activity whatever the units of expression). NOELs for food consumption and enzyme activity were reported to be 51.7 mg/kg/d for DEHP. No testicular atrophy was reported at the highest dose tested: 1,093 mg/kg/d for DEHP and 1,287 mg/kg/d for DIDP.

Administrative Data

Purpose flag	key study
Study result type	experimental result
Reliability	1 (reliable without restriction)
Rationale for reliability	This study is rated a "1" because it applied GLP and used appropriate testing procedures.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
	Barber ED, Astill BD, Moran E J, Schneider BF, Gray TJB, Lake BG and Evans JG	1987	Peroxisome Induction studies on Seven Phthalate Esters	Toxicology and Industrial Health 3(2):7-22					
study report		1986							

Materials and methods

Test type

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument9633.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-66bf7f5b-551c-4049-9690-51dae7210741%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

subchronic

Limit test

no

Principles of method if other than guideline

Method: other: not specified

GLP compliance

yes

Test materials

Details on test material

IUCLID4 Test substance: other TS: DIDP with different CAS#

Test animals

Species

rat

Strain

Fischer 344

Sex

male/female

Details on test animals and environmental conditions

TEST ANIMALS - Source: Olac 1976 Ltd., Bicester, Oxon, UK - Age at study initiation: - Weight at study initiation: - Fasting period before study: - Housing: individually - Diet (e.g. ad libitum): - Water (e.g. ad libitum): - Acclimation period: 7 days (males) 8 days (females) ENVIRONMENTAL CONDITIONS - Temperature (°C): 20-24 - Humidity (%): 45-65 - Air changes (per hr): at least 15/hr with no recirculation-filtered air (0.5um) - Photoperiod (hrs dark / hrs light): 12 hours dark/12 hours light)

Administration / exposure

Route of administration

oral: feed

Details on oral exposure

PREPARATION OF DOSING SOLUTIONS: DIET PREPARATION - Rate of preparation of diet (frequency): The mixtures were prepared once for the whole study. - Mixing appropriate amounts with (Type of food): Rat and Mouse No.1., Special Diet Services, Witham, Essex) - Storage temperature of food: 2-6 deg C

Analytical verification of doses or concentrations

yes

Details on analytical verification of doses or concentrations

Mixing efficiency and stability tests were performed.

Duration of treatment / exposure

21 days

Frequency of treatment

daily

Doses/concentrations

0.3, 1.2, 2.5% (approx. 280, 1100, and 2000 mg/kg/day)
Basis

No. of animals per sex per dose

5 rats/sex/dose

Control animals

yes, concurrent no treatment

Details on study design

Post-exposure period: no

Examinations

Observations and examinations performed and frequency

CAGE SIDE OBSERVATIONS: Yes - Time schedule: Daily - Cage side observations included variations in behavior or condition, and once weekly more detailed examination occurred during weighing. DETAILED CLINICAL OBSERVATIONS: Yes / No / No data - Time schedule: BODY WEIGHT: Yes / No / No data - Time schedule for examinations: Three days before the start of

treatment, on the day treatment began, and subsequently twice weekly until the end of the treatment period. FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study): - Food consumption for each animal determined and mean daily diet consumption calculated as g food/kg body weight/day: Yes - Compound intake calculated as time-weighted averages from the consumption and body weight gain data: Yes OPHTHALMOSCOPIC EXAMINATION: No HAEMATOLOGY: Yes - Time schedule for collection of blood: Prior to autopsy - Anaesthetic used for blood collection: No - Animals fasted: Yes - How many animals: All animals - Parameters examined: Triglycerides and total cholesterol CLINICAL CHEMISTRY: No URINALYSIS: No NEUROBEHAVIOURAL EXAMINATION: No OTHER:

Sacrifice and pathology

On the day of sacrifice, each animal was weighed and killed by exsanguination from the dorsal aorta under diethyl ether anaesthesia. Any abnormalities of the external condition and of the thoracic or abdominal viscera were noted. The liver, the left and right kidneys and, from the males, the left and right testes were weighed, and samples were preserved in 10% neutral buffered formalin. Samples of other tissues seen to be abnormal were also preserved. For electron microscopy, two thin slices of liver, one from the left lobe, the other from the median lobe, were each cut into four or five pieces and fixed for two hours with continuous agitation. The remainder of the liver was used for biochemical analysis

Other examinations

Whole homogenates of liver were prepared for each animal. These were assayed for protein and cyanide-insensitive palmitoyl-CoA. Microsomal lauric acid hydroxylation was also determined.

Statistics

Data from the control and test substance treated groups were subject to analysis of variance, and if this was significant the treated groups were compared with the controls using the Least Significant Difference test. The data from the controls and DEHP groups were compared using a two sample or pooled Student t test with Welch's correction. These methods were applied to the following data: body weights, food intakes, organ weights, serum analysis, and liver biochemistry. In all cases a probability level of $p<0.05$ was taken to indicate statistical significance.

Results and discussions

Effect levels

Endpoint	Effect level	Sex	Basis for effect level / Remarks
NOAEL	ca. 280 mg/kg bw/day (nominal)	male/female	
LOAEL	ca. 1100 mg/kg bw/day (nominal)	male/female	

Observations

Clinical signs and mortality

yes

Body weight and weight gain

yes

Food consumption and compound intake (if feeding study)

yes

Food efficiency

not examined

Water consumption and compound intake (if drinking water study)

not examined

Ophthalmoscopic examination

not examined

Haematology

yes

Clinical chemistry

yes

Urinalysis

not examined

Neurobehaviour

not examined

Organ weights

yes

Gross pathology

no effects

Histopathology: non-neoplastic

yes

Histopathology: neoplastic

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument9633.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-66bf7f5b-551c-4049-9690-51dae7210741%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934
not examined

Details on results

CLINICAL SIGNS AND MORTALITY No animals died during the study. No variations in behavior were observed which could be considered to be related to treatment; however, two of the male rats administered 2.5% test substance showed piloerection. BODY WEIGHT AND WEIGHT GAIN The male rats fed 2.5% test substance lost weight during the first three days of treatment and remained significantly lighter than the controls (69-82% of control) throughout the treatment period. The difference from the controls increased as the study progressed. Males given 1.2% test substance faild to gain as much weight as the controls but the difference was significant on day 17 only. The female rats showed the same trends but to a lesser extent. Females given 2.5% test substance were significantly lighter than the controls from day 10 onwards (83-87% of control) but no significant weight reductions were observed in the other treated female groups. FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study) Male rats fed 1.2% and 2.5% test substance consumed significantly less diet than the controls during the first 3 days of treatment, but only in the 2.5% group was the food intake significantly reduced throughout the treatment period. Rats given 1.2% test substance showed a gradual recovery in food intakes as treatment continued, returning to normal levels by the end of the treatment period. The females showed a similar trend but to a lesser extent. During the first 3 days of treatment, only the female rats fed 2.5% test substance consumed significantly less food than the controls. Food intake in all female groups returned to normal levels by the end of the treatment period. The intake of DIDP by each rat was calculated over each food intake interval using the analyzed dietary concentrations. Calculated intakes for males were 304, 1134, 2100, and 1077 mg/kg/day for the 0.3, 1.2, and 2.5% dietary levels, respectively. Calculated intakes for females were 264, 1042, 1972, and 1022 mg/kg/day for the 0.3, 1.2, and 2.5% dietary levels, respectively. OBSERVATIONS POST-MORTEM Enlarged livers were reported in one male rat given 1.2% test substance and one male given 2.5%. Areas of pale tissue were seen in the liver of one male control rat, and a female rat given 2.5% test substance had a raised area on the median liver lobe which was of normal color and texture. CLINICAL CHEMISTRY Triglyceride and Cholesterol: Apart from the isolated low mean value for cholesterol concentration in rats fed 0.3% test substance (78% of control), the serum triglycerides and cholesterol concentraitons of the female rats were not significantly influenced by treatment. In males the triglyceride values were 66% of the controls in the groups fed 1.2 and 2.5%. In the male 1.2% treatment group, the cholesterol level was 75% of the control value. These three differences were statistically significant. Hepatic Enzyme Levels: The hepatic palmitoyl CoA oxidation was significantly increased in both sexes after treatment with 1.2 or 2.5 %. At the 1.2% dose level, values were 1014 and 748% of control and at the 2.5% level they were 1553 and 1287% of control in males and females, respectively. In males there was a small though not statistically signifiant increase after feeding with 0.3%. In both sexes treated with the test substance, there was an increase in the 11- and 12-hydroxylation of lauric acid. The males were more sensitive than the females in this respect. For example, there were statistically significant increases of 12-hydroxylation at all dose levels in the males but at only the highest dose in females, while 11-hydroxylation was elevated to a

statistically significant extent at all dose levels in the males but did not reach significance in females. In the males the increase in 12-hydroxylation (400-1138% of control) was greater than that of 11-hydroxylation (183-350% of control). Hepatic Protein Levels: Total hepatic protein concentrations were significantly higher in both sexes of rats fed 1.2% (119 (males) and 120% (females) of control) and 2.5% (118 (males) and 121% (females) of control). Microsomal protein levels did not show any obvious change in any of the treated groups. ORGAN WEIGHTS In both sexes there was a significant increase in the absolute and relative weight of the liver at dose levels of 1.2 and 2.5%. In the males, absolute weights were 186 and 172% of control for levels of 1.2 and 2.5% respectively, while relative liver weights for these groups were 201 and 254% of control. In the females absolute weights for the same levels were 160 and 192% of control and relative weights were 176 and 238% of control, respectively. In the males there were also significantly higher liver weights in rats given 0.3% test substance (121% of control for absolute and relative weights). Males given the two lower doses of test substance had heavier kidneys than the controls (111%) while in both sexes given 2.5% test substance the kidney weights were lower than the controls (81% and 88% for the males and females, respectively). Relative kidney weights were significantly higher than the controls in all the treated groups except the females given 0.3%. Values were 110% of control in males given 0.3% test substance and 119% in those given 1.2 or 2.5%. in females at the same levels they were 109% of control. The testes from the males given 2.5% test substance were slightly but significantly lighter than the controls. However, when expressed relative to the low body weight, the value was significantly greater. HISTOPATHOLOGY: NON-NEOPLASTIC There was a marked increase in peroxisomes in male rats fed 2.5% test substance with some degree of variation between moderate and marked proliferation. There was a variable but always a very marked increase in peroxisomes in female rats fed 2.5% test substance. There was a reduction of the normal cytoplasmic basophilia in the livers of both sexes of rats fed 1.2% or 2.5% diets. In liver sections from rats given 2.5%, this was associated with an increase in cytoplasmic eosinophilia. All treated groups showed a reduction of neutral lipid but there was no obvious dose relationship in the magnitude of the response. No testicular atrophy was seen after treatment and there was no effect on the kidney which could be associated with treatment. The test substance caused liver enlargement, with a reduction of the normal cytoplasmic basophilia. This was associated with an increase in cytoplasmic eosinophilia in rats given 2.5% test substance in the feed. The degree of the reduction of the histochemically demonstrable neutral fat in the livers of treated rats was similar in both sexes, but the effect was not clearly dose-related.

Remarks on results including tables and figures

RS-Freetext:
Absolute and relative LIVER WEIGHTS and relative KIDNEY WEIGHTS were INCREASED in animals given 1.2 or 2.5% DIDP. Both sexes given 2.5% DIDP showed INCREASES IN PEROXISOME NUMBERS AND SIZE, with the females showing a greater response. INCREASES IN PALMITOYL CoA OXIDATION and TOTAL HEPATIC PROTEIN LEVELS were also observed at these doses.

Applicant's summary and conclusion

Conclusions

Under the conditions of this study, the test substance induces a marked proliferation of peroxisomes in both male and female rats at a dose of 2.5% which was accompanied by changes in measurements associated with peroxisome stimulation. Rats administered 1.2 or 2.5% showed reduced food intake and body weights, increased absolute and relative liver and kidney weights, and decreased hepatocyte cytoplasmic basophilia, serum cholesterol and triglycerides. Therefore the NOAEL = 0.3% (280 mg/kg/day) and LOAEL = 1.2% (1100 mg/kg/day).

