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NATIONAL INDUSTRIAL CHEMICALS NOTIFICATION AND ASSESSMENT SCHEME (NICNAS)

FULL PUBLIC REPORT

1,2-Benzenedicarboxylic acid, bis(2-propylheptyl) ester (Palatinol 10-P)

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Director
Chemicals Notification and Assessment

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FULL PUBLIC REPORT

1,2-Benzenedicarboxylic acid, bis(2-propylheptyl) ester (Palatinol 10-P)

1. APPLICANT AND NOTIFICATION DETAILS

APPLICANT(S)
BASF Australia Limited of 500 Princes Highway Noble Park VIC 3174
Orica Australia Pty Ltd of 1 Nicholson Street Melbourne VIC 3000

NOTIFICATION CATEGORY
Standard: Chemical other than polymer at more than one tonne per year.

EXEMPT INFORMATION (SECTION 75 OF THE ACT)
Data items and details claimed exempt from publication:

- Customer names and details
- Proportion of stabiliser in products

VARIATION OF DATA REQUIREMENTS (SECTION 24 OF THE ACT)
Variation to the schedule of data requirements is claimed as follows:

- Physical and chemical properties
- Induction of germ cell damage
- Acute toxicity test - fish
- Bioaccumulation study

PREVIOUS NOTIFICATION IN AUSTRALIA BY APPLICANT(S)
CEC419 and CEC608

NOTIFICATION IN OTHER COUNTRIES
It has been listed on EINECS in EU, NDSL in Canada, TSCA in USA, ENCA in Japan and ECL in Korea.

Di-isodecyl phthalate (DIDP), a close analogue of the notified chemical, has been assessed as a priority substance in the EU (by France) in accordance with Council Regulation (EEC) 793/93 on the evaluation and control of the risks of existing substances (EU, 2001).

2. IDENTITY OF CHEMICAL

CHEMICAL NAME
1,2-Benzenedicarboxylic acid, bis(2-propylheptyl) ester

OTHER NAME(S)
Bis(2-propylheptyl) phthalate;
Di-2-propylheptyl phthalate;
Phthalic acid, bis(2-propylheptyl) ester.

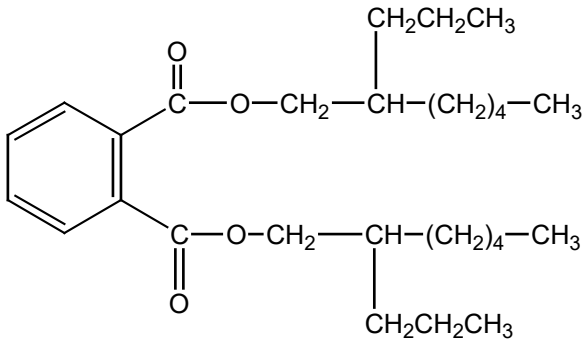
Remarks The notified chemical is a specific isomer of the complex chemical di-isodecyl phthalate (DIDP) (CAS No. 68515-49-1 and 26761-40-0).

MARKETING NAME(S)
Palatinol 10-P

CAS NUMBER
53306-54-0

MOLECULAR FORMULA
$C_{28}H_{46}O_4$

STRUCTURAL FORMULA



MOLECULAR WEIGHT
446.68

SPECTRAL DATA & METHODS OF DETECTION AND DETERMINATION

ANALYTICAL METHOD Infra-red spectroscopy

Remarks Principal peaks at: 2957.3, 2929.5, 2859.4, 1728.8, 1466.1, 1379.6, 1273.2, 1122.7, 1072.3, 742.1 cm-1

3. COMPOSITION

DEGREE OF PURITY
>99.5%

HAZARDOUS IMPURITIES
None.

NON HAZARDOUS IMPURITIES/RESIDUAL MONOMERS (>1% by weight)

Chemical Name 1,2-Benzenedicarboxylic acid, bis(4-methyl-2-propylhexyl) ester
CAS No. 103270-94-6 *Weight %* 2

Chemical Name 1,2-Benzenedicarboxylic acid, 4-methyl-2-propylhexyl 2-propylheptyl ester
CAS No. 170153-71-6 *Weight %* 15

4. INTRODUCTION AND USE INFORMATION

MODE OF INTRODUCTION OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS
Importation as a raw material

MAXIMUM INTRODUCTION VOLUME OF NOTIFIED CHEMICAL (100%) OVER NEXT 5 YEARS

Year	*1*	*2*	*3*	*4*	*5*
Tonnes	100-1000	100-1000	100-1000	100-1000	100-1000

USE

The notified chemical is a plasticiser for polyvinyl chloride (PVC) and vinyl chloride copolymers. The end use products containing the notified chemical include automobile undercoating, building materials, wires, cables, shoes, carpet backing, pool liners and gloves. The typical concentration of the notified chemical in end-use products is 30-60%.

The notifiers state that the major applications for the notified chemical will be wire and cable (70%), automotive (20%), plastisols (9%) and other (1%). The notified chemical is not intended for use in toys, food packaging or medical products.

5. PROCESS AND RELEASE INFORMATION

5.1. Distribution, Transport and Storage

PORT OF ENTRY
Victoria

IDENTITY OF IMPORTERS/RECIPIENTS
Imported by BASF Australia Limited and Orica Australia Pty Ltd. Formulated by customer in Victoria.

TRANSPORTATION AND PACKAGING

The notified chemical will be imported in 200 L steel drums, 1000 kg intermediate bulk containers (IBCs) or 20 tonne bulk isotainers. The majority of the imported chemical will be entering Australia in isotainers.

The notified chemical will be formulated into PVC compound or plastisols in Australia. If the product is a solid, such as compound for flexible PVC, it will be produced in the form of pellets and packaged in 25 kg bags or 500 kg bulky bins. If the product is in liquid form, it will be packaged in 200 L steel drums.

5.2. Operation Description

In Australia, the imported notified chemical will be formulated into PVC compound or plastisols at 30-60%. In both cases, the notified chemical will be transferred to a weighing vessel and then pumped into a closed mixing vessel for blending with PVC and other additives such as stabilisers. Mixing will occur at elevated temperatures for dry blending (100-200°C) or at room temperature for plastisols. Dry blends will be compounded by extrusion and pelletised for packing into bags or bins. Plastisols, which vary from thin liquid dispersions to thick pastes, will be drummed off. The mixing vessels are cleaned only when required; otherwise, production is sequenced. There may be clean downs required during routine or breakdown maintenance periods, where lines and vessels are purged and cleaned with inert materials.

Compounded PVC is then converted into end-use products by processes such as extrusion, calendering and injection moulding, for example, extrusion for the production of wire and cable, calendering for film, sheeting and automotive upholstery. For plastisols, the liquid or paste is poured into a mould which is then placed in air heated tunnel ovens (130-160°C). Handling of the plastisol is typically automated using vacuum pumps directly to the mould. Plastisols are used for underbody coating, sealing, rotational coating, dipping, slush moulding, and spread coating such as manufacture of tarpaulins.

