Annex XV dossier

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CMR 1A or 1B, PBT, vPvB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN

Substance Name(s): dipentyl phthalate (DPP)

EC Number(s): 205-017-9

CAS Number(s): 131-18-0

Submitted by: *Bureau for Chemical Substances, Poland*

In cooperation with: *Environment Agency Austria on behalf of the Austrian Competent Authority (Austrian Federal Ministry of Agriculture, Forestry, Environment and Water Management)*

BAuA, German Federal Institute for Occupational Safety and Health, Federal Office for Chemicals and BFR, German Federal Institute for Risk Assessment

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ABBREVIATIONS

BCF	Bioconcentration factor
CAS	Chemical Abstracts Service
CLP	Classification, Labelling and Packaging
CMR	Carcinogenic, Mutagenic and toxic to Reproduction
DNEL	Derived No Effect Level
DPP	Dipentyl phthalate
EC	European Community
EC_{50}	Effective Concentration 50%
ECHA	European Chemicals Agency
EU	European Union
ERC	Environmental release category
HSDB	Hazardous Substances Data Bank
LPVM	Low Production Volume Material
NOAEL	No Observed Adverse Effect Level
PBT	Persistent, Bioaccumulative and Toxic
REACH	Registration, Evaluation, Authorisation and Restriction of Chemical substances
SPIN	Substances in Preparations in the Nordic countries
SU	Sector of end use
SVHC	Substance of Very High Concern
vPvB	Very Persistent and very Bioaccumulative

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE AS A CMR 1A OR 1B, PBT, VPVB OR A SUBSTANCE OF AN EQUIVALENT LEVEL OF CONCERN

Substance Name(s): **dipentyl phthalate**

EC Number(s): **205-017-9**

CAS number(s): **131-18-0**

The substance is proposed to be identified as substance meeting the criteria of Article 57 (c) of Regulation (EC) 1907/2006 (REACH) owing to its classification as toxic for reproduction category 1B[1].

Summary of how the substance meets the criteria set out in Article 57 (c) of REACH

Dipentyl phthalate (DPP) is covered by Index number 607-426-00-1 of Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, Table 3.1 (list of harmonised classification and labelling of hazardous substances) as toxic for reproduction, Repr. 1B (H360FD: "May damage fertility. May damage the unborn child."). The corresponding classification in Annex VI, part 3, Table 3.2 (list of harmonised classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC) of Regulation (EC) No 1272/2008 is toxic for reproduction, Repr. Cat. 2 (R60-61: "May impair fertility. May cause harm to the unborn child").

Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification as toxic for reproduction in accordance with Article 57(c) of REACH.

Registration dossier submitted for the substance: No

[1] Classification in accordance with Regulation (EC) No 1272/2008 Annex VI, part 3, Table 3.1 List of harmonised classification and labelling of hazardous substances.

PART I

JUSTIFICATION

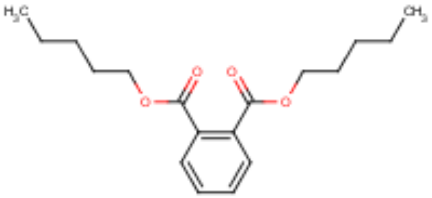
1 IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

1.1 Name and other identifiers of the substance

Table 1: Substance identity

EC number:	205-017-9
EC name:	dipentyl phthalate
CAS number (in the EC inventory):	131-18-0
CAS number:	131-18-0
CAS name:	1,2-Benzenedicarboxylic acid, 1,2-dipentyl ester
IUPAC name:	dipentyl phthalate
Index number in Annex VI of the CLP Regulation	607-426-00-1
Molecular formula:	$C_{18}H_{26}O_4$
Molecular weight range:	306,397 g/mol
Synonyms:	1,2-Benzenedicarboxylic acid, dipentyl ester Amoil Amyl phthalate Di-N-Pentyl Phthalate Di-n-pentylphthalatediamyl phthalate Dipentyl 1,2-benzenedicarboxylate Dipentyl phthalate Phthalic acid, diamyl ester Phthalic acid, dipentyl ester di-n-pentylphthalate Diamyl Phthalate Dipentyl phthalate

Structural formula:



