Annex XV dossier

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

Substance Name(s): Diisopentylphthalate (DIPP)
EC Number(s): 210-088-4
CAS Number(s): 605-50-5

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

In cooperation with: **BAuA, German Federal Institute for Occupational Safety and Health, Federal Office for Chemicals and BFR, German Federal Institute for Risk Assessment**

and the Polish Competent Authority (Bureau for Chemical Substances)

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TABLES

ABBREVIATIONS

CAS	Chemical Abstract Service
CMR	Carcinogenic, Mutagenic and toxic to Reproduction
DBP	Di-n-butyl phthalate
DIBP	Diisobutyl phthalate
DIPP	Diisopentylphthalate
EC	European Community
ECHA	European Chemicals Agency
EDA	European Defence Agency
EEC	European Economic Community
HPVC	High Production Volume Chemical
LOD	Limit of detection
LOQ	Limit of quantification
LPVC	Low Production Volume Chemical
OEL	Occupational exposure limit
REACH	Registration, Evaluation, Authorisation and Restriction of Chemical substances
SIN	Substitute it now
SPIN	Substances in Preparations in the Nordic countries
SVHC	Substance of Very High Concern

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- 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.

Summary of how the substance(s) meet(s) the CMR 1A or 1B criteria

Diisopentylphthalate (DIPP) is listed as entry 607-426-00-1in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008[1] as Repr. 1B, H360FD (May damage fertility. May damage the unborn child.). This corresponds to a classification as toxic to reproduction Repr. Cat. 2; R60-61 ("May impair fertility; May cause harm to the unborn child") in Annex VI, part 3, Table 3.2 of Regulation (EC) No. 1272/2008 (list of harmonised classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC).

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

Registration dossiers submitted for the substance?

Yes

[1]Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006

PART I

JUSTIFICATION

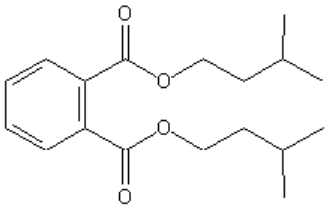
1 IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES

1.1 Name and other identifiers of the substance

Table 1: Substance identity

EC number:	210-088-4
EC name:	diisopentyl phthalate
CAS number (in the EC inventory):	605-50-5
CAS number:	605-50-5
CAS name:	1,2-Benzenedicarboxylic acid, 1,2-bis(3-methylbutyl) ester
IUPAC name:	Bis(3-methylbutyl) 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:	306,40 g/mol
Synonyms:	1,2-Benzenedicarboxylic acid, bis(3-methylbutyl) ester Diisoamyl phthalate Isoamyl phthalate

Structural formula:



1.2 Composition of the substance

Name: Diisopentyl phthalate
Description: clear slightly yellow liquid
Degree of purity: see confidential Annex II

1.3 Physico-chemical properties

Table 2: Overview of physico-chemical properties

Property	Value	Remarks
Physical state at 20°C and 101.3 kPa	*Clear liquid, slightly yellow*	*Registration data from dissemination database*[2]
Melting/freezing point	*Freezing point less than -25°C*	*Registration data from dissemination database*
Boiling point	*339°C*	*Registration data from dissemination database*
Vapour pressure	*0.025Pa at 25°C*	*Registration data from dissemination database*
Water solubility	*1.1mg/l at 20°C*	*Registration data from dissemination database*
Partition coefficient n-octanol/water (log P_{OW})	log P_{OW} *=5.6*	*Registration data from dissemination database*
Flashpoint	*166°C*	*Registration data from dissemination database*
Auto Flammability at 1013hPa	*>=400°C*	*Registration data from dissemination database*
Oxidising property	*No oxidising properties.*	*Registration data from dissemination database (QSAR)*
Density	*1.02 g/cm³*	*Registration data from dissemination database*

[2] http://apps.echa.europa.eu/registered/registered-sub.aspx

2 HARMONISED CLASSIFICATION AND LABELLING

DIPP is covered by index number 607-426-00-1 in Annex VI, part 3 of Reg. (EC) No 1272/2008 as follows:

Table 3: Classification according to part 3 of Annex VI, 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			Spec. Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)	Pictogram, Signal Word Code(s)	Hazard statement code(s)	Suppl. Hazard statement code(s)		
607-426-00-1	diisopentyl phthalate	210-088-4	605-50-5	Repr. 1B Aquatic Acute 1	H360-FD H400	GHS08 GHS09 Dgr	H360FD H400			

Table 4: Classification according to part 3 of Annex VI, 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	Concentration Limits	Notes
607-426-00-1	diisopentylphthalate	210-088-4	605-50-5	Repr. Cat. 2; R60-61 N; R50	T; N R: 60-61-50 S: 53-45-61		

Self-classification:
According to registration information, the substance is additionally classified as Skin Sens. 1, H317. For additional confidential information from the C&L inventory see Annex II Chapter 4.