5.3. Occupational exposure

Number and Category of Workers

Category of Worker	*Number*	*Exposure Duration (hour/day)*	*Exposure Frequency (day/year)*
Transport and storage			
Polymer stage	15	2	50
Product stage	15	1-2	40-50
Compounding & Manufacturing			
Reactor operating	50	12	20
Maintenance	20	1-2	240
QC testing	10	2	240
Transport & storage	10	2/4	240
End use	1000s	1-12	240

Exposure Details

Transport and storage
The notified chemical will be transported by road to a warehouse and then to the compounding facility. Exposure of receivers and transport personnel should only occur in the event of an accidental spillage.

Formulation
Incidental skin contact with the notified chemical may occur when the storemen place the drum lance inside the 200L drum, or when connect the IBC or isotanks to the weighing vessel. Inhalation exposure to vapours may also occur during the transfer process. After mixing, intermittent skin contact may occur during the packaging process, whether it be powdered blend or liquid plastisol. Samples may be taken at this stage, as the technical personnel will make up small-scale compounds by hand in the laboratory. During the subsequent compounding of dry blend into pellets, closed systems are used and any exposure will be incidental. However, manual handling operations during this process may include opening of packages, connection/insertion of line/hose, pumping liquid products, and eventual removal of connections and closing the containers. In addition, workers who clean the system may experience skin contact with the notified chemical.

For the specific formulation sites in Australia, approximately one third of the production time for the operators will be dedicated to running compound. During production runs (which can be up to 5 days long), the operators work two 12-hour shifts, 5 days per week, and 48 weeks per year. Workers prepare approximately 8 batches per day. Given the time that it takes to connect up and transfer product, the estimated period of direct contact with the notified chemical is less than 30 minutes per day for one person per shift.

Local exhaust ventilation is employed at all workplace areas where natural ventilation is considered inadequate. Workers involved in the above processes minimise their potential exposure by wearing appropriate protective equipment including industrial overalls, safety glasses/chemical goggles and face splash shields, protective gloves, and by use of proper industrial hygiene practices, particularly for those operators involved in any open transfer operations.

Product manufacture
Exposure to the notified chemical may occur during processing of the PVC compound or plastisol to manufacture the end-use product. Once compounded with PVC, the notified chemical is bound within the PVC matrix and skin contact is unlikely. However, product manufacture by processes such as extrusion, calendering and injection moulding at elevated temperatures may result in inhalation exposure to the notified chemical, whether to vapours or aerosols.

The methods for product manufacture from plastisols include spread coating, underbody coating, sealing, rotational coating, dipping and slush moulding. Although the process is largely automated and enclosed, incidental skin contact with the notified chemical may occur when transferring plastisol form drums to the moulding equipment. Intermittent inhalation exposure may occur in the vicinity of the drying ovens if ventilation is not adequate. Workers are expected to wear personal protective equipment including overalls, gloves and eye protection.

End-use of products
Under normal circumstances, occupational exposure to the notified chemical is not expected during handling of PVC products containing the chemical as the latter is physically bound within the PVC

matrix. However, as the notified chemical is not chemically bound to PVC, exudation may occur during heat, leading to possible skin and inhalation exposure.

5.4. Release

RELEASE OF CHEMICAL AT SITE

Import and Transport
Release of the notified chemical to the environment as a result of importation and transport of the notified chemical is expected to be minimal, unless exposure occurs as a result of accidental spillage.

The notifier estimates that at the maximum import volume less than 500 kg of the notified chemical would remain in the import containers. This will be either disposed of to landfill, with the bladders from flexitainers or drums, or as rinsings from isotainers and drums by waste disposal contractors.

Addition of Stabiliser
In some instances a stabiliser may need to be added to the imported product. This will be achieved by pumping the contents of isotainer into a mixing vessel adding the stabiliser mixing and returning to the isotainer. The mixing vessel will be rinsed and the rinsate disposed of to the sewer. Assuming 30% of the import volume is stabilised, approximately 105 kg will be disposed of to the sewer with the rinsate.

PVC Compounding
There are two main methods of compounding for processing of PVC, dryblending and plastisiol blending. Losses for these methods are described below. In addition to these sources of release, residues in containers may be released. Empty drums of Palanitol 10-P will be triple rinsed with washings processed to EPA regulations. IBCs and isotainers are expected to be reused.

Dryblending
Dryblending is conducted in lidded vessels. The method is based on suspension or mass grade PVC and typically consists of mixing all ingredients with a high speed rotating agitator which heats the material by friction. Temperatures of 100-200ºC are reached and the liquid plasticiser is completely adsorbed by the fine PVC powder grain. Residence times in the in the lidded blender are of the order of fifteen minutes and the hot blend is dropped into a cooling blender for rapid cooling to avoid lumping. During the process the exposure of the hot material to open air is small. Assuming, one air exchange per run, the amount of emitted plasticiser is 0.0037%. It is anticipated that these emissions would largely be trapped by local exhaust ventilations systems.

Plastisol Blending
Plastisol blending takes place stirred vessels at ambient temperature. To avoid the development of high viscosities by swelling of the PVC particles due to plasticiser uptake, the vessels have to be cooled to remove the heat of friction. Any significant emission of plasticisers at ambient temperature is excluded (emission = 0%).

PVC Product Manufacture
An estimated 0.035% per annum would be released into the environment due to the manufacture of PVC products. This release primarily resulting from volatilisation during processing into finished articles.

Periodically, extrusion equipment will be cleared of off-grade polymer by a purging process. This purging process accounts for approximately 0.4% waste. The purged material would be recycled or collected and buried in an approved landfill as general waste.

RELEASE OF CHEMICAL FROM USE

Some recycling of PVC products occurs at specialised PVC recyclers (eg cryogrind, Nylex SRM). However, ultimately the majority of the objects containing the notified chemical will be disposed of to landfill at the end of their useful life. As the notified chemical is not bound within the PVC matrix it will be lost from PVC articles containing it. This release may occur through volatilisation or leaching.

5.5. Disposal

The recommended method of disposal of liquid wastes containing materials such as the notified chemical is by burning in an approved incinerator.

5.6. Public exposure

Once imported, the notified chemical is only available to industrial processors, not to the general public. The potential for public exposure during compounding and moulding processes is low.

The notified chemical is used mainly for wire, cable and automotive parts, and does not intend for use in toys, food packaging or medical products. Members of the public may have limited dermal contact with wires and cables, but make more frequently dermal contact with automotive parts containing the notified chemical. As the notified chemical will not be chemically bound, it may be released from end-products over time, for example, volatilisation from car upholstery. Therefore, all members of the public, including children, may be potentially exposed to the notified chemical.

6. PHYSICAL AND CHEMICAL PROPERTIES

Unless indicated otherwise, the physical and chemical properties presented below are those taken from the EU report on di-isodecylphthalate (DIDP) (EU, 2001). The data are considered to be representative of the notified chemical.

Appearance at 20ºC and 101.3 kPa A clear mobile liquid with a faint odour.

Melting Point Not provided

Remarks Melting point for DIDP is approximately - 45ºC (EU, 2001).

Boiling Point 250-267ºC

Remarks The calculated boiling point for DIDP is >400°C as the data were measured at low pressures (EU, 2001).