1.2 Composition of the substance

Name: Dipentyl phthalate

Description: Colorless, oily liquid

Degree of purity: The substance has not been registered. Information on purities in the range between 95% and 99% is provided at supplier websites (http://www.chemicalbook.com/ProductChemicalPropertiesCB4197568_EN.htm#MSDSA)

Table 2: Constituents

This information is not relevant for identification of a mono constituent substance

Constituents	Typical concentration	Concentration range	Remarks
Name and EC number			

Table 3: Impurities

Impurities	Typical concentration	Concentration range	Remarks
Name and EC number			

Table 4: Additives

Additives	Typical concentration	Concentration range	Remarks
Name and EC number			

1.3 Physico-chemical properties

Table 5: Overview of physicochemical properties

REACH ref Annex, §	Property	IUCLID section	Value	[enter comment/reference or delete column]
VII, 7.1	Physical state at 20°C and 101.3 kPa	4.1	Colorless, oily liquid	Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 346
VII, 7.2	Melting/freezing point	4.2	-55°C	Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 346
VII, 7.3	Boiling point	4.3	342°C	Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 14th Edition. John Wiley & Sons, Inc. New York, NY 2001., p. 346
VII, 7.4	Density	4.4	1.03 g/cm^3	
VII, 7.5	Vapour pressure	4.6	1.96 x10^{-4} mmHg at 25°C	HSDB
VII, 7.7	Water solubility	4.8	0.8 mg/L at 25°C	Leyder Y, Boulanger P; Bull Environ Contam Tox 30: 152-7 (1983)
VII, 7.8	Partition coefficient n-octanol/water (log value)	4.7	log P_{ow} 5.62 at 20°C	Ellington JJ, Floyd TL; Octanol/water partition coefficients for eight phthalate esters. USEPA-600/S-96-006. Athens,GA: USEPA, Natl Exp Res Lab (1996)
IX, 7.9	Flashpoint	4.11	118-180^{0}C	HSDB

2 HARMONISED CLASSIFICATION AND LABELLING

Dipentyl phthalate (DPP) is listed by Index number 607-426-00-1 of Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, Table 3.1 (list of harmonised classification and labelling of hazardous substances) as follows:

Table 6: Classification according to Annex VI, Part 3, Table 3.1 (list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008

Index No	International Chemical Identification	EC No	CAS No	Classification		Labelling	
				Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)
607-426-00-1	di-n-pentyl phthalate	205-017-9	131-18-0	Repr. 1B Aquatic Acute 1	H360FD H400	GHS08 GHS09 Dgr	H360FD H400

Dipentyl phthalate (DPP) is covered by Index number 607-426-00-1 of Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, Table 3.2 (list of harmonised classification and labelling of hazardous substances from Annex I to Council Directive 67/548/EEC) as follows:

Table 7. Classification according to Annex VI, Part 3, Table 3.2 (list of harmonised classification and labelling of hazardous substances from Annex I of Council Directive 67/548/EEC) of Regulation (EC) No 1272/2008

Index No	International Chemical Identification	EC No	CAS No	Classification	Labelling
607-426-00-1	di-n-pentyl phthalate	205-017-9	131-18-0	Repr. Cat. 2; R60-61 N; R50	T; N R: 60-61-50 S: 53-45-61

3 ENVIRONMENTAL FATE PROPERTIES

Not relevant.

4 HUMAN HEALTH HAZARD ASSESSMENT

See section 2 Harmonised Classification and Labelling and Supplementary Information in Annex I.

5 ENVIRONMENTAL HAZARD ASSESSMENT

Not relevant.

6 CONCLUSIONS ON THE SVHC PROPERTIES

6.1 PBT, vPvB assessment

Not relevant.

6.2 CMR assessment

Dipentyl phthalate (DPP) is covered by Index number 607-426-00-1 of Regulation (EC) No 1272/2008 and classified in Annex VI, part 3, Table 3.1 (list of harmonised classification and labelling of hazardous substances) as toxic for reproduction, Repr. 1B (H360FD: “May damage fertility. May damage the unborn child.”). The corresponding classification in Annex VI, part 3, Table 3.2 (list of harmonised classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC) of Regulation (EC) No 1272/2008 is toxic for reproduction, Repr. Cat. 2 (R60-61: “May impair fertility. May cause harm to the unborn child”).