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

Diisopentylphthalate (DIPP) is listed as entry 607-426-00-1 in Annex VI, part 3, Table 3.1 (the list of harmonised classification and labelling of hazardous substances) of Regulation (EC) No 1272/2008[3] as Repr. 1B, H360FD (May damage fertility. May damage the unborn child.) This corresponds to a classification as toxic to reproduction Repr. Cat. 2; R60-61 ("May impair fertility; May cause harm to the unborn child") in Annex VI, part 3, Table 3.2 of Regulation (EC) No. 1272/2008 (list of harmonised classification and labelling of hazardous substances from Annex I to Directive 67/548/EEC).
Therefore, this classification of the substance(s) in Regulation (EC) No 1272/2008 shows that the substance 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.

3Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006

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

DIPP has not been reported by EU Industry as an HPVC or LPVC according to previous existing substances regulation[4]. It has been registered in a total tonnage band of 10 – 100 tonnes per year as stated in the ECHA dissemination database[5]. Based on the existing registration data there is no production of the substance in the EU in quantities > 1 tonne/year but the substance is imported into the EU.

For detailed information on tonnages see confidential Annex II, Chapter 2.

7.2 Uses of the Substance

DIPP has been registered for its use in the manufacture of propellants.

As other low molecular weight phthalates of carbon backbone lengths of C4 – C6 DIPP may also be used as plasticiser for PVC products and other polymers due to their similar structure and physico-chemical properties. Di-n-butyl phthalate (DBP) and diisobutyl phthalate (DIBP) (linear and branched C4 esters) are used in many PVC formulations, principally for ease of gelation. Owing to their relatively high volatility, in comparison with other phthalates, they are often used in conjunction with higher molecular mass esters. Diisopentyl phthalate (DIPP) is generally used in a similar manner (Ullmann, 2012). However there is currently no registration for that use.

The SPIN database[6] was searched for information on DIPP in products on the national markets of Norway, Sweden, Finland and Denmark. Only Sweden is listed in SPIN (1999-2007) but with no information on tonnages and uses due to confidentiality. For the years 2008-2010 no products with DIPP were found in the Swedish Product register.

The database chemical book has listed four potential suppliers (2 in Germany, 1 in Canada and 1 in Europe). All these suppliers are specialized[7].

In the following chapters further information on the uses of DIPP is given.

[4] http://esis.jrc.ec.europa.eu/

[5] http://apps.echa.europa.eu/registered/registered-sub.aspx

[6] Substances in Preparations in the Nordic countries http://195.215.251.229/DotNetNuke/default.aspx

[7] http://www.chemicalbook.com/Search_EN.aspx?keyword=605-50-5

7.2.1 DIPP in the manufacture of propellants

In general phthalates are used in nitrocellulose propellants as plasticisers (to reduce danger of low temperature embrittlement) and for surface conditioning (reduction of burn rate). A typical formulation for propellants contains 3-5% of phthalates.

The registration data confirm the use of DIPP in the manufacture of propellants and explosives and to coat them to regulate the rate of burn. The propellants are used for the production of ammunition. Most of the uses of this ammunition are military; however a part is also used for civil applications and by consumers for ammunition of different size (calibre) (registration information from dissemination database and ARWT, 2012).

Information on process categories from the registration (dissemination database) is given in Table 5 (workers) and 6 (consumers).