Density 960-968 kg/m^3

Remarks The density for DIDP is 966 kg/m^3 (EU, 2001).

Vapour Pressure 3.7 x 10^{-9} kPa at 20ºC

Remarks The vapour pressure for DIDP at 20°C and 25°C were 2.8x10^{-8} and 5.1x10^{-8} kPa, respectively (EU, 2001).

Water Solubility ~ 0.2 µg/L

Remarks Based on a series of studies using different analytical techniques the above value for the water solubility of DIDP was adopted in the risk assessment of DIDP (EU, 2001). Note that the maximum concentration reached in the daphnia toxicity study was 0.24 mg/L.

Hydrolysis as a Function of pH Not Determined

Remarks The notified chemical contains ester functionalities that may be expected to undergo hydrolysis. Modelling with HYDROWIN v1.67 of the notified chemical indicates a half-life ~200 days at pH 8 and in excess of 5 years at pH 7. These results are consistent with the observation that phthalates are not readily

hydrolysed at the pH conditions usually found in the environment (Drew and Frangos, 2001).

Partition Coefficient (n-octanol/water) Not Determined

Remarks The partition coefficient has been estimated to be greater than 6 by comparison with DIDP and other phthalates (EU, 2001). Modelling with the KOWKIN (v1.66) program using an atom fragment method estimated the Log Kow at 10.36.

Adsorption/Desorption Not Determined

Remarks Modelling the adsorption/desorption behaviour of the notified chemical with PCKOC (v1.66) gave a estimated Log Koc of 6.28, indicating that the chemical would be expected to strongly bind to soils and sediments.

Dissociation Constant Not Determined

Remarks The notified polymer does not contain any functional groups expected to dissociate in the environmental pH range of 4-9.

Particle Size Not determined for a liquid.

Flash Point Approximately 238ºC

METHOD DIN 51758
Remarks The flash point for DIDP is >200°C.

Flammability Limits Not determined. The notified chemical is a combustible liquid.

Autoignition Temperature Approximately 345ºC

METHOD DIN 51794
Remarks Autoignition temperature for DIDP is approximately 380°C.

Explosive Properties The chemical structure does not indicate any explosion hazard.

Reactivity It is not considered reactive but incompatible with strong oxidising agents.

Viscosity Not determined.

Remarks Viscosity for DIDP is 130 mPa.s.

7. TOXICOLOGICAL INVESTIGATIONS

A number of studies, listed in Table A below, were submitted for the notified chemical and a further set of studies, listed in Table B, were submitted for DIDP, the more general form of the notified chemical. In addition, the notifier submitted reports of international assessments conducted on DIDP, namely an EU risk assessment (EU, 2001) and an NTP evaluation of the risks to human reproduction (NTP, 2000). These toxicological data of DIDP are considered to be relevant to the notified chemical due to the similarity in chemical structure.

Table A

Endpoint and Result	*Assessment Conclusion*
Rat, acute oral	LD50>5000 mg/kg bw, low toxicity

Rabbit, acute dermal	LD50 >2000 mg/kg bw, low toxicity
Rat, acute inhalation	LC50 >20.5 mg/L/1 hour
Rabbit, skin irritation	slightly irritating
Rabbit, eye irritation	slightly irritating
Guinea pig, skin sensitisation - non-adjuvant test.	no evidence of sensitisation.

Table B

Endpoint and Result	*Assessment Conclusion*
Rat, diet, repeated dose toxicity - 90 days	NOAEL 39 mg/kg bw/day (500 ppm)
Genotoxicity - bacterial reverse mutation	Non mutagenic
Rat, oral, developmental toxicity and teratogenicity	Maternal NOAEL 200 mg/kg bw/day Developmental NOAEL 40 mg/kg bw/day Teratogenicity

7.1. Acute toxicity – oral

TEST SUBSTANCE	Notified chemical
METHOD	Similar to OECD TG 401 Acute Oral Toxicity.
Species/Strain	Rat/Sherman-Wistar
Vehicle	None.

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	5/sex	5000	0

LD50	>5000 mg/kg bw
Signs of Toxicity	No unusual behavioural signs were noted.
Effects in Organs	Gross pathological examination revealed nothing remarkable.
CONCLUSION	The notified chemical is of low toxicity via the oral route.
TEST FACILITY	Biosearch Inc. (1979a).

7.2. Acute toxicity - dermal

TEST SUBSTANCE	Notified chemical
METHOD	Similar to OECD TG 402 Acute Dermal Toxicity.
Species/Strain	Rabbit/unknown strain
Vehicle	None
Type of dressing	Occlusive

RESULTS

Group	*Number and Sex of Animals*	*Dose mg/kg bw*	*Mortality*
1	3/sex	2000	0

LD50	>2000 mg/kg bw

Signs of Toxicity - Local	Not reported.
Signs of Toxicity - Systemic	No unusual behavioural signs were noted.
Effects in Organs	Gross pathological examination revealed nothing remarkable.

CONCLUSION — The notified chemical is of low toxicity via the dermal route.

TEST FACILITY — Biosearch Inc. (1979b).

7.3. Acute toxicity - inhalation

TEST SUBSTANCE — Notified chemical

METHOD	Similar to OECD TG 403 Acute Inhalation Toxicity.
Species/Strain	Rat/unknown strain
Vehicle	None
Method of Exposure	Whole-body exposure.
Exposure Period	1 hour
Physical Form	Liquid aerosol
Particle Size	0-5 μm
Remarks - Method	The rate of flow was 10.0 L per minute at 21°C, and the concentration was 20.5 mg/L during the exposure period.

RESULTS

Group	*Number and Sex of Animals*	*Concentration (mg/L)*		*Mortality*
		Nominal	*Actual*	
1	5/sex	Not reported	20.5	0

LC50	>20.5 mg/L/1 hour (maximum concentration)
Signs of Toxicity	Animals were wet, ruffled, agitated with raspy sounding after exposure. They appeared to be normal after 24 hours.
Effects in Organs	Gross pathological examination revealed nothing remarkable.

CONCLUSION — The notified chemical had LC50 > 20.5 mg/L after one hour exposure.

TEST FACILITY — Biosearch Inc. (1979c).

7.4. Irritation – skin

TEST SUBSTANCE — Notified chemical

METHOD	OECD TG 404 Acute Dermal Irritation/Corrosion. EC Directive 92/69/EEC B.4 Acute Toxicity (Skin Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	2 female and 1 male
Vehicle	None
Observation Period	72 hours
Type of Dressing	Semi-occlusive.
Remarks - Method	GLP & QA.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Erythema/Eschar	0.3	0	0	1	24 h	0
Oedema	0	0	0	-	-	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.

Remarks - Results	The Primary Irritation Index (PII) is 0.25
CONCLUSION	The notified chemical is slightly irritating to skin.
TEST FACILITY	BASF (2002a).

7.5. Irritation - eye

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 405 Acute Eye Irritation/Corrosion. EC Directive 92/69/EEC B.5 Acute Toxicity (Eye Irritation).
Species/Strain	Rabbit/New Zealand White
Number of Animals	3
Observation Period	72 hours
Remarks - Method	GLP & QA.