Executive summary

Di-isodecyl phthalate (the test substance) was fed to groups of five male and five female F344 rats at dietary levels of 0, 0.3, 1.2, or 2.5% for 21 days. A further group of five rats of each sex, fed 1.2% DEHP, served as a study control. Male rats given 1.2 or 2.5% showed decreased body weights as compared to control; this was seen in the females but to a lesser extent. Food intakes were reduced initially in both sexes given 1.2 or 2.5%, the effect persisting throughout treament in males given 2.5%. Absolute and relative liver weights and relative kidney weights were increased in both sexes given 1.2 or 2.5% test substance in the feed. In males given 2.5%, relative testis weights were significantly greater and no lesions were seen histologically. There was a reduction in hepatocyte cytoplasmic basophilia in rats fed 1.2 or 2.5% and in the latter group this was associated with an increase in eosinophilia. Lower periportal lipid levels were seen but this was not dose related. Serum tyiglycerides and cholesterol levels were reduced in males given 1.2 or 2.5% test substance, but no dose relationship was apparent. Both sexes given 2.5% in feed showed a marked but variable increase in peroxisome numbers and size, the females showing a greater response. Cyanide-insensitive palmitoyl-CoA oxidation was significantly increased in all treated animals except those given 0.3% in feed. There was a significant increase in the 11- and 12-hydroxylation of lauric acid in all treated males, but in the females the only significant increase was in the 12- hydroxylase level in those given 2.5% of the test substance. Therefore, the NOAEL = 0.3% (280 mg/kg/day) and LOAEL = 1.2% (1100 mg/kg/day).

Administrative Data

Purpose flag	key study		
Study result type	read-across from supporting substance (structural analogue or surrogate)	Study period	1969
Reliability	2 (reliable with restrictions)		
Rationale for reliability	An old study conducted before GLP or standard guidelines were introduced. However, the study was undertaken at a recognised laboratory, and there are sufficient data reported to provide a supplementary assessment for a second route of exposure.		

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1969							1969-08-01

Materials and methods

Test type

subacute

Limit test

no

Test guideline

Qualifier	Guideline	Deviations
no guideline available		no data

Principles of method if other than guideline

A standard design for repeat dermal application toxicity study

GLP compliance

no

Test materials

Test material equivalent to submission substance identity

no

Details on test material

A clear, oily liquid with a faint, unpleasant odour. Received on 10 January1969 and assumed to be 100% active.

Test animals

Species

rabbit

Strain

New Zealand White

Sex

male/female

Administration / exposure

Type of coverage
occlusive

Vehicle

unchanged (no vehicle)

Analytical verification of doses or concentrations

no

Duration of treatment / exposure

24 hours per day, five days per week for six weeks

Frequency of treatment

0nce a day, five days a week

Doses/concentrations

Basis nominal per unit body weight

No. of animals per sex per dose

Four male at 0.5 ml/Kg and four males at 2.5 ml/Kg

Control animals

yes, sham-exposed

Results and discussions

Effect levels

Endpoint	Effect level	Sex	Basis for effect level / Remarks
NOEL (Systemic)	> 2.5 ml/kg/day	male	No systemic toxicity
NOAEL (Local)	0.5 ml/Kg/day	male	Mild dermal irritation

Observations

Remarks on results including tables and figures

There was no evidence of systemic toxicity from repeated dermal exposures to MRD-69-4 as based on general appearance and behavior, clinical laboratory studies, and gross and microscopic visceral pathology.

Compound effect was confined to gross and microscopic alterations of the skin. Grossly, MRD-69-4 at the 0.5 ml/kg/day level produced generally mild dermal irritation which was slightly more severe than irritation produced by mineral oil at 2.5 ml/kg/day; at the 2.5 ml/kg/day level, slight or moderate (abraded skin only) erythema and slight desquamation were noted through the fifth week of application.

Histologically, skin sections showed slight acanthosis, slight hyperkeratosis, and slight dermatitis of comparable severity in control and compound-treated animals. Sections of kidney, liver, and skin from control and test animals were comparable histologically; lesions encountered were consistent with incidental disease.

Applicant's summary and conclusion

Conclusions

There was no evidence of systemic toxicity from repeated daily dermal exposure to MRD-69-4 for six weeks. Mild irritation was observed at the application sites of animals treated with MRD-69-4, although there was no histopathological difference in the severity of the skin changes between test and control animals.

Executive summary

In a six week dermal toxicity study, groups of four New Zealand White rabbits received 24-hour daily applications of MRD-69-4 at 0.5 or 2.5 ml/Kg, five times a week, to the closely clipped intact (two animals per group) or abraded (two animals per group) abdominal skin, wrapped with gauze adhesive tape and fitted with neck collars. Control animals (three males and one female) received mineral oil at 2.5 ml/Kg. Clinical signs were recorded daily, haematology and urinalysis undertaken initially and terminally, and histopathology was performed on the liver, kidneys and skin. There was no evidence of systemic toxicity. Mild irritation was observed at the application sites of animals treated with MRD-69-4, although there was no difference in the severity of histopathological skin changes apparent between test and control animals. The systemic NOEL was considered to be 2.5 ml/kg/day (estimated to be 2500 mg/kg/day) and the local NOAEL was considered to be 0.5 mg/kg/day (estimated to be 500 mg/kg/day).

The dermal toxicity study was considered to be a suitable supporting study for classification.

Administrative Data

Purpose flag	key study
Study result type	experimental result
Reliability	2 (reliable with restrictions)
Rationale for reliability	The study is rated a "2" because appropriate testing methods were used; however, the study does not follow and accepted guideline or indicate compliance with GLP.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1981							

Materials and methods

Test type

subchronic

Limit test

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument81c4.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-7bfbdb03-ce36-435e-8335-2f57c9523fd8%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934
no

Principles of method if other than guideline

As described previously, Pegg (1979) GM Research Reports

GLP compliance

no data

Test materials

Test material equivalent to submission substance identity
yes

Details on test material

Unspecified DIDP; CAS No not provided

Test animals

Species
rat

Strain

Sprague-Dawley

Sex

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument81c4.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-7bfbdb03-ce36-435e-8335-2f57c9523fd8%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

male

Details on test animals and environmental conditions

TEST ANIMALS - Age at study initiation: adult - Weight at study initiation: 125g - Housing: individually in polycarbonate wire top cages - Diet: ad libitum - Water: ad libitum - Acclimation period: 7 days

Administration / exposure

Route of administration

inhalation: aerosol

Type of inhalation exposure

whole body

Vehicle

unchanged (no vehicle)

Details on inhalation exposure

GENERATION OF TEST ATMOSPHERE / CHAMBER DESCRIPTION Data not available TEST ATMOSPHERE Repeated exposures to nonradioactive DIDP were conducted through whole body exposure in a 30L cylindrical glass jar. Animals were restrained in wire mesh cylinders and supported on a suspended screen floor. The chamber atmosphere was assayed for DIDP content on each exposure day. Cascade impactor samples for determination of aerosol particle size taken every other day during the exposure period.

Analytical verification of doses or concentrations

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument81c4.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-7bfbdb03-ce36-435e-8335-2f57c9523fd8%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934
no data

Duration of treatment / exposure

5 consecutive days, 2 days recovery and another 5 days exposure (10 total exposures)

Frequency of treatment

6 hours/ day

Doses/concentrations

500 mg/m3
Basis nominal conc.

MMAD / GSD

MMAD = 0.98 um

No. of animals per sex per dose

8 rats/dose 6 control rats

Control animals

yes, concurrent no treatment

Details on study design

Body weights of the animals were taken immediately before and after each 6 hour exposure period. After exposure, animals were returned to the vivarium. Control animals were exposed simultaneously in an identical chamber flushed with filtered room air. Rats were observed daily for body weight gain, appearance and gross behavior. At the end of the exposure regimen animals were held for observation for 3 weeks. Animals were sacrificed at the end of the observation period and tissue samples taken for histopathology.

Results and discussions

Effect levels

Endpoint	Effect level	Sex	Basis for effect level / Remarks
NOAEC	500 mg/m³ air	male	No systemic toxicity

Observations

Clinical signs and mortality

no effects

Body weight and weight gain

yes

Food consumption

no data

Food efficiency

no data

Water consumption

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument81c4.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-7bfbdb03-ce36-435e-8335-2f57c9523fd8%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

no data

Ophthalmoscopic examination

no data

Haematology

no data

Clinical chemistry

no data

Urinalysis

no data

Neurobehaviour

no data

Organ weights

no data

Gross pathology

no data

Histopathology: non-neoplastic

yes

Histopathology: neoplastic

no data

Details on results

The nominal chamber atmosphere concentration for the repeated exposure toxicity studies was 500 mg/m3. Daily, mean analytical concentrations ranged from 468 to 571 mg/m3. The mean analytical concentration for the ten exposure periods was 505 mg/m3. The mass median aerodynamic diameter of the DIDP aerosol was 0.98 um. Animals exposed repeatedly to 500 mg/m3 DIDP exhibited no marked outward signs of toxicity during exposures. The rate of body weight gain was not different between control and exposed animals. Occasional changes in focal pulmonary histology were observed. Animals sacrificed 3 weeks following termination of exposure exhibited moderate increases in the weidth of alveolar septa with slight interstitial mixed inflammaotry reactions. Alveolar macrophages and type II pneumocytes were increased in number. Peribronchial lymphoid tissue appeared slightly more prominent in exposed animals. Liver, kidney and spleen from DIDP treated animals exhibited no obvious histologic alteration except for slight hepatic fatty metamorphosis.

Remarks on results including tables and figures

Applicant's summary and conclusion

Conclusions

The exposure regimen did not result in lethality when animals were observed for up to 3 weeks following treatment. Pulmonary irritation, however was apparent.

Executive summary

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument81c4.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-7bfbdb03-ce36-435e-8335-2f57c9523fd8%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

In a 2-week study (General Motors Research Laboratories, 1981) designed to evaluate the fate of DIDP (see Section 5.1), toxicity was also assessed. DIDP was administered to 8 male rats (6 for control) by inhalation (aerosol) at analytical concentration of 505±7 mg/m^3(MMAD: 0.98 µm) 6 hours a day, 5 times per week. Rats were observed daily for body weight gain, appearance and gross behavior. Animals were sacrificed at the end of the observation period (3 weeks) and tissue samples taken for histopathology. There were no marked outward signs of toxicity during exposure. The rate of body weight gain was not different between control and exposed animals. Effects in the lungs were: moderate increase in the width of alveolar septa with slight interstitial mixed inflammatory reactions, alveolar macrophages and type II pneumocytes were increased in number, peribronchial lymphoid tissue appeared slightly more prominent. In liver, spleen and kidneys, no obvious histologic alterations were noted except for a slight hepatic fatty metamorphosis. No systemic toxicity, but local irritant effects were observed at the concentration tested, thus a NOAEL of 0.5 mg/l (500 mg/m^3) can be assumed.

Administrative Data

Purpose flag	supporting study
Study result type	experimental result
Reliability	2 (reliable with restrictions)
Rationale for reliability	This study is rated a "2" because it applied GLP, used appropriate testing procedures, but did not follow an accepted testing guideline.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		2000							
study report		1986							

Materials and methods

Type of genotoxicity

other: Morphologic Transformation

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumenta0ca.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-6ee4099c-3e68-4cce-929f-3ff63c4a9ab7%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Type of study

other: cell transformation assay

Principles of method if other than guideline

Method: other: Methods used in the assays for in vitro cell transformation were bsed on those presented by Kakunaga, 1973.