Table 5: Uses by workers in industrial settings[8]

Identified Use	Use descriptors
Used in the manufacture of propellants and explosives and to coat them to regulate rate of burn	**Process category (PROC)** PROC 2: Use in closed, continuous process with occasional controlled exposure **Environmental release category (ERC)** ERC 5: Industrial use resulting in inclusion into or onto a matrix **Market sector by type of chemical product (PC)** PC 0: Other: Manufacture of propellants and explosives **Sector of end use (SU)** SU 0: Other: Manufacture of propellants and explosives **Article category related to subsequent service life (AC)** AC 0: Other: Propellants and explosives

8http://apps.echa.europa.eu/registered/registered-sub.aspx

Table 6: Uses by consumers[8]

Identified Use	Use descriptors
Used to coat the propellant to regulate rate of burn	**Chemical product category (PC)** PC 0: Other: Propellants and explosives **Environmental release category (ERC)** ERC 5: Industrial use resulting in inclusion into or onto a matrix **Article category related to subsequent service life (AC)** AC 0: Other: Propellants and explosives

According to Article 2 (3) of the REACH Regulation Member States may allow for exemptions from REACH in specific cases for certain substances, on their own, in a mixture or in an article, where necessary in the interests of defence. An enquiry performed by the European Defence Agency (EDA) (EDA, 2012) among its national points of contact showed that no exemption for DIPP has been requested or allowed so far.

Propellants containing DIPP may be further used by producers of ammunition or used directly to load cartridges. This may be done by professional users or consumers e.g. sport shooters and hunters. For example, smokeless rifle powder containing DIPP in a content < 3% is sold in the EU in packaging of 2,27kg and 0,45kg[9].

7.2.2 DIPP as plasticiser for plastics

According to ECPI (European Council for Plasticisers and Intermediates) C4 to C6 phthalates (low molecular weight phthalates) with 3 to 6 carbon atoms in their backbone are used in applications where high solvating plasticisers and stain resistance are required[10]. Due to its high reproductive toxicity DIPP has not been used widely as general purpose plasticiser.

According to Wilson, 1996 some diisopentyl phthalate based on a synthetic C_5 alcohol has been used as a fast fusing plasticiser for PVC, giving the advantage of reduced volatility relative to dibutylphthalate/diisobutylphthalate. A material described as “diisoamyl phthalate” produced from a fermentation by-product of alcohol has been used in the past in small volumes for non-plasticiser applications.

On the internet several sources mention DIPP as plasticiser for different applications:

- A patent for an adhesions membrane (using soft PVC) identifies DIPP as possible plasticiser (http://www.patent-de.com/20010927/DE10012261A1.html) for that use.

[9] http://www.alliantpowder.com/downloads/msds/Reloder15.pdf

http://www.lhs-germany.de/pulververtrieb/treibladungspulver/

[10] http://www.plasticisers.org/plasticisers

- Schaeffler Technologies GmbH & Co. KG, 2011 lays down requirements for their suppliers with regard to prohibited and declarable substances across the entire supply chain and for all materials (chemicals, mixtures, products and packaging materials) which are supplied: DIPP is listed as restricted substance with the following example for application: plasticiser in plastics. http://www.schaeffler.com/remotemedien/media/_shared_media/supplier/environment_1/S132030-1_en.pdf
- The chemical substance index database of the Chinese drug portal lists DIPP for uses as plasticiser for nitrocellulose and resin lacquers, as preventing foam in manufacture of glue, and in rubber cements. http://www.drugfuture.com/chemdata/isoamyl-phthalate.html
- The German Center of Competence in Civil Engineering (DeutschesInstitutfürBautechnik (DIBt)) lists DIPP as one of several plasticisers used to ensure flexibility of PVC. http://www.dibt.de/de/data/Aktuelles_Ref_II_4.pdf
- DIPP is commercially available as it can be found in product catalogues on the websites of chemical suppliers in the EU.

These findings show the possible use of DIPP as plasticiser and its potential to substitute other phthalates. No information is available on the amounts of DIPP potentially present in final articles and possible releases.

7.2.3 Use restrictions

DIPP is listed in Annex XVII, Group 30, of the REACH regulation[11] and 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”. This restriction was introduced by Directive 2005/90/EC amending Council Directive 76/769/EEC for the 29th time.

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 DIPP 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%.

According to the Cosmetics Directive 76/768/EEC (amended by Commission Directive 2005/80/EC), Annex II, no 1151, DIPP (CAS No 605-50-5) must not be a part of the composition of cosmetic products.

No EU wide occupational exposure limit for DIPP has been established.

[11]Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), establishing a European Chemicals Agency, amending Directive 1999/45/EC and repealing Council Regulation (EEC) No 793/93 and Commission Regulation (EC) No 1488/94 as well as Council Directive 76/769/EEC and Commission Directives 91/155/EEC, 93/67/EEC, 93/105/EC and 2000/21/EC. Currently DIPP is listed in Annex XVII of this Regulation with the CAS-No 42925-80-4, that refers to a different isomer. A corrigendum to this entry, which will refer to the CAS No 605-50-5, is in preparation by the Commission.