RESULTS

Lesion	*Mean Score* Animal No.*			*Maximum Value*	*Maximum Duration of Any Effect*	*Maximum Value at End of Observation Period*
	1	2	3			
Conjunctiva: redness	0.3	0.3	0.3	2	24 hours	0
Conjunctiva: chemosis	0	0	0	-	-	0
Conjunctiva: discharge	0	0	0	1	1 hour	0
Corneal opacity	0	0	0	-	-	0
Iridial inflammation	0	0	0	-	-	0

*Calculated on the basis of the scores at 24, 48, and 72 hours for EACH animal.

Remarks - Results

CONCLUSION	The notified chemical is slightly irritating to the eye.
TEST FACILITY	BASF (2002b).

7.6. Skin sensitisation

TEST SUBSTANCE	Notified chemical
METHOD	Similar to OECD TG 406 Skin Sensitisation – non-adjuvant test
Species/Strain	Guinea pig/unknown strain
PRELIMINARY STUDY	Maximum Non-irritating Concentration: not reported
MAIN STUDY	
Number of Animals	Test Group: 5/sex Control Group: nil
INDUCTION PHASE	Induction Concentration: topical application 100% (10 applications)
Signs of Irritation	3-4/10 animals had Draize score of 1 (erythema) during 5th to 10th inductions.
CHALLENGE PHASE	
1st challenge	topical application: 100%
Remarks - Method	No controls were included in the study.

RESULTS

Animal	*Challenge Concentration*	*Number of Animals Showing Skin Reactions after challenge*	
		24 h	*48 h*
Test Group	100%	0/10	0/10

Remarks - Results

CONCLUSION	There was no evidence of reactions indicative of skin sensitisation to the notified chemical under the conditions of the test.
TEST FACILITY	Biosearch (1979d).

7.7. Repeat dose toxicity

TEST SUBSTANCE	DIDP
METHOD	OECD TG 408 Repeated Dose 90-Day Oral Toxicity Study in Rodents. EC Directive 88/302/EEC B.26 Sub-Chronic Oral Toxicity Test: 90-Day Repeated Oral Dose Study using Rodent Species.
Species/Strain	Rat/Wistar
Route of Administration	Oral – diet
Exposure Information	Total exposure days: 90 days; Dose regimen: 7 days per week.
Vehicle	DIDP was directly mixed with food.
Remarks - Method	GLP & QA. The dose selection was based on a preliminary study using 5/sex per group at the concentrations of 0, 1000, 10000 and 20000 ppm.

RESULTS

Group	*Number and Sex of Animals*	*Nominal Concentration (ppm)*	*Actual Dose (mg/kg/day)*	*Mortality*
I (control)	10/sex	0	0	0
II (low dose)	10/sex	500	39 (36 for males and 42 for females)	0
III (mid dose)	10/sex	2500	196 (181 for males and 211 for females)	0
IV (high dose)	10/sex	15000	1266 (1187 for males and 1344 for females)	0

Mortality and Time to Death

No mortality.

Clinical Observations

The high-dose animals had lower bodyweights than the controls. No treatment-related effects were observed in clinical observations, food consumption, and ophthalmoscopy tests.

Laboratory Findings – Clinical Chemistry, Haematology, Urinalysis

In blood chemistry tests, the high-dose animals had lower serum chloride concentrations and higher albumin concentrations, and the mid-dose males also had higher albumin concentrations. In addition, the high-dose males had lower triglycerides levels, and the high-dose females had higher creatinine concentrations and lower glucose levels.

In enzyme assays, serum alkaline phosphatase activities and liver cyanide-insensitive palmitoyl-CoA-oxidation were increased in the high-dose animals. A marginal increase in cyanide-insensitive palmitoyl-CoA-oxidation was observed in mid-dose females.

In haematological tests, the high-dose animals had lower haemoglobin concentrations in the peripheral blood samples. Furthermore, the high-dose males had lower hematocrit values and higher platelet counts, and the high-dose females had lower mean corpuscular haemoglobin (MCH). In the high-dose male animals, there was a trend towards reduced MCH. There were no changes in the clotting parameter measured.

The urinalysis showed that the high-dose animals produced slightly larger volumes of urine than the controls.

Pathological Findings
In the male and female animals of the mid and high-dose groups, some treatment-related effects were observed including increased liver weight and/or liver cell hypertrophy due to peroxisome proliferation, increased basophilic cells in the anterior part in the pituitary gland of males, and hypertrophy of the follicular epithelium in the thyroid glands.

Remarks – Results
From this study, it can be concluded that liver is the target organ of DIDP toxicity. The following changes were considered to be treatment related:

High-dose group (15000 ppm or 1266 mg.kg/day)

		Increase	***Decrease***
Both sexes	Chemistry:	Alkaline phosphatase, cyanide-insensitive palmitoyl-CoA-oxidation, and albumin,	Chloride
	Haematology:		Haemoglobin and mean corpuscular haemoglobin
	Urinalysis	Urinary volume	
	Pathology	Absolute and relative liver weights, liver cell hypertrophy due to peroxisome proliferation, and hypertrophy of the follicular epithelium of the thyroid glands.	Bodyweight and bodyweight gain
Male rats	Chemistry		Triglycerides
	Haematology	Platelets	Haematocrit
	Pathology	Basophilic (thyrotrophic) cells in the anterior part of the pituitary gland	
Female rats	Chemistry	Creatinine	Glucose
	Pathology		Mean terminal bodyweights.

Mid-dose group (2500 ppm or 196 mg/kg/day)

		Increase
Both sexes	Pathology	Hypertrophy of the follicular epithelium of the thyroid glands.
Male rats	Chemistry	Albumin
	Pathology	Relative liver weight, and basophilic (thyrotrophic) cells in the anterior part of the pituitary gland; liver cell hypertrophy in one animal.
Female rats	Chemistry	Cyanide-insensitive palmitoyl-CoA-oxidation
	Pathology	Absolute liver weight

Low-dose group (500 ppm or 39 mg/kg/day)
No treatment-related effects were observed.

CONCLUSION
The No Observed Adverse Effect Level (NOAEL) for DIDP was established as 39 mg/kg bw/day (500 ppm) in this study based on effects on the liver and thyroid at 196 mg/kg/day.

TEST FACILITY BASF (1995a).

7.8. Genotoxicity - bacteria

TEST SUBSTANCE DIDP

METHOD OECD TG 471 Bacterial Reverse Mutation Test.
EC Directive 2000/32/EC B.13/14 Mutagenicity – Reverse Mutation Test using Bacteria.
Plate incorporation procedure & Pre incubation procedure

Species/Strain *S. typhimurium*: TA1535, TA1537, TA98, TA100.
Metabolic Activation System S-9 mix

Concentration Range in Main Test	a) With metabolic activation: 20-5000 µg/plate. b) Without metabolic activation: 20-5000 µg/plate.
Vehicle	Acetone
Remarks - Method	GLP & QA.