Therefore, this classification of the substance in Regulation (EC) No 1272/2008 shows that it meets the criteria for classification as toxic for reproduction in accordance with Article 57(c) of REACH.

6.3 Substances of equivalent level of concern assessment.

Not relevant.

PART II

INFORMATION ON USE, EXPOSURE, ALTERNATIVES AND RISKS

7 INFORMATION ON MANUFACTURE, IMPORT/EXPORT AND USES – CONCLUSIONS ON EXPOSURE

7.1 Volumes for manufacture import and export

Dipentyl phthalate has been pre-registered under REACH with indication of registration by 30 November 2010, but no registration has been done up to now. However, the substance could be registered at a later date.

According to C&L Inventory database (status on 18.02.2013) (http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database) 102 companies have notified the substance.

According to the available information, use of DPP in Europe is limited. The European Chemicals Bureau (ECB) listed DPP as a "low production volume chemical" (LPVC), with tonnage band 10-1000 t/year per producer or importer.

There is limited information available on the current production and use of the substance as well as on consumer exposure. The Chemical Book website lists 62 DPP suppliers worldwide (15 within Europe). http://www.chemicalbook.com/ChemicalProductProperty_EN_CB4197568.htm

The SPIN online database[2] indicates a use of DPP in Sweden as a component to gunpowder at 11, 15 and 11 tons in 2008, 2009 and 2010 respectively in 18 registered products used in explosives materials like gunpowder. The Swedish register is updated each year and no tonnage is reported for 2011.

[2] Database on the use of Substances in Products in the Nordic Countries. The database is based on data from the Product Registries of Norway, Sweden, Denmark and Finland.

Table 8. Total quantity of DPP in the registered products in Sweden

Year	Used amounts [t]	Number of products
1993	24.3	3
1994	39.7	16
1995	15.4	15
2008	10.9	18
2009	15.8	18
2010	11.4	18

No additional information could be identified on current annual EU import/export volumes. It can therefore be assumed that DPP is not manufactured in the EU or placed on the market in quantities of one ton or more per year.

7.2 Uses of the Substance

The main use of DPP in EU is as a plasticizer in polyvinyl chloride (HSDB, 2011).

7.3 Use restrictions

DPP is listed in Annex XVII, Group 30 of the REACH regulation. It shall not be placed on the market or used for supply to the general public as substance or in mixtures in concentrations equal to or greater than 0,5% (from 1st of June 2015 Regulation (EC) No 1272/2008 has to be applied giving a generic concentration limit for reproduction toxicants of >=0.3%). Suppliers shall ensure before the placing on the market that the packaging of such substances and mixtures is marked visibly, legibly and indelibly as follows: “Restricted to professional users” (Directive 2005/90/EC).

DPP is covered by restrictions in toys and cosmetic products:

- n-pentyl-isopentylphthalate, **di-n-pentyl phthalate**, diisopentylphthalate, benzyl butyl phthalate, dibutyl phthalate, bis(2-ethylhexyl) phthalate (diethylhexyl phthalate) and bis(2-methoxyethyl) phthalate are prohibited in cosmetic products (Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products, Annex II, Reference number: 675, 677, 678, 1151 and 1152)
- According to Directive 2009/48/EC (Safety of toys) substances classified as CMR of category 1A, 1B or 2 shall not be used in toys or in components of toys in individual concentrations above the specific concentration limits established for the classification of mixtures containing these substances according to Directive 1999/45/EC (till May 2015). Therefore for DPP a concentration limit of >=0.5% applies. From 1st of June 2015 Regulation (EC) No 1272/2008 has to be applied giving a generic concentration limit for substances toxic to reproduction of >=0.3%.

No workplace exposure limit has been established for DPP in the EU.

7.4 Human exposure

Occupational exposure to DPP may occur through inhalation of aerosols and dermal contact with this compound at workplaces where DPP is used as a plasticizer or where plastics are produced and/or processed. No data are available on DPP exposure concentration at the workplace (HSDB 2011).

Data indicate that the general population may be exposed via dermal contact with consumer products (e.g. textiles, paper or paints) containing this compound (HSDB 2011).

Ten house-dust samples (of commercial and private origin) have been analysed in Austria for their content of phthalates (Umweltbundesamt, 2010a). The limit of detection (LOD) of 0.02 mg/kg for DPP was exceeded in eight of these samples with concentrations ranging from 0.045 mg/kg to 0.43mg/kg.