Since 1987 Sweden has a national binding 8h-OEL for phthalates of 3mg/m^3 with a short time limit value of 5mg/m^3 [12].

Conclusion on manufacture, import, export and uses:

DIPP is imported in a tonnage range of 10 to 100t into the European Market. The substance is used for the manufacture of propellants and their coating to regulate the rate of burn and has the potential to be used as plasticiser. Due to existing restrictions the use of the substance as such or in mixtures by consumers is not expected. However these restrictions do not apply to articles and consumer exposure via articles like ammunition is possible.

7.3 Exposure

7.3.1 Human exposure

Exposure to DIPP may mainly occur through dermal contact (log P_{ow}=5.6). Due to the low volatility of DIPP (0.025Pa at 25°C) inhalation exposure will be relevant when heating the substance to high temperatures or when aerosols are formed[13]. The saturation concentration at 20°C is 3.1mg/m^3 (ideal gas law). Inhalation exposure to unburned propellant dust at indoor shooting sites or to powder dust during manual reloading of cartridges may be possible, there is however no information available on the extent of exposure, on particle size and the concentration of DIPP in the dust.

7.3.1.1 Workplace exposure

On industrial sites exposure at the workplace may be possible during the production of propellants (confidential information is given in Annex II, Chapter 3). It may further be possible during the manufacture of ammunition and explosives containing propellants with DIPP, during dismantling and disposal of ammunition. Ammunition is manufactured by encasing the propellant in a special container (e.g. cartridge case) therefore no release during storing and handling is assumed.

Exposure of professional users may occur to the propellant powder during reloading of empty cartridges with the propellant and to dust from unburned propellant residues.

During the use of ammunition DIPP burns together with the other components of the propellant and should be destroyed at the same time. However according to literature the combustion of propellant powders in general is not complete. The amount of unburned propellant residues depends on the propellant itself, the calibre of the projectile and the barrel length. In indoor shooting ranges these residues are mainly deposited in the floor area in the first five to ten meters from the shooter in the firing direction. The unburned amount of propellant can range from 1 – 100g per 1.000 shots. In professional shooting operations a daily amount of 0.5 kg of unburned residues may be assumed (Jorczyk, 2012; VBG SP 25.7, 2000). Therefore exposure to DIPP from unburned propellant residues is possible for professionals during shooting activities and for cleaning personnel of indoor shooting ranges.

[12] http://www.av.se/dokument/inenglish/legislations/eng0517.pdf

[13]: http://gestis-en.itrust.de/nxt/gateway.dll?f=templates$fn=default.htm$vid=gestiseng:sdbeng

7.3.1.2 Consumer exposure

Ammunition including DIPP as part of the propellant may be sold to the general public. In ammunition the propellant is encased in a special container (e.g. cartridge case) where no release during storing and handling is assumed. However, consumer exposure to the propellant powder containing DIPP in concentrations up to 3% during reloading of empty cartridges is possible. Exposure to DIPP from unburned propellant residues may also be possible (see chapter 7.3.1.1).

10 house-dust samples (of commercial and private origin) have been analysed for their content of phthalates (Umweltbundesamt, 2010a). The limit of detection (LOD) of 0.02 mg/kg for DIPP was neither exceeded in the product samples nor in the house dust samples.

Since beginning of 2010 the content of DIPP in articles was analysed several times by the Austrian Umweltbundesamt: 164 articles (toys, flip flops, floating devices, packaging material, paper, etc.) were measured. In one non food packaging material the content of DIPP was above the LOD but below the limit of quantification (LOQ) (< 0,010 mg/kg). DIPP was not found in any of the remaining samples. No propellants or ammunition were analysed (Umweltbundesamt, 2010a, b).Although these results only show slightly increased levels in a single case, in general consumer exposure to articles containing DIPP cannot be excluded. DIPP is normally not included in routine phthalate measurements in articles and therefore its presence might be underestimated.

7.3.2 Environmental Exposure

7.3.2.1 General Aspects

In general, phthalates used as plasticisers are easily released into the environment (leaching, migration) because phthalates are not covalently bound into plastics. Because of their physicochemical properties exposure to phthalates does not result in bioaccumulation (Heudorf, 2007). Their concentration in water is declining fast while they can be found in water sediments, soil and waste water sludge (Römpp, 1985).Studies on phthalates have shown that they can be biodegraded by many species of bacteria (Ullmann, 2012).