RESULTS

Metabolic Activation	*Test Substance Concentration (µg/plate) Resulting in:*			
	Cytotoxicity in PreliminaryTest	*Cytotoxicity in Main Test*	*Precipitation*	*Genotoxic Effect*
Absent				
Test 1 (Plate incorporation)		Not observed	≥500	Not observed
Test 2 (Pre incubation)		Not observed	≥500	Not observed
Present				
Test 1 (Plate incorporation)		Not observed	≥500	Not observed
Test 2 (Pre incubation)		Not observed	≥500	Not observed

Remarks - Results

CONCLUSION DIDP was not mutagenic to bacteria under the conditions of the test.

TEST FACILITY BASF (1995b).

7.9 Developmental Toxicity

TEST SUBSTANCE DIDP

METHOD OECD TG 414 Teratogenicity.
EC Directive 87/302 Teratogenicity study.

Species/Strain	Rat/Wistar
Route of Administration	Oral – gavage.
Exposure Information	The duration of treatment was from day 6 to day 15 to female rats post coitum.
Vehicle	Olive oil DAB 10
Remarks - Method	GLP & QA

RESULTS The study was terminated on day 20 post coitum.

Group	*Number of Animals*	*Dose mg/kg bw/day*	*Mortality*
I (control)	10 females	0	0
II (low dose)	9 females*	40	0
III (mid dose)	10 females	200	0
IV (high dose)	10 females	1000	0

*one low-dose animal was not pregnant and excluded from the study.

Mortality and Time to Death

None death occurred before the termination of the study.

Effects on Dams

No significant treatment-related effects were observed in the organ weights of uterus, liver and kidney, in the conception rate, in the mean number of corpora lutea and implantation sites, or in the values calculated for pre- and post-implantation losses, the number of resorptions ane viable foetuses.

Effects on Foetus

No treatment-related effects were observed in sex distribution of foetuses, weight of placentae or weight of

foetuses. In external examination of foetuses, one external malformation, namely, microphthalmia, was noted in one high dose foetus. In view of the occasional occurrence of this effect from historical control data, it was not considered treatment-related.

In soft tissue examination of the organs of the foetuses, one type of malformation, namely, dextrocardia, was observed in the control and low-dose groups but not at 400 and 1000 mg/kg/day. No significant soft tissue variations were observed.

In skeletal examination of the foetuses, various malformations, variations and retardations were observed.

Malformations – vertebral column and sternum. No statistically significant differences between treated rats and controls; comparable to historical control data.

Skeletal variations – additional 14th rib. Increased incidence in high dose foetuses, greater than incidences from historical control data.

Skeletal retardation – incomplete or missing ossification of skull bones, vertebral column, sternabra(e) and metacarpal bones. Statistically significant findings were (i) increase in dumb-bell shaped thoracic vertebral bodies at low dose, and (ii) increase in incompletely ossified thoracic vertebral bodies at mid dose. Taking into account the similar incidence of both effects in historical control data and the absence of a clear dose-response relationship, there was some doubt on the significance of these observations.

Remarks - Results
The study provided for assessment was the 1995 BASF screening study on DIDP. From the EU and NTP reports on DIDP, it appears that further details on the study may have been provided later in the published literature (Hellwig et al, 1997 in EU, 2001 and NTP, 2000). The conclusions presented here are based on information provided in the screening study. That is, based on the lack of a clear dose-response relationship in some skeletal observations and historical control data, it was concluded that some foetal effects observed in the study may not have been treatment-related. However, it is noted that similar developmental toxicity was observed in later studies after DIDP administration (Waterman et al, 1999).

CONCLUSION
Based on the absence of statistically significant effects in dams, the No Observed Adverse Effect Level (NOAEL) for maternal toxicity was established as 1000 mg/kg bw/day in this screening study. Based on the statistically significant and dose-related incidence of skeletal variations in foetuses, the NOAEL for developmental toxicity is 400 mg/kg bw/day.

TEST FACILITY BASF (1995c).

7.10 Literature reviews

The notifier provided several published papers on DIDP and other phthalate compounds to support their notification.

7.10.1 EU Risk Assessment for DIDP

The final EU risk assessment report on DIDP was prepared by France and published in 2001 (EU, 2001). The report indicated that there is at present no need for further information and/or testing and for risk reduction measures beyond those which being applied already for workers and consumers. However, risk reduction measures should be taken if DIDP is used in toys. This concern was reached because of concerns for hepatic toxicity as a consequence of repeated exposure of infants and newborn babies arising mainly by oral route from toys and baby equipment.

The report addressed the toxicokinetics and metabolism of DIDP and some of the toxicological endpoints not adequately covered by the study reports submitted by the notifier. The main conclusions are summarised below for the purposes of a consolidated health hazard assessment.

Toxicokinetics, metabolism and distribution

The absorption of DIDP via the oral route was concluded to be saturable since the absorption decreases when dose increases. The absorption of DIDP through dermal route is very low with most of the unabsorbed dose remaining at the skin area at day 7. The maximum percentage of dermal absorption is approximately 4% of the applied dose in 7 days in rat, with comparative *in vitro* studies indicating that the rate will be lower in humans. Inhaled DIDP aerosol seems readily absorbed as a part of insoluble particles are cleared from the nasopharyngeal region and swallowed. Similarly, the mucociliary transport system in the tracheobronchial tree leads the deposited particles upward to the oropharynx where these particles are swallowed and pass through the gastrointestinal (GI) tract. The report concluded that, for absorption by inhalation, 75% bioavailability be used for the risk characterisation.

DIDP is mainly distributed in the GI tract, liver and kidneys if absorbed by the oral or inhalation routes. For dermal exposure, DIDP is distributed in muscle and adipose tissue. Following inhalation, DIDP in fat tissue is very low but remains constant from the end of exposure to the end of the observation period.

In DIDP and mono-isodecyl phthalate (MIDP) metabolism studies, only metabolites such as the oxidative monoester derivative and phthalic acid are excreted in urine, rather than the parent compound. No DIDP was detected in bile extracts at 24 and 72 hours after dosing. Data on end-products indicate a cleavage to the monoester and an alcohol moiety. Both MIDP and DIDP were detected in faeces that indicate the metabolic pathway leading to phthalic acid is saturable.

DIDP is rapidly eliminated and not accumulated in tissues. Excretion is shared between urine and faeces.

In addition, results from a two-generation study suggest a possible transfer of DIDP through the milk when dam are exposed by oral route.

Repeated dose toxicity
A number of studies by different routes in various species were reviewed in the EU report. The principal conclusions are summarised below.

The target organ for oral sub-acute and sub-chronic DIDP toxicity in animals is the liver, based on increased liver weights and significant changes in proliferator peroxisome enzyme activities at higher dose in rodents. Peroxisome proliferation liver effects are generally assumed to be species-specific, with humans expected to be far less sensitive than rats.

In a 13-week dietary study in dogs, a NOAEL of 15 mg/kg/day was established, based on liver effects, namely, swollen and vacuolated hepatocytes at higher doses. As the dog is not considered to be responsive to peroxisome proliferation, it was considered to be a more relevant species for the human health risk assessment. As the dog study was not considered reliable, the NOAEL of 60 mg/kg/day, based on increased relative liver weights in female rats in a 90-day study, was also used in the human health risk assessment.

The EU report concluded that the effects observed in the repeated dose toxicity tests did not justify the classification with R48 according to the EU criteria.