7.5 Environmental exposure

Due to their persistence in the environment, phthalates are commonly found in groundwater, rivers and drinking water (Jobling et al., 1995). Bioaccumulation does not take place (Heudorf, 2007) and the concentration in water is declining fast while phthalates can be found in water sediment, soil and waste sludge (Römpp, 1985).

DPP production and use as a plasticizer may result in its release to the environment through various waste streams. If released to air, an estimated vapor pressure of $2.0x10^{-4}$ mm Hg at 25°C indicates DPP will exist solely as a vapor in the atmosphere. Vapor-phase di-n-pentylphthalate will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 32 days. If released to soil, DPP is expected to have no mobility based upon an estimated Koc of 27,000. Volatilization from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry's Law constant of $8.9x10^{-7}$ $atm.m^3$/mole. Limited data suggest that DPP may biodegrade under aerobic conditions yielding phthalic acid and amyl alcohol. If released into water, DPP is expected to adsorb to suspended solids and sediment based upon the estimated Koc. Volatilization from water surfaces is not expected to be an important fate process based upon this compound's estimated Henry's Law constant. An estimated BCF of 420 suggests the potential for bioconcentration in aquatic organisms is high, provided the compound is not metabolized by the organism. However, bioconcentration studies on compounds which are structurally similar suggest that bioconcentration may be lower than that indicated by the regression-derived equations due to the ability of aquatic organisms to readily metabolize this class of compounds. Estimated hydrolysis half-lives of 3.4 years and 130 days at pHs 7 and 8, respectively, suggest hydrolysis is not expected to be an important process (HSDB 2011).

8 CURRENT KNOWLEDGE ON ALTERNATIVES

A number of substances have been identified as alternative plasticizers. These alternatives include citrates, sebacates, adipates, and phosphates. They are used as substitutes in products that traditionally use phthalates, such as toys, childcare articles and medical devices. In addition to their

application as alternative PVC plasticizers, these substances are also being used as solvents and fixatives in cosmetic products, inks, adhesives, and other consumer products (Technical Briefing, 2011).

DPP has been put on the SIN list containing hazardous substances which should be substituted by safer alternatives (http://www.sinlist.org/).

9 RISK-RELATED INFORMATION

No risk assessment has been carried out for DPP according to Regulation EEC/793/93. A comprehensive risk assessment is outside the scope of this dossier.

DPP is listed as phase-out substance in Kemi PRIO data base due to its classification as Repr. 1B. (http://www.kemi.se/templates/PRIOEngframes__414.aspx). PRIO phase-out substances mean substances with hazardous environmental or health properties for which all uses are unsuitable. For these substances the substitution principle should be applied if they can be replaced by products that are assumed to be less hazardous.

However, as DPP is not yet included into the REACH candidate list and is not covered in REACH Annex XVII, DPP might be considered as a possible substitute for already regulated phthalates. Therefore it cannot be excluded that the substance could be registered at a later date based on its properties, functions and uses. In this case, exposure to DPP might arise. Possible substitution of hazardous phthalates by DPP should be prevented by equal treatment of all phthalates classified as toxic to reproduction. Based on the inherent toxic properties and its classification DPP represents a hazardous phthalate which toxicity might be even higher than that of already regulated phthalates (Hannas, 2011).

Occupational exposure to DPP may occur through inhalation of aerosols or dermal contact (HSDB 2010). The general population may be exposed via dermal, oral, or inhalation contact with consumer products containing this compound. The information on toxicokinetic and health effect is included in Annex I.

DPP as a substance toxic for reproduction Repr. 1B with hazard statement H360FD (May damage fertility. May damage the unborn child) is already restricted for sale to the general public in individual concentration equal to or greater than 0.5% (Annex II, part B, Table VI, Directive 1999/45/EC). The remaining concerns are connected with the exposure of workers and with the exposure of consumers in contact with articles containing that substance. At present, there are not sufficient data available which allow to identify all remaining specific uses and to conclude whether there are cases of unacceptable risk which would trigger restriction according to REACH article 68 (1).