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

IUCLID4 Test substance: other TS: unspecified DIDP

Method

Target gene

None; Transformation is associated with certain phenotypic changes such as loss of contact inhibition and the ability to form colonies in soft agar medium.

Species/strain

Species/strain	other: BALB/C-3T3 mouse cell line cells
Details on mammalian cell lines (if applicable)	
Additional strain characteristics	not applicable
Metabolic activation	without
Metabolic activation system	

Test concentrations

0.2 to 20 ul/ml

Vehicle

Solvent was not used; test chemicals were diluted in culture media and added directly to the flasks.

Details on test system and conditions

METHOD OF APPLICATION: 1-3 (x10^4) Balb/3T3 cells were seeded into a series of glass tissue culture flasks and incubed for 24 hours. Five concentrations of the test chemical (0.2 - 20 ul/ml), preselected for toxicity to the cell line, were added to the flasks containing the cells. The highest dose tested in each assay was anticipated to reduce survival to ca. 10-20% of the control values. Positive (3-methylcholanthrene and methyl-N-nitro-N-nitrosoguanidine) and negative (untreated) controls were also tested. The cultures were incubated with the test chemical for 3 days, washed free of test chemical and cultured for an additional 27 days . The assays were terminated by fixing the monolayers with methanol and staining with Giemsa. Stained dishes were examined by eye and also by microscope for scoring of transfomed foci. Transformed cells formed a dense mass (focus) that stained deeply (usually blue) and was superimposed on the surrounding monolayer of normal cells. Scored foci had several variations in morphological features. Most scored foci consisted of a dense piling-up of cells and exhibited a random, criss-cross orientation of fibroblastic cells at the periphery of the focus and extensive invasiveness into the continuous monolayer. Other scored foci were composed of 1) more rounded cells with little criss-crossing at the periphery but with necrosis at the center caused by the dense piling-up of a large number of cells, or 2) foci without the necrotic center and large number of cells but which exhibited the criss-cross pattern of overlapping cells throughout most of the colony. Foci that had these characteristics and exceeded 2 mm in diameter were scored as +++ and those <2mm diameter were designated as ++. DETERMINATION OF CYTOTOXICITY - Method: Other; A concomitant cytotoxicity assay was performed by plating 200 cells per flask (3 flasks/group), treating with the same concentrations of test chemical and

incubating for a further 7-8 days. Viability in the control cultures was ca. 50%. Colonies were stained and evaluated as described.

Evaluation criteria

Criteria for a valid test were an average negative control transformation frequency of less than or equal to 0.5 focus per dish, and positive control with significantly more foci than the negative control at the 99% confidence level.

Statistics

Transformation data were compiled and evaluated as the number of transformed colonies per flask at each dose level. Log10 transformation of the data was applied in order to convert the distribution of values to a normal distribution. Bailey's modification of Student's t-test, applied to the log-transformed data, was used to determine whether results from a given treatment were significantly different from the corresponding negative controls. Sporadic increases attaining significance at the 95% confidence level were not considered sufficient for a test chemical to be judged as 'transforming' in this assay. Rather, responses at more than one dose level exhibiting significance at the 95% confidence level, and/or a dose-dependent response, were considered necessary to conclude that transformation had been included.

Results and discussions

Test results

Species/strain	other: BALB/C-3T3 mouse cell line cells
Metabolic activation	without
Test system	other: BALB/C-3T3 mouse cell line cells
Genotoxicity	negative Even at concentrations that were clearly in excess of the water solubility limits, no significant increases in transformed foci were observed with DIDP
Cytotoxicity	no data
Vehicle controls valid	not applicable

Negative controls valid	yes
Positive controls valid	yes

Remarks on results including tables and figures

No statistically significant increases in the numbers of transformed foci were observed for DIDP. In each assay, the positive controls produced significant increases in transformed foci, indicating that the assay was responsive to known transformats.

Table 1. Results from the Balb/3T3 in vitro transformation assay for DIDP

DIDP (ul/ml)	% Relative Suvival	No. of Cultures	Total foci	Foci per flask	t-Statistic
Control (0)	100	36	22	0.61	Control
0.200	73.5	18	5	0.28	-1.464
0.632	68.3	17	7	0.41	-0.687
2.000	66.9	18	6	0.33	-1.172
6.320	51.2	18	3	0.17	-2.343
20.00	60.6	18	5	0.28	-1.464
3 -MCA[a]	25.2	18	61	3.388	6.17*
MNNG[b]	2.8	18	47	2.610	5.89*

* Statistically significant using Bailey's modification of Student's t-test

a, 3 -methylcholanthrene

b, methyl-N-nitro-N-nitrosoguanidine

Applicant's summary and conclusion

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumenta0ca.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-6ee4099c-3e68-4cce-929f-3ff63c4a9ab7%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Conclusions

Under the conditions of this study, DIDP did not increase the transformation frequency in the Balb/3T3 cell transformation assay.

Executive summary

The Balb/3T3 cell transformation assay was used to test the ability of DIDP to transform (morphologically alter) cells in culture. The test material, DIDP, was incubated with Balb/3T3 cells in culture at concentrations ranging from 0.200 to 20.00 ul/ml for 3 days. Following a 4 week growth period, the assays were terminated and the monolayers were stained for examination by eye and by microscope for scoring of transformed foci. Positive and negative controls were also tested. No statistically significant increases in the numbers of transformed foci were observed for DIDP. In each assay, the positive controls produced significant increases in transformed foci, indicating that the assay was responsive to known transformants. Therefore, the test substance was negative in that it did not increase the transformation frequency in the Balb/3T3 cell transformation assay.

Administrative Data

Purpose flag	key study
Study result type	experimental result
Reliability	2 (reliable with restrictions)
Rationale for reliability	This study is rated a "2" because it applied GLP, used appropriate testing procedures, but did not follow an accepted testing guideline.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		2000							
study report		1986							

Materials and methods

Type of genotoxicity
gene mutation

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument2ebb.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-6622ec71-977f-446b-8c21-f9d69fb4ddd7%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Type of study

mammalian cell gene mutation assay

Principles of method if other than guideline

Method: other: not specified Based on Clive and Spector, 1975 and Clive et al., 1979.

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity
no

Details on test material

IUCLID4 Test substance: other TS: unspecified DIDP

Method

Target gene
thymidine kinase locus (TK)

Species/strain

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument2ebb.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-6622ec71-977f-446b-8c21-f9d69fb4ddd7%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Species/strain	other: TK locus of mouse lymphoma cells, L5178Y cell line
Details on mammalian cell lines (if applicable)	Mouse lymphoma L5178Y cells in culture were used in the study. The cells were properly maintained in RPMI 1640 supplemented with F68 pluronic solution, antibiotics, and horse serum (10%, v/v) and periodically checked for mycoplasma contamination. In addition they were periodically "cleansed" against high spontaneous background.
Additional strain characteristics	
Metabolic activation	with and without
Metabolic activation system	S9 derived from Aroclor 1254, rat liver

Test concentrations

The w/v concentrations of the doses assayed and density of test substance were not provided. The concentrations reported were in v/v. Six doses (2.0, 4.0, 5.0, 6.0, 8.0 and 10.0 ul/ml) were tested without S9 activation. Four doses (0.25, 0.50, 1.00, and 2.00 ul/ml) were tested with S9 activation. Mutant frequencies were determined for all evaluated levels.

Vehicle

- Vehicle(s)/solvent(s) used: acetone - Justification for choice of solvent/vehicle: None provided

Details on test system and conditions

IUCLID4 Type: Mouse lymphoma assay Mouse lymphoma cells cultured in vitro were exposed to the test substance at 4 or 6 doses in the presence or absence of S9 mammalian metabolic activation for 4 hours. Duplicate tubes were prepared. After washing, cells were cultured for 2 days (expression period) before cell selection. After expression, 1x10^6 cells/dish (3dishes/group) were cultured for 12 days in selection medium to determine numbers of mutants and 200 cells/dish (3 dishes/group) were cultured for 12 days without selective agent to determine cloning efficiency. Selection media consisted of cloning medium with a final concentration of 3ug/ml trifluorothymidine. This nucleoside analog is phosphorylated and, if incorporated into nucleic acid by wild-type cells, results in cell death. Colonies were counted at a size setting of 1.3 using an Artek Model 880 counter. Mutant frequency values were calculated by

dividing the total number of mutant colonies appearing in each set of three dishes containing trifluorothymidine (10^6 cell per dish) by the total viable colony count in the set of three viable count dishes (200 cells per dish) and multiplying by 200 to account for dilution.

Evaluation criteria

The assay was considered valid if all of the following criteria were satisfied: 1. The average cloning efficiency of the negative controls must be in the range of 60-130%. 2. The suspension growth, calculated as [(Day 1 cell count/3x10^5)] x [(Day 2 cell count)/(Day 1 split back volume density)], for the negative controls must be greater than or equal to 8.0. 3. The mutant frequency for the negative controls should be within the range of 10 x 10^-6 to 100x10^-6. 4. The mutant frequencies induced by the positive controls for either the nonactivation assay (using 0.3 ul/ml ethylmethanesulfonate) or the activation assay (using 2.5 ug/ml 3-methyl cholanthrene) must be greater than or equal to 200x10^-6. 5. For test materials determined to be non-mutagenic, the concentrations assayed must include one that will induce a reduction in the percent relative growth to 10-20% of the average for the negative controls, or a maximum concentration of 5ul/ml. The percent relative growth is an expression of toxicity calculated as the relative suspension growth x relative cloning efficiency/100. 6. The relative cloning efficiency must be greater than or equal to 10%; the total number of viable clones must be > 60 in order to accept an experimental mutant frequency. 7. A minimum of two dishes per set, with colony numbers that differ by no more than 3-fold, must be used to derive the mutant frequency. 8. A minimum of three test doses must be analyzed to evaluate the mutagenicity of the test substance. In order to demonstrate mutagenesis for any given dose level, the mutant frequency must be greater than or equal to 150% the concurrent background mutant frequency plus 10x10^-6. To be considered a mutagen, 1. A toxicity-related or dose-related increase in the mutant frequencies must be demonstrated, or 2. if for a single dose near the max tested, mutant frequency is > 300% the concurrent background mutant frequency plus 20x10^-6.

Statistics

The data were not evaluated for statistical significance.

Results and discussions

Test results

Species/strain	mouse lymphoma L5178Y cells

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument2ebb.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-6622ec71-977f-446b-8c21-f9d69fb4ddd7%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Metabolic activation	with and without
Test system	other: TK locus of mouse lymphoma cells, L5178Y cell line
Genotoxicity	negative not mutagenic
Cytotoxicity	other: Doses were selected to cover toxicity from little or no survival to 80-100% growth relative to the solvent control.
Vehicle controls valid	yes
Negative controls valid	yes
Positive controls valid	yes

Additional information on results

pH: At the end of the 4 hour treatment period, the pH of the culture medium containing the highest concentration of test chemical was measured. All pH values were in the range of 7.21-7.68. ADDITIONAL INFORMATION ON CYTOTOXICITY: Doses were selected to cover toxicity from little or no survival to 80-100% growth relative to the solvent control.

Remarks on results including tables and figures

The test material formed a clear, colorless liquid in acetone at 1000 ul/ml. Dilutions of stock solutions were made in the growth medium prior to addition to the cells. The test material, dissolved in acetone, was incompletely soluble in the growth medium at all test concentrations (0.25 - 10 ul/ml) as it formed oily droplets. Under the nonactivation conditions, a white precipitate formed on day 1 after the 4 hour treatment period at all test concentrations, indicating that the posttreatment washings did not remove all of the test material. Under the S9 activation conditions, a white precipitate formed on day 1 posttreatment at test concentrations > 1 ul/ml, again indicating that the washings did not remove all of the test material at these concentrations. Each trial included two cultures per dose level, four negative controls, and two concentrations for the positive control.