The water solubility of DIPP is very low (1.1mg/l) and the substance is predicted to be readily biodegradable by QSAR modelling (information from registration).

DIPP has been found in samples of landfill leachates from municipal solid wastes in Brazil as described by NascimentoFilho, 2003, in a study for method development for extraction of plasticiser compounds from landfill leachates. No concentration of DIPP is given in this paper.

During use of ammunition it is possible that phthalate residues from unburned propellant powder are released into the environment. No information on the level of DIPP residues is available.

7.3.2.2 Exposure data

Confidential information from the registrant see Annex II, Chapter 3.

8 CURRENT KNOWLEDGE ON ALTERNATIVES

8.1 General aspects

The effects of phthalates on reproduction appear to be associated predominantly with the transitional phthalates of carbon backbone lengths of C4-C6. In general, lower molecular weight phthalates (<=C3) and high molecular weight phthalates (>=C7) do not appear to induce developmental effects (NICNAS, 2008). However it is noted that there may be exceptions from this general rule and it has to be kept in mind that some low and high molecular weight phthalates show effects at higher levels of exposure. Alternative substances might be phthalates with short or long carbon backbones, depending on the physicochemical property needed. Furthermore, substances not belonging to the group of phthalates are currently being discussed or used as alternative plasticisers (discussed in detail in section 8.3).

8.2 Alternatives for use in propellants

According to ARWT, 2012 DIPP is not a very common additive in the production of propellants and alternatives might exist. Dibutylphthalate is the most common phthalate used for ammunition However, it should be noted that dibutylphthalate is already included in Annex XIV of the REACH-Regulation. Therefore the importance of DIPP for the use in propellants may rise. Instead of phthalates additives like Campher and diphenylureaderivates (Akardit, Centralit) are used for the manufacture of propellants. Also diisooctylphthalate or dioctylphthalate are used (Mindef, 2012). According to registration information there is no suitable alternative substance for their production of propellants available for the time being.

8.3 Alternatives for uses as plasticiser

A number of substances have been identified as alternative plasticisers on the market but without considering their suitability for propellants. These alternatives include citrates, sebacates, adipates and phosphates. Table 7 gives an overview on possible alternative plasticisers (Lowell Center, 2011). It is noted that none of these possible alternatives listed are harmonized classified according to CLP regulation 1272/2008/EC. Like phthalates these alternative plasticisers are not chemically bound to the polymer and can leach out of products. None of the alternatives offers a “one-for-all” solution for every application: its choice depends not only on the inherent properties but also on the performance requirements (temperature performance, viscosity, ageing, fogging, price) of the article being manufactured (Ullmann, 2012).

Table 7: Alternative plasticisers (Lowell Center, 2011)

Chemical name	Function/product	Human Health Concerns	Environmental Concerns
Acetyl tributylCitrate **CAS 77-90-7**	• Primarily used as a plasticiser in cosmetic products, toys, vinyl, adhesives, medical devices, pharmaceutical tablet coatings, food packaging, flavoring substance in foods, printing inks and plastics in concrete. • Also used as a surface lubricant in the manufacture of metallic articles that contact food	• Intravenous exposure affects the central nervous system and blood in laboratory animals. May have moderate irritation effects on eyes and lead to increased liver weights • Studies show that it inhibits the proliferation of Lymph node T cells • Exhibits fire and explosive hazard in the presence of strong oxidizers and nitrates	Can bioaccumulate and is inherently biodegradable (in an inherent biodegradation test, 80 percent was degraded). However, in a nonstandard test aerobic degradation was slow and no data is available on anaerobic degradation
Di-isononylcyclohexane-1,2-dicarboxylate **CAS 166412-78-8**	• Primarily used as a plasticiser in PVC medical devices (blood tubes or packaging for nutrient solutions), toys, food packaging, cosmetics products, shoes, exercise mats and cushions, textile coatings, printing inks	Acute toxicity is low. However, an increase in testes weight, liver weight, thyroid weight, serum gammaglutamyltransferase and thyroid-stimulating hormone was observed in laboratory animals after repeated exposure. Blood and transitional epithelium cells in urine were also observed	No data
Dioctyl terephthalate **CAS 6422-86-2**	Primarily used as a plasticiser for PVC toys, childcare articles, consumer products, beverage closures and other polymer materials including cellulose acetate-butyrate, cellulose nitrate, and chloroprene rubbers	• Slightly irritating to eyes but will not damage eyes. • Prolonged exposure may cause dermatitis. Studies involving rodents showed inflammatory damage to the kidneys	Potential for bioconcentration in aquatic organisms is low. Likely to be biodegradable under aerobic and anaerobic conditions
Epoxidized soybean oil **CAS 8013-07-8**	• Primarily used as a plasticiser in closure gaskets used to seal glass jars, and as a stabilizer to minimize the ultraviolet	• A worker developed asthma from exposure to vapors from heated PVC film. Vapor may also produce asthmatic symptoms in as	Toxic to the crustacean Daphnia magna. Estimated to be bioaccumulative. Two standard tests administered