Genotoxicity
The EU report concluded that DIDP was not genotoxic. It is not mutagenic *in vitro* in bacterial mutation assays with and without metabolic activation, and is negative in a mouse lymphoma assay. It is not clastogenic in a mouse micronucleus assay *in vivo* either.

Carcinogenicity
Among the two in vitro transformation studies reviewed in the EU report, one test showed positive in the Balb/3T3 cell line at the highest tested concentration. This positive result is considered to be in accordance with those of well-known peroxisome proliferators.

No carcinogenicity long term study is available for DIDP, but an increase in incidence of hepatocellular tumours in rats related to peroxisome proliferation might be anticipated. An increased incidence in tumour liver cells was observed in rats treated with DEHP and di-isononyl phthalate (DINP). However, the carcinogenic effects of peroxisome proliferators are generally considered to be specific to rodent species, while humans are essentially non-responsive or refractory.

Toxicity for reproduction

The EU report concluded that DIDP was a developmental toxicant, based on a decrease in survival indices in two-generation studies; a NOAEL of 0.06% (33 mg/kg/day) was used in the risk assessment. For developmental effects, NOAELs of 500 mg/kg/day, for skeletal variations, and 253 mg/kg/day, for body weight decrease in offspring, were used in the risk assessment. No fertility effects were observed in any studies.

Overall, the effects observed were not severe enough to warrant classification against the EU criteria.

Endocrine disrupter effects
Overall, no overt effect related to endocrine disruption of the reproductive system was observed in any of the studies considered in the EU report.

7.10.2 NTP Evaluation of Risks to Human Reproduction from DIDP

The US National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) expert panel report on DIDP was published in 2000 (NTP, 2000).

The expert panel concluded that there was sufficient evidence from the toxicology database to determine that DIDP can cause foetotoxicity after oral exposure. The NOAEL for developmental toxicity in the two prenatal developmental studies in rats was 40-100 mg/kg/day based on the effects on the developing skeletal system. In the two oral two-generation reproductive toxicity studies in rats, adverse effects on pup survival and growth were observed, the NOAELs being 38-44 mg/kg/day during pregnancy and 52-114 mg/kg/day during lactation.

However, the reproductive studies showed that DIDP had no effect on reproductive structure or function, and the top doses, 427-929 mg/kg/day for males and 508-927 mg/kg/day for females, were selected as the NOAELs.

7.10.3 Doull paper on Cancer Risk Assessment of DEHP

The notifier provided a published paper by Doull et al (1999), titled "A cancer risk assessment of di-(2-ethylhexyl) phthalate (DEHP): Application of the new US EPA risk assessment guidelines". The paper indicated that the hepatocarcinogenic effects of DEHP were resulted directly from the receptor-mediated, threshold-based mechanism of peroxisome proliferation in rodents. Since humans are quite refractory to peroxisomal proliferation, even following exposure to potent proliferation agents, the hepatocarcinogenic response of rodents to DEHP is not relevant to human cancer risk at any anticipated exposure level. The paper was specific to DEHP.

7.10.4 CSIRO papers on PVC

The notifier provided two published papers on issues concerning the use of PVC (Smith, CSIRO Molecular Science, 1998, and Coghlan, CSIRO Molecular Science and ANU, 2001). The papers contain information on phthalates, particularly DEHP, however, no specific toxicological data on DIDP was included.

8. ENVIRONMENT

8.1. Environmental fate

8.1.1. Ready biodegradability

TEST SUBSTANCE	Notified chemical
METHOD	OECD TG 301 B Ready Biodegradability: CO_2 Evolution Test.
Inoculum	Activated sludge from laboratory wastewater treatment plant treating municipal waste.
Exposure Period	28 days
Auxiliary Solvent	None
Analytical Monitoring	
Remarks - Method	Inoculum was aerated overnight in culture medium prior to the addition of test materials (~27 mg/L). Samples were collected from the first CO_2 absorber vessel on Days 1, 3, 5, 7, 10, 12, 14, 17, 21, 24, 27 and 28.

RESULTS

Test substance		*Aniline*	
Day	*% degradation*	*Day*	*% degradation*
1	2	1	0
10	5	10	48
12	17	12	55
21	59	21	71
28	75	28	79

Remarks - Results: The extent of degradation of the reference material validates the test. A toxicity control containing test material and aniline reached 77% degradation on day 28 indicating that the notified chemical is not toxic to sewage treatment organisms since >25% degradation occurred as required.

CONCLUSION: The degradation of the notified chemical exceeded 60% pass value within the 28 d duration of the test. These pass values have to be reached in a 10 d window within the 28 d period, beginning when degradation reaches 10%. The test material does not quite achieve this latter criterion. However, it is close to achieving the required degradation within the 10 d window and is not expected to be persistent in the environment.

TEST FACILITY: BASF (2002c)

8.1.2. Bioaccumulation

No studies on the bioaccumulation of the notified chemical were provided. One study for the bioaccumulation of DIDP has been reported, where the parent compound is measured in biota and the water phase (EU 2001). A bioconcentration factor of <14.4 was determined for fish (*Cyprinus carpio*). However it should be noted that bioconcentration factors between 1.3 and 29.7 were measured for DEHP under the same test conditions in this study and that much higher BCFs have been determined for DHEP in other studies.

8.2. Ecotoxicological investigations

8.2.1. Acute toxicity to fish

A study on the toxicity to fish has not been submitted. However, the notifier supplied the European risk assessment for di-isodecyl phthalate (DIDP). This report summarises a number of studies for DIDP all of which indicate no acute effects reported with fish up to the limit of solubility for DIDP in the test systems (EU 2001). DIDP is a mixture of isomeric compounds which includes the notified chemical. Hence, the notified chemical is not expected to be toxic to fish up to the limit of its water solubility.

8.2.2. Acute toxicity to aquatic invertebrates

TEST SUBSTANCE: Dipropylheptylphthalate

METHOD: OECD TG 202 Daphnia sp. Acute Immobilisation Test – Static test.

Species	*Daphnia magna STRAUS*
Exposure Period	48 hours
Auxiliary Solvent	None
Water Hardness	2.56 mmol $CaCO_3$/L
Analytical Monitoring	Liquid-liquid extraction followed by GC.
Remarks - Method	The stock solution was prepared by suspending a known amount of the

test substance in the test medium and stirring (about 20 h at 20ºC). This stock solution (nominally 100 mg/L) was centrifuged and used to prepare the test concentrations by dilution. Water quality parameters of pH, water temperature, O_2 content were within normal limits throughout study.

RESULTS — Four parallel tests with 5 daphnia in each were conducted.

Concentration mg/L		*Number of D. magna*	*Number Immobilised*	
Nominal	*Actual*		*24 h*	*48 h*
0	<0.1	20	0	0
1.56	<0.1	20	0	0
3.13	-	20	0	0
6.25	-	20	0	0
12.5	<0.1	20	0	0
25	-	20	0	1
50	-	20	0	1
100	0.24	20	0	3

EC50 — >100 mg/L at 24 hours
>100 mg/L at 48 hour

NOEC — 12.5 mg/L at 48 hours

Remarks - Results — The 48-hour NOEC for the test material was determined in the report to be at the third highest test level with a nominal concentration of 12.5 mg/L (actual <0.1mg/L). Concentrations in excess of 0.24 mg/L could not be achieved due to the low water solubility of the test substance. The 48-hour EC50 for the test substance could not be determined for *Daphnia magna* as the test substance had little toxic effect on the test daphnia up to its highest concentration which could be achieved in the test media. Hence, the 48-hour EC50 is greater than 0.24 mg/L.