Using non activation conditions, six dose levels were tested (2 -10 ul/ml). The percent relative growth values were tested 7.3 -33.3% indicating moderate to high toxicities. In order to demonstrate mutagenesis, the mutant frequency of any given dose level had to be > 30.2 x 10^-6 (150% of the concurrent background mutant frequency plus 10x10^-6). The mutant freqencies for the assayed dose levels were 13.2 x 10^-6 to 28.9 x 10^-6. Because moderate to high toxicity was observed, but mutagenesis was not observed at any dose

level assayed, the test substance was determined not to be a mutagen under nonactivation conditions.

Using activation conditions, four dose levels were tested (2 -10 ul/ml). The percent relative growth values were tested 10.3 -88.6% indicating low to high toxicities. In order to demonstrate mutagenesis, the mutant frequency of any given dose level had to be > 58.4 x 10^-6. The mutant freqencies for the assayed dose levels were 27.8 x 10^-6 to 43.1 x 10^-6. The S9 activation assay confirmed the findings of the nonactivation assay and the test substance was determined not to be a mutagen under activation conditions.

Applicant's summary and conclusion

Conclusions

The data presented in this report confirm the general lack of genotoxicity for DIDP. Phthalate esters do not contain substructures that would be considered 'alerting' for mutagenicity.

Executive summary

In a mammalian cell gene mutation assay at the thymidine kinase locus, L5178Y mouse lymphoma cells cultured*in vitro*were exposed to the test substance, in acetone, at concentrations of 0.25, 0.50, 1,2, 4, 5, 6, 8, or 10 ul/ml (concentration could not be verified; refer to deficiencies section) in the presence and absence of S9 mammalian metabolic activation.

The test substance was tested up to cytotoxic concentrations. Under nonactivation conditions (dose levels 2 -10 ul/ml), the percent relative growth values were 7.3 -33.3%, indicating moderate to high toxicities, and the mutation frequencies were 13.2 x $10^{-6}$to 28.9x10^{-6}. Because moderate to high toxicity was observed, but mutagenesis was not observed at any dose level assayed, the test substance was determined not to be a mutagen under nonactivation conditions. In the S9 activation assay, the test substance was assayed at low to highly toxic dose levels, and the mutant frequencies for the assayed dose levels were 27.8 x $10^{-6}$to 43.1 x 10^{-6}. The test substance was determined not to be a mutagen under S9 -activation conditions. In both the nonactivated and activated conditions, the positive controls induced the appropriate response. There was no evidence of induced mutant colonies over background as a result of exposure. The test material is considered inactive in the mouse lymphoma forward mutation assay with and without metabolic inactivation.

Dissemination Dossier
Genetic in vitro Endpoint.003

Administrative Data

Data waiving study scientifically unjustified

Materials and methods

Test materials

Test material equivalent to submission substance identity
yes

Dissemination Dossier
Genetic in vitro Endpoint.004

Administrative Data

Purpose flag key study
Study result type experimental result
Reliability 1 (reliable without restriction)
Rationale for reliability This study is rated a "1" because it applied GLP and used appropriate testing procedures.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Zeiger E, et al	1992	Phthalate Ester Testing in the National Toxicology Program's Environmental Mutagenesis Test Development Program	Environ Health Perspect 45:99-101					
publication	Zeiger E, et al	1985	Mutagenicity Testing of di(2-ethylhexyl) Phthalate and Related Chemicals in Salmonella	Environ Mutagen 7(2):213-232					

Materials and methods

Type of genotoxicity
gene mutation

Type of study

bacterial reverse mutation assay (e.g. Ames test)

Principles of method if other than guideline

Method: other: Ames BN et al. Mutat Res. 31:347-364.

GLP compliance

no

Test materials

Test material equivalent to submission substance identity
no

Details on test material

IUCLID Test substance: other TS: DIDP with different CAS#

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	homogenates of Aroclor 1254-induced Sprague-Dawley rat and Syrian hamster liver S9

Test concentrations

from 100 up to 10,000 ug/plate

Vehicle

95% ethanol

Details on test system and conditions

IUCLID Type: Ames test

Evaluation criteria

A positive mutagenic response was defined as a reproducible, dose-related increase in his+ revertants over spontaneous level

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	other: Salmonella strains TA98, TA100, TA1535, TA1537
Genotoxicity	negative not mutagenic
Cytotoxicity	no not cytotoxic
Vehicle controls valid	no data
Negative controls valid	no data
Positive controls valid	no data

Applicant's summary and conclusion

Conclusions

The test substance was not mutagenic in the preincubation modification of the Salmonella microsome test.

Administrative Data

Purpose flag	key study
Study result type	experimental result
Reliability	1 (reliable without restriction)
Rationale for reliability	The study was rated a "1" because it was conducted in accordance with international guidelines, used appropriate testing procedures, and applied GLP.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		2000							
study report		1994							1994-05-16

Materials and methods

Type of genotoxicity

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentbdec.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-1e8dcf6e-bdfb-4018-a508-1e92f5b65c15%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

chromosome aberration

Type of study

micronucleus assay

Test guideline

Qualifier	Guideline	Deviations
equivalent or similar to	OECD Guideline 474 (Mammalian Erythrocyte Micronucleus Test)	yes 1000 polychromatic erythrocytes were scored per animal.

Principles of method if other than guideline

Method: other: as described by Schmid (1975). Mutat. Res. 31:9-15 and modified from Heddle et al. (1983) Mutat Res. 123:61-118.

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

IUCLID4 Test substance: other TS TS-Freetext: CAS #68515-49-1; 1,2-benzenedicarboxylic acid, di-C9,C10 and C11 branched alkyl ester, C10 Rich

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Test animals

Species
mouse

Strain

CD-1

Sex

male/female

Details on test animals and environmental conditions

TEST ANIMALS - Source: Charles River Laboratories, Portage, MI - Age at study initiation: 6-9 weeks of age - Weight at study initiation: 29.9-37.6g males and 21.1-27.9 g females - Assigned to test groups randomly: [no/yes, under following basis:] yes - Fasting period before study: - Housing: group housed by sex up to 7/cage - Diet (e.g. ad libitum): ad libitum for the duration of the study - Water (e.g. ad libitum): ad libitum for the duration of the study - Acclimation period: 7 days ENVIRONMENTAL CONDITIONS - Temperature (°C): 72+/- 6 deg F - Humidity (%): 55 +/- 15% - Air changes (per hr): - Photoperiod (hrs dark / hrs light): 12 hour light/12 hour dark cycle IN-LIFE DATES: From: 1994-3-1 To: 1994-3-31

Administration / exposure

Route of administration
oral: gavage

Vehicle(s)

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentbdec.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-1e8dcf6e-bdfb-4018-a508-1e92f5b65c15%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

- Vehicle(s)/solvent(s) used: Duke's Corn Oil - Justification for choice of solvent/vehicle: In the solubility test 1.0072 g of the test substance was added to 2.0 ml of corn oil. This resulted in a clear, light yellow solution upon mixing, at a final concentration of 503.6 mg/ml. This solution passed readily through a 20 G needle. - Concentration of test material in vehicle: Stock solution prepared by adding 19ml corn oil to 11.000 g of test substance with a final concentration of 500 mg/kg. Dilutions of this stock were prepared for the 2500 and 1250 mg/kg dose levels. - Lot/batch no. (if required): Lot #2B

Details on exposure

The vehicle control consisted of corn oil and was administered concurrently with the test substance at a volume of 10 ml/kg. The postive control, cyclophosphamide, was solubilized in sterile deionized water and was administerd by oral gavage at 80 mg/kg.

Duration of treatment / exposure

Mice were sacrificed 24, 48, and 72 hours following dosing. Mice administered the positive control were sacrificed 24 hours after administration.

Frequency of treatment

Single administration of test substance.

Doses / concentrations

1250, 2500, and 5000 mg/kg
Basis actual ingested

No. of animals per sex per dose

5 animals per sex per dose

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Positive control(s)

cyclophosphamide - Route of administration: oral gavage - Doses / concentrations: 80 mg/kg

Examinations

Tissues and cell types examined

Polychromatic and normochromatic erythrocytes from mouse bone marrow were counted.

Details of tissue and slide preparation

At 24, 48, and 72 hours after dosing, animals from each dose group were sacrificed by CO2 asphyxiation. Bone marrow from each femur was aspirated with fetal bovine serum and and suspended. Cells were placed on slides, air dried, fixed in methanol, and stained with May-Grunwald solution then Giemsa. Slides were air dried and coverslipped, then coded prior to scoring.

Evaluation criteria

The criteria for a positive response were a statistically significant dose-related increase in micronucleated PCEs or the detection of a reproducible and statistically significant increase at at least one dose level.

Statistics

Analysis of variance was performed on the proportion of cells with micronuclei per animal (square root arscine proportion). Tukey's Studentized range test, with adjustment for multiple comparisons, was used at each harvest time to determine which dose groups were significantly different ($p<0.05$) from vehicle controls.

Results and discussions

Test results

Sex	male/female
Genotoxicity	negative
Toxicity	no effects . A range finding study was used to select doses for each of the definitive micronucleus tests, but because there was no evidence of toxicity, the highest doses utilized were based on limit tests. The study followed EPA Toxic Substances Control Act guide
Vehicle controls valid	yes
Negative controls valid	yes
Positive controls valid	yes

Additional information on results

All animals were observed immediately after dosing and periodically throughout the duration of the assay for signs of toxicity and mortalities. All animals in the vehicle and positive control groups appeared normal after dosing and remained healthy until sacrifice. All experimentally dosed groups appeared normal immediately after dosing and remained healthy until sacrifice. The test substance induced no significant increases in micronucleated polychromatic erythrocytes over the levels observed in the vehicle controls in either sex or at any time point. The positive control induced significant increases in micronucleated polychromatic erythrocytes in both sexes with means and standard errors of 2.04% +/- 0.34% and 1.76% +/- 0.28% for the males and females, respectively.

Remarks on results including tables and figures

Applicant's summary and conclusion

Interpretation of results

negative

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumentbdec.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-1e8dcf6e-bdfb-4018-a508-1e92f5b65c15%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Conclusions

The test substance did not induce a significant increase in micronuclei in bone marrow polychromatic erythrocytes under the conditions of this assay and is considered negative in the mouse bone marrow micronucleus test.

Executive summary

In an in vivo mouse bone marrow micronucleus assay, groups of 15 male and 15 female CD-1 mice received a single oral gavage dose of 1,250, 2,500, or 5,000 mg/kg test substance. Bone marrow cells were harvested at 24, 48, or 72 hours post-treatment. The test material was administered in corn oil.

There were no clinical signs of toxicity during the study. The test substance was not cytotoxic to the target cell. The positive control induced significant increases in micronucleated polychromatic erythrocytes in both sexes. The test substance did not produce a significant increase in the frequency of micronucleated polychromatic erythrocytes in bone marrow after any treatment time.