	degradation of PVC resins baby food jars, fillers, paint and lacquers, adhesives, printing inks, and packaging	little as 5 minutes • Studies involving rats have reported skin and eye irritations, secondary agent in bronchospastic reaction • Suspected to cause some effects on the kidney, liver, testis and uterus by repeated oral administration	by OECD concluded it is biodegradable in aerobic environments
Alkylsulphonic phenyl ester **CAS 91082-17-6**	Used as a plasticiser in PVC, polyurethanes, natural rubber, styrene-butadiene rubber, blends of styrenebutadiene rubber and butadiene rubber, isobutyleneisoprene rubber, acrylonitrilebutadiene rubber, and chloroprene rubber .	Has not been comprehensively studied for toxiceffects.	The main constituents of sulphonic acids, C10-21- alkane, Ph esters are not considered as PBT. They do not meet the P/vP criteria based on screening data but they meet the screening B criteria (COWI, 2009).
Tri-2-ethylhexyl trimellitate **CAS 3319-31-1**	Primarily used for heatresistant PVC articles, PVC-products used in the hospital sector (blood platelet bags), packing,cables, profiles, and floor/ wall coverings	• May cause irritation, nausea and vomiting in humans from exposure to mists and fumes. • Toxic to laboratory animals through inhalation. • Shown to irritate the skin of guinea pigs, rabbits and mice and the eyes of rabbits. • Studies in dogs (14d) showed an increase in weight of liver and spleen. • In rats, exposure through diet (28d) resulted in slightly increased liver weights and peroxisome proliferation	• Very limited data on environmental effects is available. • Potential for environmental effects is associated with the accumulation of the compound in biota, in aquatic sediments and in soils treated with sewage sludge. • Available data indicate that it does not biodegrade readily
Acetylated monoglycerides of fully hydrogenated castor oil **CAS 736150-63-3**	• Used in PVC-containing films, tubes, bottles, food packaging materials and other polymers such as polyolefin, styrene, and PET	•No data found describing human exposure. • Slightly lower migration rate was found when compared to DEHP	No data

bis(2-ethylhexyl)-1,4-benzenedicarboxylate (Eastman 168) **CAS 6422-86-2**	• Used as a plasticiser in PVC toys, bottle caps and closures, coatings for cloth, electric connectors, flexible film, pavement, striping compounds, walk-off mats, sheet vinyl flooring, other vinyl products, and PVC/VA copolymer resins.	•Limited data suggest that acute oral toxicity is low based on an LD50 of >3200 mg/kg in both rats and mice. •DEHT is irritating and sensitizing to guinea pig skin and is only slightly irritating to rabbit eyes (Versar, 2010)	No data
Di(2-ethyl hexyl)adipate **CAS 103-23-1**	• Used as a plasticiser in toys, vinyl flooring, wire and cable, stationery, wood veneer, coated fabrics, gloves, tubing, artificial leather, shoes, sealants, and carpet backing. • Also used in films employed in food packaging materials, fillers, paint and lacquers, adhesives, plastic in concrete, and rubber products. • Expected to be widely used in the near future in products for the hospital sector, printing inks and other PVC products	•Slightly toxic when administered intravenously in animal studies. • May produce dose-dependent changes in the body. • Reported to cause liver tumors, reduced bodyweight and increased liver weight (may be a result of hepatic peroxisome proliferation) in mice and rats	• Toxic to algae, crustaceans and fish. • Chronic data on crustaceans show adverse effects on reproduction of Daphnia magna. • Not a bioaccumulative substance. • Available data indicate evidence of biodegradability
Di-butyl adipate **CAS 105-99-7**	• Primarily used as a plasticiser for resins. Also used in floor wax	Combustible. Mildly irritating to skin. Causes coughing when inhaled • No data found on long-term exposure effects.	Moderately toxic to fish, daphnids and algae. • Readily biodegradable. • No data found on bioaccumulation
Butylatedhydroxytoluene **CAS 128-37-0**	• Used in childcare articles intended to be mouthed such as teething products and as an antioxidant in EVA and polyethylene plastics. Also used as a food additive	May cause impaired blood clotting, hemorrhage, cytotoxicity, hepatocellular injury and carcinogenesis	No data
Hyperbranched Poly (Є-caprolactone)	• Intended primary use is in PVC applications including coating	• No data found. • According to one study, it does	No data