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ANNEX I

SUPPLEMENTARY INFORMATION ON THE LEADING HEALTH EFFECTS AND TOXICOKINETICS

1. Toxicokinetics (absorption, metabolism, distribution and elimination)

No data were identified specific to the absorption of DPP. Dermal absorption of phthalate diesters depends on several competing factors, such as lipophilicity, molecular size, and metabolism. Dermal uptake decreases with increasing side chain length beyond four carbons, and uptake decreases progressively with side chain length beyond four carbons, despite the fact that the lipophilicity increases.
Histological data from acute toxicity studies suggest that DPP is distributed quickly.
Following oral exposure, DPP is rapidly metabolized in vivo to its corresponding monoester by nonspecific esterases in the intestinal mucosa and other tissues.
For phthalate esters in general, after formation of the monoester, there can be further hydrolysis in vivo to phthalic acid or the corresponding alcohol, which can be excreted or further oxidized to an aldehyde, ketone, or carboxylic acid. The monoester can also undergo glucuronidation.
The monoester and oxidative metabolites and conjugants of phthalate diesters are excreted in the urine and feces (HSDB 2010).

2. Reproductive and Developmental Toxicity

DPP demonstrates testicular atrophy and a fertility impairing effect in dose ranges of relevance for classification (Gangolli 1982; Creasy et al., 1983; Granholm et al. 1992; Jones et al. 1993; Gray and Gangoli 1986; Foster at al., 1980).
In a study of the reproductive toxicity of eight phthalate esters to rats (2100 mg/kg bw/day for four days), DPP caused the most severe testicular atrophy (Foster et al. 1980).
Treatment of rats via gavage with 7.2 mmol/kg bw DPP (~2200 mg/kg bw) was shown to decrease testicular cytochrome P-450, cytochrome P-450 dependent microsomal steroidogenic enzymes (17 alpha-hydroxylase, 17-20 lyase) and the maximal binding of a natural substrate (progesterone) to microsomes of the testes. The study authors concluded that DPP has a direct effect on cytochrome P-450-dependent steroid production, which may be directly responsible for the toxic effects on testicular structure and function (Foster et al. 1983).
Lindstrom et al. (1988) described the effect of DPP on fertility. Fischer 344 rats received single gavage doses of 0, 250, 1000, or 2000 mg/kg bw DPP. Treated males were mated with untreated females at 3, 6, and 10 weeks post-exposure. The percentage of high-dose rats successfully impregnating at least one female was 65 percent of controls at week 3; 15 percent at week 6; and 35 percent at week 10. The number of live fetuses per pregnant female crossed with a high-dose male was 35 percent, 43 percent, and 72 percent of controls at weeks 3, 6, and 10, respectively. Preimplantation loss in cross-matings was three times that of controls. There was no significant difference in the number of resorptions or dead fetuses (i.e., post-implantation loss) at any time. All males showed typical phthalate ester-induced testicular lesions, which did not recover within the 30-week monitoring period. There were no effects on fertility at the mid- or low- doses.
The National Toxicology Program (NTP) tested the reproductive toxicity of DPP in mice. Male and female mice received DPP in the diet at concentrations of 0.5, 1.25, or 2.5% (approximately

equivalent to 760, 2160, and 4800 mg/kg/day, respectively) for 7 days prior to and during a 98-day cohabitation. The reproductive NOAEL was determined to be less than 760 mg/kg/day, based on significant decreases in the proportion of fertile pair groups, number of litters per pair, number of live pups per litter, and the proportion of live births. At the two high doses, there was a complete inhibition of fertility (Heindel et al. 1989; NTP 1985).

More recent study revealed changes in reduction of anogenital distance of male foetuses exposed in utero to 500 mg/kg/day DPP on gestation days 12-19 (Liu et al. 2005).

Howdeshell et al. (2008) compared the reproductive toxicity of a number of individual phthalates. Doses of 0, 25, 50, 100, 200, 300, 600, or 900 mg/kg/day DPP were administered by gavage on gestation days (GD) 8-18 to Sprague-Dawley rats.

The NOAEL for reproductive and maternal effects was 200 mg/kg/day based on significant changes in maternal body weight gain, number of live fetuses, total resorptions, and fetal mortality. Testicular testosterone production was measured on gestation day 18. The effective dose which inhibited fetal testosterone production by 50% (ED50) was calculated to be 130 mg/kg/day.