Administrative Data

Purpose flag	key study
Study result type	read-across from supporting substance (structural analogue or surrogate)
Reliability	2 (reliable with restrictions)
Rationale for reliability	The study is rated a "2" because it used appropriate test methods but no information is available concerning application of a test guidline or compliance with GLP.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Wan-Seob Cho, Beom Seok Han, Byeongwoo Ahn, Ki Taek Nam, Mina Choi, Sang Yeon Oh, Seung Hee Kim, Jayoung Jeong, Dong Deuk Jang	2008	Peroxisome proliferator di-isodecyl phthalate has no carcinogenic potential in Fischer 344 rats	Toxicology Letters 178 (2): 110-116					

Materials and methods

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument6adf.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-5aadce34-498e-4c09-bfba-457ec6447b18%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Test materials

Test material equivalent to submission substance identity

no

Details on test material

- Name of test material (as cited in study report): Di-isodecyl phthalate - Analytical purity: 99.9% - Stability under test conditions: - Storage condition of test material: - Other:

Test animals

Species

rat

Strain

Fischer 344

Sex

male/female

Details on test animals and environmental conditions

TEST ANIMALS - Source: Charles River Japan Inc. - Age at study initiation: 6 wks - Weight at study initiation: - Fasting period before study: - Housing: 2/cage - Diet: ad libitum - Water: ad libitum - Acclimation period: 10-14 days ENVIRONMENTAL CONDITIONS - Temperature (°C): 23 +/- 1deg - Humidity (%): 55 +/- 5% - Air changes (per hr): - Photoperiod (hrs dark / hrs light): 12 hours light/12 hours dark

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument6adf.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-5aadce34-498e-4c09-bfba-457ec6447b18%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Administration / exposure

Route of administration
oral: feed

Vehicle

unchanged (no vehicle)

Details on exposure

PREPARATION OF DOSING SOLUTIONS: DIET PREPARATION - Rate of preparation of diet (frequency): Test diets were prepared on a monthly basis - Mixing appropriate amounts with (Type of food): DIDP was added to Purina Certified Rodent Chow 5002, on a fixed weight percentage (w/w) basis, and mixed thoroughly to ensure homogeneity. - Storage temperature of food: 4 degrees Celcius VEHICLE -unknown

Analytical verification of doses or concentrations

yes

Details on analytical verification of doses or concentrations

The homogeneity and stability of the test chemical in the diet were verified analytically by HPLC.

Duration of treatment / exposure

2 years

Frequency of treatment

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daily

Doses / concentrations

0, 400, 2,000, and 8,000 ppm. Actual exposures for male rats were 21.9, 110.3 and 479.2 mg/kg-bw/day and for female rats 22.9, 128.2 and 619.6 mg/kg-bw/day.

Basis actual ingested

No. of animals per sex per dose

52 animals/sex/dose

Control animals

yes, concurrent vehicle

Details on study design

- Dose selection rationale: Maximum toterated dose of DIDP (9,000 ppm) was determined in a preliminary 13 week repeated dose toxicity study (Hong et al., 1999) - Rationale for animal assignment (if not random): - Rationale for selecting satellite groups: Experiment for Assessment of peroxisome proliferating activity: For assessment of peroxisomal proliferation, a total of 50 male F344 rats were fed diets containing a vehicle control, 400, 2,000, 8,000 ppm DIDP or 12,000 ppm DEHP. The rats were sacrificed at 12 or 32 weeks after the treatment for the analysis of enzyme catalase. Liver samples were taken for western blotting, enzyme activity assay and immunohistochemistry.

Positive control

DEHP was included as a postive control for induction of peroxisome proliferation.

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Examinations

Observations and examinations performed and frequency

CAGE SIDE OBSERVATIONS: Yes - Cage side observations were included. All animals were observed twice daily for moribundity and mortality. DETAILED CLINICAL OBSERVATIONS: Yes, recorded daily BODY WEIGHT: Yes, recorded weekly through week 13, and every two weeks thereafter until terminal sacrifice FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study): - Food consumption for each animal determined and mean daily diet consumption calculated as g food/kg body weight/day: Yes - Compound intake calculated as time-weighted averages from the consumption and body weight gain data: No data FOOD EFFICIENCY: - Body weight gain in kg/food consumption in kg per unit time X 100 calculated as time-weighted averages from the consumption and body weight gain data: No data WATER CONSUMPTION AND COMPOUND INTAKE (if drinking water study): No data OPHTHALMOSCOPIC EXAMINATION: No HAEMATOLOGY: No CLINICAL CHEMISTRY: No URINALYSIS: No NEUROBEHAVIOURAL EXAMINATION: No OTHER: Assessment of peroxisome proliferating actiivty. Liver samples were taken for western blotting, enzyme activity assay, and immunohistochemistry.

Sacrifice and pathology

GROSS PATHOLOGY: Yes - all organs and tissues were examined for grossly visible lesions HISTOPATHOLOGY: Yes - all major tissues were fixed and preserved in 10% neutral buffered formalin, processed and trimmed, embedded in parafin, sectioned to a thickness of 4-6 um and stained with hematoxylin and eosin for microscopic examination. The following organs were weighed at the interim and terminal sacrifices: adrenal glands, brain, heart, kidneys, liver, ovaries, spleen and testes.

Statistics

The probability of survival was estimated using the product-limit procedure of Kaplan and Meier (1958). Statistical analyses for possible dose-related survival effects were conducted using Cox's (1972) method and Tarone's (1985) life table test for testing two groups for equality and to identify dose related trends, respectively. Feed consumption, as well as organ and body weight data were analyzed using the parametric multiple compaison procedures of Dunnet (1955) and Williams (2002). Extreme values were identified using the outlier test of Dixon and Massey (1951). Average severity values were analyzed for significance using the Mann-Whitney U-test. The Poly-k test (Bailer and Portier, 1988; Portier and Bailer, 1989) was used to assess the prevalence of meoplastic and non-neoplastic lesions. The catalase assay data were compared using the Dunnett t test after an ANOVA analysis. For all comparisons, p values less than 5% ($p<0.05$) were considered statistically significant.

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Results and discussions

Effect levels

Endpoint	Effect type	Effect level	Sex	Basis for effect level / Remarks
NOAEL	carcinogenicity	ca. 8000 ppm	female	Increased incidences of MNCL at 8,000 ppm were observed; however, these effects are considered not relevant to humans.
NOAEL	carcinogenicity	ca. 8000 ppm	male	Increased incidences of MNCL at 8,000 ppm were observed; however, these effects are considered not relevant to humans.

Observations

Clinical signs and mortality

no effects

Body weight and weight gain

yes

Food consumption and compound intake (if feeding study)

no effects

Food efficiency

not examined

Water consumption and compound intake (if drinking water study)

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not examined

Ophthalmoscopic examination

no data

Haematology

no data

Clinical chemistry

no data

Urinalysis

no data

Neurobehaviour

no data

Organ weights

yes

Gross pathology

yes

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument6adf.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-5aadce34-498e-4c09-bfba-457ec6447b18%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Histopathology: non-neoplastic

yes

Histopathology: neoplastic

no effects

Details on results

CLINICAL SIGNS AND MORTALITY A significant decrease in overall survival was noted in both sexes of the high-dose groups compared with the vehicle control group (males: vehicle control 44/52, low dose 38/52, mid dose 43/52, high dose 19/52; females control 44/52, low dose 39/52, mid dose 39/52, high dose 29/52). The survival in the control groups was 85% similar to that observed in chronic feeding studies on F344 rats sponsored by the National Toxicology Program (Cameron et al., 1985; Solleveld et al., 1984). There were no clinical findings related to DIDP exposure. BODY WEIGHT AND WEIGHT GAIN The mean body weights of rats exposed to 8,000 ppm were generally less than those of the other treatment groups throughout the study. ORGAN WEIGHTS The relative kidney and liver weights of both males and females exposed to 8,000 ppm were significantly increased compared to those of the control animals. No treatment-related changes were observed in the relative organ weights for the spleen, testes, ovary, brain, adrenal glands, and heart. HISTOPATHOLOGY: NON-NEOPLASTIC Males: The incidence of animals with altered cell foci in the liver was significantly decreased in rats exposed to 2,000 and 8,000 ppm DIDP, in a dose-dependent manner. The fatty change in the liver decreased in the 8,000 ppm group. Oval cell hyperplasia, hypertrophy, necrosis and peliosis of the liver were increased in the 8,000 ppm group. Microgranuloma and spongiosis hepatis of the liver were increased in all treatment groups compared to control. Medullary hyperplasia of the adrenal gands was inccreased in the 400 and 2,000 ppm exposed males. Mineralization and interstitial nephritis of the kidneys were increased in the high dose. Degeneration and inflammation of the prostate and hyperplasia were increased in the 400 ppm, and 400 and 2,000 ppm exposed males, respectively. C-cell hyperplasia of the thyroid gland was decreased in the 2,000 ppm group. Females: The incidence of altered cell foci in the liver was generally decreased in the exposed females, with those decreases significant at 8,000 ppm. Inflammation of the liver and necrosis were increased in the 400 and 2,000 ppm and the 8,000 ppm groups, respectively. Microgranuloma of the liver was decreased with the high dose. Hyaline cast, interstitial nephritis and chronic progressive nephropathy of the kidney were decreased in the high dose. Inflammation of the kidney was increased in the 400 and 2,000 ppm treatment groups. The incidence of extramedullary hematopoiesis was decreased in the 2,000 and 8,000 ppm groups. C-cell hyperplasia in the thyroid gland was increased in the 400 and 2,000 ppm groups. HISTOPATHOLOGY: NEOPLASTIC (if

applicable) DIDP produced no treatment-related neoplastic lesions of the liver in either sex. However, the incidences of mononuclear cell leukemia (MNCL) in the males and females exposed to 8,000 ppm were significantly increased compared with the vehicle control, but were within historical ranges in the controls. The C-cell adenomas of the thyroid gland were significantly decreased in the males exposed to 400 ppm and females exposed to 2,000 and 8,000 ppm compared with the vehicle control, but were again within the NTP historical ranges. OTHER FINDINGS: CELLULAR CATALASE EXPRESSION LEVELS AND ACTIVITY Western blot, catalase assay and immunohistochemical staining for the H2O2-degrading enzyme catalase contained within the peroxisome were performed. After 12 weeks of treatment, the levels of catalase in the high dose DIDP and 12,000 ppm DEHP treated livers were significantly increased compared to control. However, after 32 weeks of treatment, no significant differences were found in the expression and activity of catalase protein among DIDP treated liver tissues. A significant increase in the expression and activity of catalase protein was seen with the positive control. Similar results were obtained when the catalase protein was investigated via immunohistochemistry. No change in the expression of catalase was seen at any dose.

Applicant's summary and conclusion

Conclusions

Under the conditions of this study, DIDP was not carcinogenic to in male or female rats at doses up to 8,000 ppm (479-619 mg/kg bw/day). A marginal increase of MNCL in the 8000 ppm groups was observed; however, it was not considered a relevant risk for humans.

Dissemination Dossier
Reproduction Endpoint.001

Administrative Data

Purpose flag supporting study

Reliability 1 (reliable without restriction)

Rationale for reliability This study is rated a "1" because it applied GLP and used appropriate testing procedures.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1986							1985-12-31
publication	Lington A, Gray T, Evans J, Lake B and Morgan B 1993 Short-term feeding studies assessing the testicular effects of new plasticizers in the F344 rat Toxicology Letters 67:123								

Materials and methods

Test type

other: Testicular atrophy

Test materials

Test material equivalent to submission substance identity

yes

Test animals

Species

rat

Strain

Fischer 344

Sex

male

Administration / exposure

Route of administration

oral: feed

Duration of treatment / exposure

Exposure period: 21 days

Frequency of treatment

daily

Administrative Data

Purpose flag	supporting study
Reliability	1 (reliable without restriction)
Rationale for reliability	This study is rated a "1" because it applied GLP, and used appropriate testing procedures.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
study report		1990							
publication	Lake B, Cook W, Worrell N, Cunninghame M, Evans J, Price R, Young P and Carpanini F	1991	Dose-response relationships for induction of hepatic peroxisome proliferation and testicular atrophy by phthalate esters in the rat	Human and Experimental Toxicology 10:67-68					

Materials and methods

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Test type
other: Investigation of testicular atrophy

Test materials

Test material equivalent to submission substance identity
yes

Test animals

Species
rat

Strain

Fischer 344

Sex

male

Administration / exposure

Route of administration
oral: feed

Duration of treatment / exposure

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument47c3.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-ed950c0c-86ad-4249-bda3-708bb4b7275b%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Exposure period: 28 days

Frequency of treatment

daily

Administrative Data

Purpose flag	key study
Study result type	experimental result
Reliability	1 (reliable without restriction)
Rationale for reliability	This study is rated a "1" because it applied GLP, used appropriate testing procedures, and followed an accepted test guideline.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
	Hushka LJ, Waterman SJ, Keller LH, Trimmer GW, Freeman JJ, Ambroso JL, Nicolich MJ and McKee RH	2001	Two-generation reproduction studies in rats fed di-isodecyl phthalate	Reproductive Toxicology (15)153-169					
study report		1997							1997-10-31