	resins, polymer additive, adhesive agents, and processing aids	not migrate when used in PVC even under harsh conditions such as high temperature	
Di(2-ethylhexyl) phosphate **CAS 298-07-7**	• Primarily used as a flame retardant in products with specific fire resistant demands. Also used as a plasticiser in PVC products used in the hospital sector, packaging, cables, floor and wall coverings	In humans, inhalation caused weakness, irritability and headache. • Causes irritation of the eyes, and first and second degree skin burns. Reported to be corrosive to the skin and eyes in rabbits	• Ecosystem toxicity data indicate it is harmful to algae, crustaceans and fish. In a test involving the microorganism thiobacillusferrooxidans, respiration was inhibited. • Has low bioaccumulation potential and is inherently biodegradable
Tri(2-ethylhexyl) phosphate **CAS 78-42-2**	• Used in fillers, paint and lacquers, adhesives, plastic in concrete and similar DEHPA applications	• May produce moderate erythema and slight irritation to eyes. • Observed effects in rats include hematological changes and reduced body weight gain. (repeated dose, 28d/30d) • A slight evidence of carcinogenicity has been observed in female mice (long-term study)	• Data show it is toxic to algae. Not readily biodegradable according to the available aerobic biodegradation data. • Slowly biodegrades under anaerobic conditions when present in weak solutions
O-toluene sulfonamide **CAS 88-19-7**	• Information on use is limited. Anticipated to be used in the future mainly in PVC cables .	• Reported to be teratogenic in rats, but only exhibiting a weak mutagenic effect (this is however based on studies without detailed descriptions of the study design) • Sulfonamides may cause hyperbilirubinemia in infants. In addition, sulfonamides may cause hemolyticanemia in glucose-6-phosphate dehydrogenase-deficient neonates	Does not readily biodegrade
2,2,4-trimethyl 1,3-pentanediol diisobutyrate	• Primarily used as a plasticiser in PVC toys, flooring, products used in the hospital sector. Also used in fillers, wallpaper, paint and	• May be associated with eye irritation and nasal allergies • Has been observed to be slightly irritating in guinea pigs.	Has some potential for bioaccumulation

CAS 6846-50-0	lacquers, printing inks, plastic in concrete, artificial leather, packaging, as well as vinyl and urethanes	• Reversible liver weight changes have also been observed in rats from chronic exposure	
Dioctylsebacate **CAS 122-62-3**	• Primarily used as a plasticiser for PVC products and elastomers. • Compatible with nitrocellulose and polyvinylidene chloride. • Anticipated to be used in printing ink	Exhibits moderate acute toxicity when administered orally to rats. Oral administration to rats also showed increased liver weight, peroxisome proliferation and increased levels of peroxisome enzymes	Has a high bioaccumulation potential and has been shown to degrade slowly.
Di-butyl sebacate **CAS 109-43-3**	• Used as a plasticiser, flavoring agent, and cosmetic and perfume additive	Combustible. • Chronic skin contact may cause skin sensitization • Mildly toxic when ingested	• biodegradable. • Low and moderate potential for bioaccumulation and bioconcentration in aquatic organisms respectively
Grindsted soft-n-safe: Made from fully hydrogenated castor oil and acetic acid	• Primarily used as a plasticiser in food contact materials (approved for use in the EU, US, South America and most of Asia), medical devices, vinyl flooring, wallpaper, shrink wrap film, textile dyes, ink applications, adhesives and sealants	According to the manufacturer (Danisco), it shows no indication of dermal absorption, dermal irritation or eye irritation. • No hormone-disrupting or mutagenic effects may result	• According to the manufacturer, there is no indication of aquatic toxicity • Biodegradable

9 RISK-RELATED INFORMATION – Human Health

No risk assessment has been carried out for DIPP according to Regulation EEC/793/93. No CSR is available from registration data. A comprehensive risk assessment is outside the scope of this dossier.