CONCLUSION — The notified chemical is not toxic to daphnia up to the limit of its water solubility in the test media.

TEST FACILITY — BASF (1995d)

8.2.3. Algal growth inhibition test

TEST SUBSTANCE — Dipropylheptylphthalate

METHOD — OECD TG 201 Alga, Growth Inhibition Test.
EC Directive 92/69/EEC C.3 Algal Inhibition Test.

Species — *Scenedesmus subspicatus*
Exposure Period — 72 hours
Concentration Range Nominal — 0, 12.5, 25, 50, 100
Concentration Range Actual — 12.5, 25, 50, 100 mg/L (nominal)
Auxiliary Solvent — None
Water Hardness — Not specified
Analytical Monitoring —

Remarks - Method — The stock solution (nominally 125 mg/L) was prepared by suspending a known amount of the test substance in the test medium and stirring (about 20 h at 20ºC). This stock solution was passed through a membrane filter. The test was conducted with further dilutions of this aqueous extract (eluate) of the test substance. Hence, the test was conducted on the water accommodated fraction (WAF). Water quality parameters of pH, water temperature, O_2 content were within normal limits throughout the study.

RESULTS

Biomass	*Growth*	*NOEC*
E_bC50 *mg/L at 72 h*	*E_rC50* *mg/L at 72 h*	*mg/L at 72 h*
>100	>100	25

Remarks - Results

The results of the study showed no inhibitory effect on the growth of *Scenedesmus subspicatus*. The 72-hour NOEC for the test material was determined to be at the third highest test level with a nominal concentration of 25 mg/L. The 48-hour E_bC50 and E_rC50 for the test substance could not be determined for *Scenedesmus subspicatus* as the test substance showed no inhibitory effect on the test algae up to the highest concentration which could be achieved in the test media. Hence, both the 48-hour E_bC50 and E_rC50 are greater than 100 mg/L (nominal).

CONCLUSION

While the EC50 of the notified chemical to algae is above the limit of its water solubility, some effects were noted below this level.

TEST FACILITY

BASF (1997)

8.2.4. Inhibition of microbial activity

TEST SUBSTANCE

Dipropylheptylphthalate

METHOD

Inhibitory Effect on Cell Multiplication of the Bacterium *Pseudomonas putida.*

Inoculum: *Pseudomonas putida*

Exposure Period: 16 hours

Concentration Range Nominal: 31.25-8,000 mg/L

Remarks – Method

A stock solution of the test substance was prepared by stirring the test substance (10,000 mg/L) in deionised water at room temperature for 17 h. The resulting emulsion was centrifuged for about 10 min and the resulting water extraction was diluted with deionised water to give the desired test concentrations. Hence the test was conducted on diluted water accommodated fractions (WAFs).

The test parameter is the cell multiplication of the bacterial culture. Therefore the optical density of the bacterial suspension after incubation is measured in a photometer at 436 nm. The inhibition of bacterial cell multiplication is determined by comparing the bacterial growth of each concentration level with an untreated control.

RESULTS

Concentration	% Growth relative to control	% Inhibition relative to control
Control	100.0	0.0
31.25	97.7	2.3
62.5	98.5	1.5
125	97.7	2.3
250	98.9	1.1
500	99.1	0.9
1000	102.8	-2.8
2000	104.8	-4.8
4000	109.9	-9.9
8000	112.8	-12.8

IC50

>8,000 mg/L (Nominal)

NOEC	8,000 mg/L (Nominal)
Remarks – Results	As the test was conducted on the dilutions of the WAFs the actual test concentration is limited by the solubility of the chemical. The test substance showed no significant inhibitory effect on the bacteria. In fact, for the less diluted samples a slight stimulation of growth may be observed. However, it is uncertain whether this is statistically significant.
CONCLUSION	No adverse effects toward bacterial activity in sewage treatment plants are expected for the substance up to the limit of its solubility in water.
TEST FACILITY	BASF (1994)

9. RISK ASSESSMENT

9.1. Environment

9.1.1. Environment – exposure assessment

The majority of the notified chemical will be incorporated into PVC articles. During the lifetime of the articles the notified chemical may be released either through evaporation or leaching.

Wastes generated during the compounding with PVC or manufacture of PVC articles will either enter landfill or the sewage system. Simpletreat modelling of the closely related DIDP (a mixture of isomeric compounds containing the notified chemical) indicates that 3.2% will be released to air, 8.1% to water, 84.8% to sludge and 3.9% degraded, resulting in 81.9% removal during passage through a sewage treatment plant (EU 2001). Studies of the leaching of DIDP from wire insulation in simulated landfills, containing genuine household waste or model waste mixtures, found that negligible amounts of DPIP were leached over the equivalent of a decade in landfill. Hence, the notified chemical is not expected to leach from landfill.

The major use for PVC containing the notified chemical will be as wire and cable insulation (~70%). The expected useful lifetime of such products is expected to be around 30 years. The European Risk Assessment for DIDP estimated that up to 80% of cables and wires would be installed below ground and assumed that any emissions from underground cables would be expected to remain in the soil compartment (EU 2001). Based on a report by the Building Research Establishment from the United Kingdom, the risk assessment assumes that the leached chemical will partition equally between soil and surface water. The European risk assessment uses an emission rate for DIDP from above ground wires and cables of 1.05g/m^2 based on a field study of roofing materials Assuming that half finds its way into the atmosphere and half into surface waters, the emission rate to surface waters is 0.525 g/m^2. Using these assumptions the emission to surface waters from wire and cable insulation in Australia for the notified chemical would be 1.17 t/annum Australia wide (based on a maximum import of 1000 t/annum, 70% of import volume is used in wire and cable insulation of which 20% is above ground and susceptible to leaching, insulation surface area of 532 m^2/tonne, with an emission rate to surface waters of 0.525 g/m^2). For a section cable with a surface area of 1 m^2, the release rate is 43 mg/d. Assuming a cylindrical cable of 5 mm diameter, the cable section would have a length of 64 m. Hence, these releases are expected to be disperse in nature and at low levels.

The following half-lives for DIDP in various environmental compartments have been taken from the European risk Assessment for DIDP (EU 2001). The half-life in air through reaction with hydroxide radicals is determined using the AOP program produced by Syracuse Corporation. The half-life in surface water is extrapolated from a biodegradation study using methods described in the technical guidance document (European Commission 1996). The half-life for soil is based on that determined for diethylhexylphthalate (DEHP) and diisononylphthlate (DINP) and is a very conservative estimate. The same half-life was assumed for aerobic sediment. The anaerobic sediment was also derived from data for DHEP.