Materials and methods

Test type

two-generation study

Test guideline

Qualifier	Guideline	Deviations
equivalent or similar to	EU Method B.35 (Two-Generation Reproduction Toxicity Test) Cited as Directive 67/548/EEC, Annex V Part B 1988	
equivalent or similar to	EPA OPPTS 870.3800 (Reproduction and Fertility Effects)	

Principles of method if other than guideline

-

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumente39e.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-56d15a54-98b5-43ea-9c43-dec4dffe0219%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

- Name of test material (as cited in study report): 1,2-benzenedicarboxylic acid, di-C9, C10 and C-11 branched alkyl ester, C10 rich - Physical state: liquid - Analytical purity: Assumed 100% pure for purposes of dosing - Expiration date of the lot/batch: April 1999

Test animals

Species
rat

Strain

Sprague-Dawley

Sex

male/female

Details on test animals and environmental conditions

TEST ANIMALS - Source: Charles River Laboratories, Inc - Age at study initiation: (P) 7-8 wks - Weight at study initiation: (P) Males: 238.2-288.4 g; Females: 148.3-201.5 g; (F1) Males: x-x g; Females: x-x g - Fasting period before study: No - Housing: individually housed during the test period, except during the mating and postpartum periods. - Diet: Purina Certified rodent Chow (5002 meal), ad libitum - Water: Automatic watering system, ad libitum - Acclimation period:16 days ENVIRONMENTAL CONDITIONS - Temperature (°F): 68-76 - Humidity (%): 40-70 - Photoperiod: 12 hrs dark / 12 hrs light IN-LIFE DATES: From: 1995-07-12 To: 1996-04-07

Administration / exposure

Route of administration
oral: feed

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumente39e.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-56d15a54-98b5-43ea-9c43-dec4dffe0219%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Vehicle

unchanged (no vehicle)

Details on exposure

DIET PREPARATION - Rate of preparation of diet (frequency): weekly - Mixing appropriate amounts with (Type of food): The basal diet consisted of Certified Rodent Chow (5002 Meal). The test material was incorporated into the feed and mixed thoroughly to assure homogeneity. The test material diet and mixtures were prepared as fixed concentrations of test material.

Details on mating procedure

After the 10-week premating exposure period, each P1 male was randomly paired with a P1 female from the same treatment group to produce the F1 generation. The mating period ended when all females were confirmed mated or approximately two weeks had elapsed. The day of confirmation of mating, based on observation of a copulatory plug or sperm in a vaginal rinse, was designated as Gestation day 0 (GD 0) and the date on which parturition was recorded was designated as PND 0. - M/F ratio per cage: 1:1 - Length of cohabitation: Continuously until mating was confirmed - Proof of pregnancy: vaginal plug referred to as day 0 of pregnancy - After successful mating each pregnant female was caged (how): Mated females were single housed in clean cages fitted with a stainless steel litter pans and provided with fresh bedding material.

Analytical verification of doses or concentrations

yes

Details on analytical verification of doses or concentrations

Concentrations of test material-diet blends were checked by the testing laboratory at least once a month in order to ensure continuing accuracy in mixing diets.

Duration of treatment / exposure

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P1 males and females received test material daily for at least 10 weeks prior to mating and during the mating period. Additionally P1 females received test material during the gestation and postpartum periods, until weaning of the F1 (offspring of the P1 generation) offspring on PPD 21. P2 (F1 generation animals chosen to mate) males were dosed from postnatal day (PND) 21 for at least 10 weeks prior to mating, through the mating period for F2 (the offspring of the P2 generation) litters, and until sacrificed. P2 (F1) females were dosed from PND 21 for at least 10 weeks prior to mating, during mating, gestation, postpartum and until they were sacrificed following weaning of the F2 animals on PPD 21.

Frequency of treatment

continuous (diet)

Details on study schedule

- Selection of parents for F1 generation when pups were 21 days of age.

Doses / concentrations

In the first study 0.2, 0.4, 0.8% were target dietary concentrations, 30/sex/group. In the second study the target concentrations were 0.02%, 0.06%, 0.2%, and 0.4% in diet, 30/sex/group.

Basis nominal in diet

No. of animals per sex per dose

Main Study (P1 Generation) 30/sex/dose for 0.2% and 0.4% concentrations 40/sex/dose for control and 0.8% concentration Satellite Animals (P1 Generation) 5 males/dose for 0.2% and 0.4% doses 10/sex/dose for control and 0.8% dose Main Study (P2 Generation) 30/sex/dose Satellite animals (P2 generation) 5 males/dose

Control animals

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumente39e.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-56d15a54-98b5-43ea-9c43-dec4dffe0219%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

yes, plain diet

Further details on study design

- Dose selection rationale: Doses for this study were selected based on the results of a one-generation reproduction toxicity range-finding study in rats with the test material. The dose levels tested in the rangefinding study (with only a 3 week pre-mating period) were 0.25%, 0.50%, 0.75% and 1.0%. Signs of toxicity were apparent at dose levels of 0.75% and 1.0%, and observed in both the parental animals and offspring. Signs of toxicity in the parental animals included decreased doby weight, suppression of body weight gain, and/or decreased food consumption. In the 0.5% dose group, adverse findings were limited primarily to decreases in food consumption compared to controls in the females during the postpartum period. Overt signs of toxicity observed in the offspring were limited to growth retardation in males and females at 0.75% and 1.0%. There also was slight evidence of growth retardation at 0.5%. The postnatal day 0 and 4 offspring mean body weights were outside the historical control range of this laboratory (although not statistically significantly less than controls) indicating possible growth retardation. Based on these results, 0.8% was selected as the high dose for the definitive two-generation reproduction toxicity study in rats with the test material. This dose was anticipated to produce signs of toxicity, primarily lower body weights, in the parental males but also in the females during gestation and postpartum. Additionally, this dose was considered low enough to allow for sufficient survivorship in the F1 generation. A low dose of 0.2% was selected because it was expected to be a level without effect, particularly in the F2 generation. Finally, 0.4% was selected as the mid dose.

Examinations

Parental animals: Observations and examinations

CAGE SIDE OBSERVATIONS: Yes - Time schedule: Daily DETAILED CLINICAL OBSERVATIONS: Yes - Time schedule: Males: On the first day of dosing (day 0) and at least weekly therafter until sacrifice. Females: Prior to P1 selection, on the first day of dosing, and at least weekly thereafter until confirmation of mating, then on GD 0, 7, 14, and 21, and on PPD0, 4, 7, 10, 14, and 21. An exam was also given to each P1 male and female on its day of sacrifice. BODY WEIGHT: Yes - Time schedule for examinations: Males: prior to P1 selection, on the first day of dosing, and at least weekly thereafter until sacrifice. Females: Prior to P1/P2 selection, on the first day of dosing and at least weekly thereafter until confirmation of mating, then on GD 0, 7, 14, and 21 and on PPD 0, 4, 7, 10, 14, and 21, and/or at least weekly until sacrifice. Body weight also was measured on the day of sacrifice for all P1 males and females. FOOD CONSUMPTION AND COMPOUND INTAKE (if feeding study): Food consumption was measured concurrently

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with body weight after Day 0, except during mating or during the postweaning period of the F1 litters.

Estrous cyclicity (Parental animals)

The estrous cycle of each P1 female was evaluated daily by vaginal smears beginning three weeks prior to mating (day 49) and continuing until the end of cohabitation. The vaginal smears were stained with Wright's stain before being evaluated. Estrous cycles were not evaluated on the day positive vaginal smears for either sperm or plugs were present.

Postmortem examinations (Parental animals)

Complete gross postmortem examinations were conducted on all animals in the study. Selected organs including liver, kidneys (paired), testes (individual), prostate, seminal vesicles, right epididymis (total and cauda), ovaries (individual), uterus, and brain from all parental animals that survived to scheduled termination were removed and weighed. The pituitary, testes, epididymides, prostate, seminal vesicles, vagina, uterus, ovaries, mammary gland, oviducts, thymus, adrenals, coagulating gland, kidney, liver and gross lesions from all parental animals in the control and 0.8% dose groups were examined microscopically. In addition, the reproductive organs of all animals in the 0.2% and 0.4% dose groups that had abnormal sperm, estrous cycles, or failed to produce viable litters were examined. The testes of teh P1 and F1 males were preserved in Bouin's solution. All other tissues were fixed in 10% neutral formalin, The tissues were processed, embedded in paraffin, sectioned at 5um and stained with hematoxylin and eosin. Five sections of each ovary from females in the control and high dose were examined for oocyte evaluation.

Results and discussions

Effect levels

Endpoint	Generation	Sex	Effect level	Basis for effect level / Remarks
NOAEL	P	male/female	> 0.8 %	Reproductive NOAEL is the highest dose tested = 0.8% Lowest estimated dose for 0.8% = 427mg/kg/bw/d (P1 males, premating) Highest estimted dose for 0.8% = 1,424 mg/kg/bw/d (P2 females, post partum)
NOAEL	F2	male/female	> 0.06	lowest estimated dose for 0.06% = 33mg/kg/bw/d

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%

Observations: parental animals

Clinical signs (parental animals)

yes

Body weight and food consumption (parental animals)

yes

Test substance intake (parental animals)

yes

Reproductive function: estrous cycle (parental animals)

yes

Reproductive function: sperm measures (parental animals)

not examined

Reproductive performance (parental animals)

yes

Organ weights (parental animals)

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocumente39e.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-56d15a54-98b5-43ea-9c43-dec4dffe0219%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

yes

Gross pathology (parental animals)

yes

Histopathology (parental animals)

yes

Observations: offspring

Remarks on results including tables and figures

Parental toxicity: In the P1 generation, there were statistically significant increases in the mean absolute and relative liver weights of the 0.4% dose males 12% and 14%, respectively) and 0.4% dose females (12% and 13%,respectively) compared with controls. These increases were consistent with findings in the previously conducted two-generation reproductive study (Exxon Biomedical Sciences, 1997d), and related to the known capability of DIDP to cause peroxisome proliferation. There were statistically significant increases in mean absolute and relative kidney weights of the 0.4% males (14% and 18%, respectively). These increases were also consistent with findings in the previously conducted two-generation reproductive study (ExxonBiomedical Sciences, 1997d). There also was a statistically significant increase in the 0.4% female mean relative kidney weight (6%) compared with the controls. In the P2 generation, there were statistically significant increases in the mean absolute and relative liver weights of the 0.4% males(13% and 14%,respectively), 0.4% females (23% and 20%, respectively), and 0.2% females (17% and 9%, respectively)compared with controls. In the kidneys, there were statistically significant increases in mean absolute and relative weights of the 0.4% dose males (20% and 19%, respectively), and the 0.2% males (10% and 7%,respectively) compared with controls. There was a statistically significant increase in mean absolute kidney weight in the 0.2% females (13%) compared with controls. There were no treatment-related deaths. There were no gross postmortem observations judged to be related directly to treatment with the test material. The majority of P1 and P2 animals throughout the groups were free of observable abnormalities at postmortem examination. In the females, there was an apparent dose-related increase in thick and/or discolored stomachs. This stomach irritation was attributed to ingestion of bedding materials since it was observed only in females and observed in all groups, including controls. Notable postmortem observations in the P2 animals surviving to termination were limited to an increased incidence (8/29) of