DIPP is classified as Repr. 1B and self-classified as skin sensitizer. For information on toxicokinetics, sensitization and effects on reproduction and development see Annex I. No DNEL´s are given in the existing registration data.

No measured or modelled data for exposure assessment (environment and human health) are available. Exposure to DIPP may mainly occur through dermal contact.

Manual handling during industrial use cannot be ruled out from the explanation of process steps during manufacture of propellants (confidential Annex II). Therefore appropriate PPE and RMMs would need to be implemented.

Exposure to DIPP during handling of propellant and via unburned propellant dust is possible for downstream users and consumers (ammunition industry, army, police, sport shooters, etc.). No risk related information is available.

The exposure to DIPP could contribute to a cumulative health risk caused by antiandrogens. Mixture toxicity of low molecular weight phthalates has been investigated by several studies. Dose addition provides fairly good predictions of the effects (Kortenkamp, 2009). The national research council (NRC) concluded that sufficient data are available to proceed with the cumulative risk assessment (dose addition approach) of phthalates and other androgens (NRC, 2008).

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ANNEX I

SUPPLEMENTARY INFORMATION ON THE LEADING HEALTH EFFECTS AND TOXICOKINETICS

1 TOXICOKINETICS (ABSORPTION, METABOLISM, DISTRIBUTION AND ELIMINATION)

For the substance DIPP a good skin penetration potential can be expected as for the structurally-related diisobutyl phthalate about 10 % of the occlusively applied 30 mg dose was absorbed by rats within 24 h.
Absorption via the gastrointestinal tract is substantiated by systemic effects in animal experiments.
Alkyl phthalates are assumed to be absorbed via the respiratory tract. Since the vapor pressure is very low, inhalative exposure is only to be expected if DIPP is strongly heated or if aerosols are formed.
Studies regarding metabolism of DIPP are not available. Analogous to other medium-chained alkyl phthalates, it is to be expected that a hydrolysis to the monoester mono-isopentyl phthalate takes place in the liver, followed be subsequent formation of phthalic acid and methyl butanol. The elimination of these metabolites or consecutive products or conjugates probably proceeds with the urine and also in part with the faeces (GESTIS).

2 TOXICITY FOR REPRODUCTION

2.1 Developmental toxicity

After oral administration of a mixture Di-n-pentylphthalate with di-iso-pentylphthalate to Wistar rats in doses of 40, 200 and 1,000 mg/kg from the 6th - 15th day of pregnancy (8 - 10 animals per group; preparation in olive oil) the following results were obtained:

In the top dose all fetuses were resorbed (100% post-implantation loss). Dams on the 20th day of pregnancy showed increases in absolute and relative liver weights together with reduced feed intake and reduced body weight gain. No connection can be seen between maternal and fetal effects. Relating the only slight maternal to the severe fetal effects, the fetal toxicity is regarded as specific and selective. No effects were observed at 200 and 40 mg/kg respectively (Hellwig et al., 1997; ECBI/65/00 Add 9).

Additional information:
According to Hannas, 2011 and earlier conducted studies (Foster, 1980) there is strong evidence that dipentylphthalate (CAS 131-18-0) is an equal or even more potent testicular toxicant than DEHP. This is likely to be valid also for other structurally related pentyl phthalates, like DIPP. This is supported by the results of the above mentioned study by Hellwig, 1997. The mixture of pentyl phthalates caused a 100% resorption at 1000mg/kg/day while DEHP caused malformations in 70% of the litters at the same dose.

2.2 Effects on fertility

There are no studies on fertility with DIPP available to date. A fertility reducing action is suspected because of the structural relationship to di-n-pentyl phthalate and dibutylphthalate and the findings available for these substances. The monoesters of phthalic acid esters of medium chain length (C4 – C6) cause damage to the germinal epithelium in the testis. Sertoli cells in the seminiferous tubules are the primary site of attack. They exhibit considerable vacuolization of the smooth endoplasmatic reticulum resulting in a reduced fertility. As a consequence the germinal epithelium may be lost. (GESTIS; BAuA, 2001; ECBI/65/00 Add2).

ANNEX II

CONFIDENTIAL DATA