dilated renal pelves in the 0.4% dose males compared with controls. Dilated renal pelves also were observed in the other treated groups (2-5/30),but the incidence generally was similar to controls (3/30). Dilated renal pelves also were noted in several females. There were no statistically significant differences in the mean body weight between the treated and control males or females during the P1 or P2 generation, including the gestation and postpartum intervals.
Offspring toxicity: There were no biologically significant differences in F1 survivorship between the treated and control offspring and all survival indices were within the historical control range for this laboratory. Statistically significant differences were limited to an increase in the live birth index of the 0.06% and 0.4% dose groups compared with controls. These increases were not considered biologically important. In the F2 generation, there was a dose-related decrease in the Day 1 and Day 4 survival indices, with statistically significant decreases being observed in the 0.2% dose group (4% and 10%, respectively) and0.4% dose group (6% and 13%, respectively) compared with controls. These values were outside the historical control range of this laboratory and were considered treatment related. These results were consistent with the decreased F2 survivorship in the previous two-generation study. There were no statistically significant differences between the control and treated animals for post-implantation loss. The live birth index for the 0.2% dose group was higher than the historical control and this was not considered biologically important. There were statistically significant increases in Day 14 and viability at weaning indices of the 0.02% and 0.06% dose groups compared with controls. These increases were not considered biologically important. The Day 21 survival indices of the 0.2% and 0.4% dose groups were marginally outside the historical control range for this laboratory, but not statistically significantly different from the control. No biological importance was assigned to these observations (cf. Table 4.31).
In the F1 offspring, there were no statistically significant differences in mean body weights between treated and control animals of either sex up to PND 21 nor statistically significant differences in mean body weight or mean food consumption between treated and control offspring of either sex during the two-week post weaning measurements. In the F2offspring, there were statistically significant lower mean body weights in the 0.4% males on PND 14, the 0.4%females on PND 14 and 21 and the 0.2% females on PND 14 compared with controls. Although, these weights were within the historical control range of the laboratory, these may have been a treatment-related effect. There also was a statistically significant increase in the 0.02% male mean body weight on PND 21. This increase was not considered biologically important. Mean post weaning body weights were significantly decreased compared to controls in the 0.4% dose males during PNDs 28 and 35, and in the 0.2% dose males at PND35 only. At PNDs 42, 49, and 56, an apparent recovery occurred in the 0.2% and 0.4% treated males and their mean body weights were no longer statistically different from controls. There were no statistically significant differences in post weaning body weights between treated and control females on PND28. There were no treatment-related clinical signs observed in the F1 or F2 offspring of any group and the majority of offspring in all groups were free of observable abnormalities from PND 0-21 and during the post weaning periods. However, there was an increased incidence of cannibalization of F2 pups at PND 1 or 2,not sporadically but a few P2 females in the 0.2 and 0.4% groups were specifically concerned (for instance in the 0.4% treated group one female cannibalized all its litter, e.g. 10 pups/10). In general, there were no gross postmortem observations in the F1 or F2 offspring judged

to be related to treatment with the test material. The majority of animals selected for necropsy were free of observable abnormalities at the scheduled terminal sacrifice on PND 21. The majority of animals that died prior to weaning (GD 22 - PND 21) also were free of observable abnormalities. In the F1 generation, there were no statistically significant differences in mean absolute or relative organ weights (kidney or liver) between treated and control animals of either sex. In the F2 generation, there were no statistically significant differences in mean absolute or relative organ weights(kidney or liver) between treated and control animals of either sex with the exception of the 0.4% dose group female mean relative liver weight. There was a statistically significant increase in the mean relative liver weight of the 0.4% dose group females compared with controls. In the absence of a similar trend in the respective absolute liver weight, this single difference was considered the result of the lower mean bodyweights of the 0.4% females at study termination and not treatment-related. There were no statistically significant differences in F1 or F2 offspring mean PND 0 anogenital distance between treated and control animals of either sex. Nipple retention was similar between treated and control offspring of both sexes: the majority of females in all groups had six nipples retained on PND 13/14, while all males in all groups had zero. In the F1 animals, there were no statistically significant differences in age or weight at preputial separation between treated and control male offspring. There were no statistically significant differences in age or weight at vaginal patency between treated and control female offspring. In the F2 animals, there was a statistically significant delay in preputial separation for the 0.4% males when compared to the control male offspring. This delay was small (1.2 days) and preputial separation was still included within the historical data of CD-rats(Bates et al., in Developmental Toxicology Handbook, 1997). There were no statistically significant differences in the mean body weight at which preputial separation occurred between treated and control male offspring. There were no statistically significant differences for age of vaginal patency between treated and control female offspring. However, there was a statistically significant decrease in the mean body weight at the time that the 0.4% females achieved vaginal patency compared with the control female offspring. This decrease was small (6%) and not considered biologically significant.
Satellite studies: Cross fostering: In the cross fostering satellite study, offspring born to high-dose dams and cross-fostered to control dams on PND 0 exhibited body weights which were not different from main study control offspring throughout the postnatal phase. Conversely, the mean body weights of the offspring cross-fostered to the high-dose dams were statistically significant lower (up to 19%) than the main study control offspring of both sexes on PND 14 and 21. This indicates that DIDP may be transferred through the milk but at a low level, evidenced by a low decrease of body weight; a statistical level of significance was obtained when lactation exposure effects and direct toxicity via feed (solid food is absorbed by pups from PND 14) were combined. Following weaning, these animals remained on control or high-dose diet corresponding with their cross fostering treatment, for the second generation premating phase. The mean body weight of the offspring cross-fostered with high-dose dams continued to be statistically significant lower (9-11% males; 7-10% females) than the mean body weight of the offspring cross-fostered with control dams during premating. In parent equivalents (adult rats stemming from cross-fostered pups), during the premating period there were statistically significant increases in the mean absolute and relative kidney weights of the pups cross fostered with high-dose dams (an increase of respectively 16% and 30% in males,

and respectively 9% and 22% in females) compared with pups cross-fostered with control dams. The same trend was observed for liver weights: the mean absolute and relative liver weight of the cross-fostered high-dose group was increased compared with the cross-fostered control group (an increase of respectively 11% and 23% in males and 22% and 35% in females). Pertaining to reproductive organ weight changes in males, mean absolute right and left testis weight of the cross-fostered high-dose group were statistically significantly decreased compared with the cross-fostered control group. Since, relative right and left testis and epididymis weights were increased, this effects is probably due to lower body weight. In females there was an increase of the uterus, right and left ovary weights, only statistically significant when expressed relative to body weights. In absence of histopathology, it could not be determined if changes in tissue structure and function occurred.
Switched diet phase: In the switched diet phase, weaning from high-dose animals was given control diet, while weaning from control animals was given high-dose diet. The high-dose offspring of both sexes switched to control diet displayed signs of recovery in body weight immediately after weaning and displayed normal growth patterns. However a trend toward lower body weight similar to the main study high-dose males was observed after day 42. The control offspring of both sexes switched to high-dose diet displayed slight reduction of body weight gain as the study progressed, similar to the main study high-dose animals during the P1 premating interval. In addition, in the switched diet high-dose P2 equivalents (adult rats stemming from the switched diet pups) there were statistically significant increases of the absolute and relative liver weights (an increase of respectively 36% and 34% in males, 31 and 39% in females) and kidney weights (an increase of 27% in males, respectively 15% and 23% in females), right and left testis and epididymis weights compared with the switched diet control P2 equivalents. The increase of testicular weight observed in males might be related to transient hypothyroidism in early phases of development. Results from the cross-fostering and switched diet satellite groups indicate that lactation exposure may participate to toxicity of DIDP (EU RAR on DIDP (2006)).
Summary: No-Observed-Adverse-Effect Levels (NOAELs) for fertility was 0.8%, and for offspring survival was 0.06% (F2 gen, PND 1 -4). There were no important or dose-dependent clinical signs of toxicity in either the P1 males or females in any dose group. There were no treatment-related deaths or gross postmortem observations judged to have been related directly to treatment with the test material in any P1 or F1 animals. Increased liver and kidney weights were found at all dose levels in male and female adults. There were no differences observed in mating, male or female fertility, gestational index, or length of gestation. Furthermore, there were no differences in mean littersize or sex ratio. The percentage of live offspring was significantly decreased in the 0.8% dose group and below the laboratory historical control range (HCR). In addition, reduced offspring survival was observed at postnatal days 1 and 4 in the F2 generation (but not in the F1 generation) at levels of 0.2% DIDP and greater. There was a statistically significant increase in age of vaginal patency in the 0.4 and 0.8% dose groups, but overall the differences were small (approximately 2 days) and with in the range of unknown biologic relevance. No clinical signs of toxicity or gross postmortem observations were noted in the offspring. There were no differences in viability at weaning during the postnatal period. There were no differences in F1 offspring developmental landmarks, anogenital distance, nipple retention, preputial separation, or vaginal patency. There were no

differences in testicular weights in either parents (P1) or offspring (F1) and there were no pathological changes in the testes. Further, there were no differences in offspring body weight during the postnatal period to PND 35. Results from the cross-fostering and switched diet satellite groups indicate that lactation exposure may participate to toxicity of DIDP (EU RAR on DIDP (2006)).

Applicant's summary and conclusion

Conclusions

There were no statistically significant differences in male mating, male fertility, female fertility, female fecundity, or female gestational indices between treated and control animals in the P1 or P2 generation. Mean days of gestation and mean litter size and of the treated and control groups were similar. There were no statistically significant differences in the mean sex ratio of the treated offspring compared with controls. Parental toxicity: In both studies, liver and kidney effects were observed in the P1 generation. Increased liver weights and associated hepatocellular hypertrophy were observed at dietary concentrations of 0.4% and greater in both studies. These dietary concentrations also produced kidney effects that were associated with alpha 2u microglobulin toxicity, a male rat specific effect and thus not relevant to humans. In the first study, minor effects on the liver were observed at 0.2% (103 – 203 mg/kg/day). In the second study, no hepatic effects were recorded at this concentration (114 – 225 mg/kg/day). As there is a range in intake levels, it is likely this dietary concentration results in ingestion of DIDP at or near the NOAEL for systemic effects from repeated doing. Up to the highest dose tested no overt signs of reproductive toxicity were reported and no effect was observed on fertility parameters. For offspring toxicity, a decrease in survival indices (day 1 and day 4) in F2 generation leads to a NOAEL of 0.06% (33 mg/kg bw/d, lowest estimated dose for 0.06% DIDP in diet). No effect was observed on developmental landmarks assessed at any dose tested.

Dissemination Dossier
Developmental Endpoint:001

Administrative Data

Purpose flag supporting study

Reliability 1 (reliable without restriction)

Rationale for reliability This study is rated a "1" because it applied GLP, used appropriate testing procedures, and followed an accepted test guideline

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Hellwig J, Freudenberger H and Jackh R	1997	Differential prenatal toxicity of branched phthalate esters in rats	Food and Chemical Toxicology 35:501-512					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	EU Method B.31 (Prenatal Developmental Toxicity Study) Cited as Directive 87/302/EEC, part B, p. 24	

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

IUCLID4 Test substance: as prescribed by 1.1 - 1.4

Test animals

Species

rat

Strain

Wistar

Administration / exposure

Route of administration

oral: gavage

Duration of treatment / exposure

day 6-15 of gestation

Frequency of treatment

daily

Doses / concentrations

40, 200, 1000 mg/kg/day

Basis

Control animals

yes, concurrent vehicle

Further details on study design

Sex: male/female
Duration of test: day 20 of gestation

Results and discussions

Effect levels

Endpoint	Effect type	Effect level	Basis for effect level / Remarks
NOAEL	maternal toxicity	200	
NOAEL	teratogenicity	200	

Dissemination Dossier
Developmental Endpoint.002

Administrative Data

Purpose flag key study

Study result type experimental result

Reliability 1 (reliable without restriction)

Rationale for reliability This study is rated a "1" because it applied GLP, used appropriate testing procedures, and followed an accepted test guideline.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication		1995							
publication		1999							
study report		1995							1995-04-28

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to other guideline:	Official Journal of European Communities L 133 Methods for Determination of Toxicity, Teratogenicity (Annex V, Adopted November 18, 1987)	no

GLP compliance

yes

Test materials

Test material equivalent to submission substance identity

yes

Details on test material

- Name of test material (as cited in study report): di-isodecyl phthalate
- CAS RN 68515-49-1

Test animals

Species

rat

Strain

Sprague-Dawley

Details on test animals and environmental conditions

TEST ANIMALS
- Source: Charles River Laboratories, Inc
- Age at study initiation: 9 weeks
- Weight at study initiation: 210 to 270 g
- Fasting period before study:
- Housing: Single house during the study period, except during mating
- Diet: ad libitum
- Water: ad libitum
- Acclimation period: 13 days

ENVIRONMENTAL CONDITIONS
- Temperature (°C): 20 to 24.4
- Humidity (%): 40 to 70
- Photoperiod: 12 hrs dark / 12 hrs light

Administration / exposure

Route of administration

oral: gavage

Details on mating procedure

- Impregnation procedure: cohoused
- If cohoused:
  - 1:1 M/F ratio per cage:
  - Length of cohabitation: until observation of proof of pregnancy.
  Mated females returned to individual cages. New females placed in males'cages until required number of mated females obtained for study.
- Proof of pregnancy: vaginal plug / sperm in vaginal smear, referred to as day 0 of pregnancy

Duration of treatment / exposure

Gd 6 through 15

Frequency of treatment

daily

Duration of test

All females euthanised on GD21

Doses / concentrations

100, 500, 1000 mg/kg
Basis actual ingested

No. of animals per sex per dose

no males; up to 25 mated females / dose

Control animals

yes, concurrent vehicle

Further details on study design

Sex: male/female
Duration of test: gestation day 21

Results and discussions

Effect levels

Endpoint	Effect type	Effect level	Basis for effect level / Remarks
NOAEL	maternal toxicity	500 mg/kg bw/day	no reduced maternal weight gain or food consumption unlike during maternal toxicity at 1000 mg/kg bw/day
NOAEL	developmental toxicity	500 mg/kg bw/day	no increased incidence of frequency of 7th cervical and rudimentary lumbar ribs unlike during maternal toxicity at 1000 mg/kg bw/day

Embryotoxic / teratogenic effects

yes

Remarks on results including tables and figures

RS-Freetext:
Maternal toxicity was indicated by reductions in body weight gain and food consumption. There was no evidence of malformations or fetal toxicity.

Developmental effects: There were no significant differences in mean foetal body weight and no statistically significant increases in total or individual external, visceral or skeletal malformations in the treated group when compared with controls. The only visceral variation observed was a single incidence of dilated renal pelves in the mid group. Three controls, one low-dose, three mid-dose, and six high-dose foetuses were stunted. Those observations were considered incidental and unrelated to treatment. There was a dose-related increase in total foetuses with skeletal variations on both a per foetus basis (38/196, 35/177, 61/193, 123/196) and a per litter basis (18/25, 17/22, 20/24, 23/24) at a dose of 0-100-500-1,000 mg/kg, respectively. When compared with controls, rudimentary lumbar ribs and cervical ribs were dose-related significantly increased (p 0.01) in the mid and high-dose groups on a per foetus basis (21%, 52% versus 8.2% in control group and 6.2%, 9.2% versus 1% in control group, respectively; the historical control ranges are 3.7-21.6% and 0.54-4.0%, respectively) and in the high-dose group on a per litter basis (23/24 vs. 10/24 for rudimentary lumbar ribs and 10/24 vs. 2/25 for rudimentary cervical ribs).

Applicant's summary and conclusion

Conclusions

The results indicate that DIDP was neither a selective developmental toxicant nor an embryotoxic agent.

Executive summary

In regard with developmental effects, skeletal variations are observed in the developmental studies at 1,000 mg/kg/d concurrently with slight signs of materna

Dissemination Dossier
Developmental Endpoint.003

Administrative Data

Purpose flag supporting study

Reliability 1 (reliable without restriction)

Rationale for reliability This study is rated a "1" because it applied GLP, used appropriate testing procedures, and followed an accepted test guideline.

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Hardin BD, et al	1987	Evaluation of 60 Chemicals in a Preliminary Developmental Toxicity Test	Terat Carcin Mutagen 7:29-48					

Materials and methods

Test guideline

Qualifier	Guideline	Deviations
according to	EU Method B.31 (Prenatal Developmental Toxicity Study) Cited as Directive 87/302/EEC, part B, p. 24	

GLP compliance

yes

Test materials

Details on test material

IUCLID4 Test substance: other TS: DIDP with different CAS #.

Test animals

Species

mouse

Strain

CD-1

Administration / exposure

Route of administration

oral: gavage

Duration of treatment / exposure

gestation days 6-13

Frequency of treatment

daily

Doses / concentrations

9650 mg/kg/day

Basis

Control animals

yes

Further details on study design

Sex: female

Results and discussions

Effect levels

Endpoint	Effect type	Effect level	Basis for effect level / Remarks
NOAEL	maternal toxicity	> 9650 mg/kg bw/day	
NOAEL	teratogenicity	> 9650 mg/kg bw/day	

Dissemination Dossier
Other Endpoint.001

Administrative Data

Purpose flag supporting study

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Benford DJ, Patel S, Sarginson N and Reavy HJ	1986	Species difference in the response of cultured hepatocytes to phthalate esters	Food and Chemical Toxicology 24(6/7):795-800					

Materials and methods

Type of information

Type: other: Evidence of species differences in response based on in vitro studies

Test materials

Test material equivalent to submission substance identity

yes

Dissemination Dossier
Other Endpoint.002

Administrative Data

Purpose flag supporting study

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Harris CA, et al	1997	The estrogenic Activity of Phthalate Esters In Vitro	Environmental Health Perspectives 105: 802-811					
publication	Zacharewski TR, et al	1999	Examination of the In Vitro and In Vivo Estrogenic Activities of Eight Commercial Phthalate Esters	Toxicological Sciences 46(2):282-293					

Materials and methods

Type of information

Type: other: Endocrine Disrupter

Test materials

Test material equivalent to submission substance identity

yes

Administrative Data

Purpose flag supporting study

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Kamendulis L, Isenberg J, Smith J, Pugh G, Lington A and Klaunig J	2001	Comparative effects of phthalate monoesters on gap junctional intercellular communication and peroxisome proliferation in rodent and primate hepatocytes	Journal of Toxicology and Enviornmental Health. Part A 62, 127-141					

Materials and methods

Type of information

Type: other: Inhibition of gap junctional intercellular communication in vitro

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument424e.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-365eda40-84c4-4141-be59-56f462fea88f%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Test materials

Test material equivalent to submission substance identity

yes

Dissemination Dossier
Other Endpoint.004

Administrative Data

Purpose flag supporting study

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Elsisi A, Carter D and Sipes I	1989	Dermal absorption of phthalate diesters in rats	Fundamental and Applied Toxicology 12:70-77					

Materials and methods

Type of information

Type: other: Dermal Absorption and Excretion

Test materials

Test material equivalent to submission substance identity

yes

Administrative Data

Purpose flag supporting study

Data source

Reference

Reference type	Author	Year	Title	Bibliographic source	Testing laboratory	Report no.	Owner company	Company study no.	Report date
publication	Smith J, Isenberg J, Pugh G, Kamendulis L, Ackley D, Lington A and Klaunig J	2000	Comparative in vivo hepatic effects of di-isononyl phthalate (DINP) and related C7-C11 dialkyl phthalates on gap junctional intercellular communication (GJIC), peroxisomal beta-oxidation (PBox), and DNA synthesis in rat and mouse liver	Toxicological Sciences 54:312-321					

Materials and methods

Type of information

Type: other: Evidence of species differences in response based on in vivo studies

Test materials

Test material equivalent to submission substance identity

yes

Administrative Data

First-aid measures

INHALATION Remove from further exposure. For those providing assistance, avoid exposure to yourself or others. Use adequate respiratory protection. If respiratory irritation, dizziness, nausea, or unconsciousness occurs, seek immediate medical assistance. If breathing has stopped, assist ventilation with a mechanical device or use mouth-to-mouth resuscitation. SKIN CONTACT Wash contact areas with soap and water. EYE CONTACT Flush thoroughly with water. If irritation occurs, get medical assistance. INGESTION First aid is normally not required. Seek medical attention if discomfort occurs.

Fire-fighting measures

EXTINGUISHING MEDIA Appropriate Extinguishing Media: Use water fog, foam, dry chemical or carbon dioxide (CO2) to extinguish flames. Inappropriate Extinguishing Media: Straight streams of water FIRE FIGHTING Fire Fighting Instructions: Evacuate area. Prevent run-off from fire control or dilution from entering streams, sewers or drinking water supply. Fire-fighters should use standard protective equipment and in enclosed spaces, self-contained breathing apparatus (SCBA). Use water spray to cool fire exposed surfaces and to protect personnel. Hazardous Combustion Products: Smoke, Fume, Incomplete combustion products, Oxides of carbon FLAMMABILITY PROPERTIES Flash Point [Method]: 225C (437F) [ASTM D-93] Flammable Limits (Approximate volume % in air): LEL: N/D UEL: N/D Autoignition Temperature: >400°C (752°F)

Accidental release measures

NOTIFICATION PROCEDURES In the event of a spill or accidental release, notify relevant authorities in accordance with all applicable regulations. SPILL MANAGEMENT Land Spill: Eliminate all ignition sources (no smoking, flares, sparks or flames in immediate area). Stop leak if you can do so without risk. Absorb or cover with dry earth, sand or other non-combustible material and transfer to containers. If liquid is too viscous for pumping, shovel it up into a suitable container for recycle or disposal. Recover by

pumping or with suitable absorbent. Water Spill: Warn other shipping. Remove from the surface by skimming or with suitable absorbents. Seek advice of a specialist Water spill and land spill recommendations are based on the most likely spill scenario for this material; however, geographic conditions, wind, temperature, (and in the case of a water spill) wave and current direction and speed may greatly influence the appropriate action to be taken. For this reason, local experts should be consulted. Note: Local regulations may prescribe or limit action to be taken. ENVIRONMENTAL PRECAUTIONS Large Spills: Dyke far ahead of liquid spill for later recovery and disposal. Prevent entry into waterways, sewers, basements or confined areas.

Handling and storage

HANDLING Avoid contact with skin. Provide adequate ventilation if fumes or vapour are generated. Prevent small spills and leakage to avoid slip hazard. DO NOT handle, store or open near an open flame, sources of heat or sources of ignition. Protect material from direct sunlight. Material can accumulate static charges which may cause an electrical spark (ignition source). Loading/Unloading Temperature: [Ambient] Transport Temperature: [Ambient] Transport Pressure: [Ambient] Static Accumulator: This material is a static accumulator. STORAGE Do not store in open or unlabelled containers. Keep container closed. Handle containers with care. Open slowly in order to control possible pressure release. Store in a cool, well-ventilated area. Storage Temperature: [Ambient] Storage Pressure: [Ambient] Suitable Containers/Packing: Drums; Barges; Tank Cars Suitable Materials and Coatings: Carbon steel; Stainless steel; Polypropylene; Teflon; Aluminium; Nylon; Viton Unsuitable Materials and Coatings: Butyl rubber; Natural rubber; Vinyls

Land transport (ADR/RID/)

Class

Not regulated for land transport.

Inland waterway transport (AND(R))

Class

Not regulated for inland waterways transport.

Marine transport (IMDG)

Class

http://apps.echa.europa.eu/registered/data/DISS-828dfa7f-a6de-1962-e044-00144fd73934/showdocument1579.html?treeUuid=DISS-828dfa7f-a6de-1962-e044-00144fd73934%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934&uuid=AGGR-aa90ae8d-17ec-4c84-8b61-824ef4ca3f8e%2FDISS-828dfa7f-a6de-1962-e044-00144fd73934

Not regulated for sea transport according to IMDG-Code.

Air transport ICAO/IATA

Class

Not regulated for air transport.