Compartment	Half-life (d)
Air	0.6
Surface water	50
Soil/aerobic sediment	300
Anaerobic sediment	3000

Based on the similarities between DIDP and the notified chemical it is anticipated that would display similar half-lives in each of the environmental compartments and potentially be persistent in some soils and sediments inspite of its ready biodegradability status.

9.1.2. Environment – effects assessment

The notified chemical is non-toxic to fish, daphnia and bacteria up to the limit of its water solubility though some inhibition of algae was observed below this limit. Since LC50 and EC50 levels could not be determined, estimation of a PNEC is not possible.

9.1.3. Environment – risk characterisation

The notified chemical is to be used as a plasticiser in PVC products. The majority of the imported product will be incorporated into insulation for wires and cables. Once the chemical has been incorporated in PVC articles the majority of the notified chemical is expected to remain within the PVC matrices. Hence, the majority of the notified chemical will share the fate of the articles into which it is incorporated. It is anticipated that these will be disposed of to landfill end of their useful lifetime. The notified chemical is not expected to leach from landfill.

The recommended method of disposal of liquid wastes containing the notified chemical is incineration. Any incineration of the notified chemical will result in the formation of water vapour and oxides of carbon.

Some leaching of the notified chemical may be anticipated during the useful lifetime of the articles into which it has been incorporated. These releases are expected to be disperse in nature and at low levels. Any material partitioning to the air through evaporation would also rapidly degrade through reaction with hydroxyl radicals.

The above considerations indicate minimal risk to the environment when the notified chemical is used in the manner and levels indicated by the notifier.

9.2. Human health

9.2.1. Occupational health and safety – exposure assessment

Formulation

The formulation process is largely enclosed, however, incidental skin contact and exposure to vapours may occur during transfer operations. Intermittent skin contact may occur during packaging operations. Local exhaust ventilation would be expected in open processes.

No monitoring data were available for the notified chemical, however, exposure estimates were included in the EU report on the close analogue DIDP. The exposure scenarios described in the EU report are similar to those to be encountered in Australia. In the EU report, a reasonable worst-case for daily external dermal exposure was 5 mg/cm2, an overestimate considering the high level of engineering control and the poor dermal absorption of the notified chemical. For inhalation, a reasonable worst-case estimate for daily exposure was 10 mg/m^3, with a typical exposure of 3 mg/m^3. The corresponding internal doses for worst-case dermal and inhalation exposures were 0.03 mg/kg/day and 1.07 mg/kg/day, assuming a 70 kg body weight (combined dose 1.10 mg/kg/day).

Product manufacture

For product manufacture, including compounding operations and plastisol processing, exposure scenarios are similar to those for formulation, that is, largely incidental or, at worst, intermittent skin and/or inhalation exposure in an environment of good engineering control.

No monitoring data were available for the notified chemical, however, exposure estimates were included in the EU report on the close analogue DIDP. Due to the similarity in exposure pattern to formulation scenarios, the estimates above were also used in the risk assessment for product manufacture.

End-use of products
The pattern of exposure is different in end-use scenarios as there is a wide variety of end-use. For example, there may be aerosol-forming activities such as spray coating and non-aerosol-forming activities. No monitoring data were available for the notified chemical, however, exposure estimates were included in the EU report on the close analogue DIDP.

In the absence of monitoring data for DIDP, exposures were assumed to be, at worst, similar to those during formulation and product manufacture. Therefore a reasonable worst-case estimate for daily external dermal exposure was taken as 5 mg/cm^2, and a reasonable worst-case estimate for daily inhalation exposure was taken as 10 mg/m^3, with a typical exposure of 1.5 mg/m^3. As exposure scenarios in Australia for the notified chemical are expected to be similar to those described in the EU report, the estimates above are used in the risk characterisation.

Transport and storage
Exposure to the notified chemical during normal transport and storage operations are assumed to be negligible.

9.2.2. Public health – exposure assessment

The exposure pattern for consumers will be similar to that experienced by workers during end-use, that is, incidental low level exposure during contact with end-use products. No monitoring data were provided, however, EU report on the close analogue DIDP. For the purposes of estimating exposures, the following scenarios were considered in the EU report:
Building materials and furniture (A)
- release of plasticiser vapour from wall and floor coverings, wire and cable into room air

Automotive interiors (B)
- release of plasticiser vapour from dashboard and upholstery into vehicle interior

Clothing, gloves and footwear (C)
- release of plasticiser during skin contact with article.

The following combined estimates were obtained for the three scenarios, assuming a 70% bioavailability for adults and 100% for children:

		Adult		Child
	External ($\mu g/m^3$)	Internal ($\mu g/kg/day$)	External ($\mu g/m^3$)	Internal ($\mu g/kg/day$)
A	20	4.2	20	21.3
B	20	0.8	20	1.9
C		0.7		
Total dose		5.7		23.2

9.2.3. Human health - effects assessment

Toxicokinetics
No toxicokinetic data were provided for the notified chemical, however, the EU report on DIDP contained information relevant to this assessment. Skin absorption was poor but DIDP aerosols were absorbed, although mainly via the oral route. The report concluded that, for absorption by inhalation, 75% bioavailability be used for the risk characterisation. The absorption of DIDP via the oral route is saturable as absorption decreases when dose increases. DIDP is mainly distributed in the GI tract, liver and kidneys if absorbed by the oral or inhalation routes. For dermal exposure, DIDP is distributed in muscle and adipose tissue.

In DIDP metabolism studies, only metabolites such as the oxidative monoester derivative and phthalic acid are excreted in urine, rather than the parent compound. No DIDP was detected in bile extracts at 24 and 72 hours after dosing. Data on end-products indicate a cleavage to the monoester and an alcohol moiety. DIDP was detected in faeces indicating saturation of the metabolic pathway leading to phthalic acid. DIDP is rapidly eliminated and does not accumulate in tissues. Excretion is shared between urine and faeces.

In addition, results from a two-generation study in rats suggested a possible transfer of DIDP through the milk when dams are exposed by the oral route.

Acute effects
Based on studies on the notified chemical, the notified chemical is of low acute oral, dermal and inhalation toxicity. The notified chemical is slightly irritating to eyes and skin. The result of the non-adjuvant skin sensitisation test provided for assessment was negative and additional information available in the EU report for DIDP indicates that the notified chemical has low sensitising potential.

Repeated dose toxicity
Based on repeated dose studies using DIDP, the more complex analogue of the notified chemical, the target organ in subacute and subchronic studies in rats is the liver, the effects observed being increased liver weight and changes in liver peroxisome proliferator enzyme activities. As the NOAELs derived are due to the latter, which is considered to be species-specific and of little relevance to humans, the NOAEL of 15 mg/kg/day from a 90-day dog study was used in the EU risk assessment. However, this study was considered to be of poor reliability. In the DIDP dietary study provided to NICNAS for assessment, the NOAEL was 39 mg/kg/day, based on liver effects and hypertrophy of the follicular epithelium of the thyroid glands.

The effects observed in the repeated dose toxicity tests do not justify classification with R48 according to the NOHSC Approved criteria.

Reproductive toxicity
In the DIDP developmental toxicity screening study in rats provided to NICNAS for assessment, the NOAEL for maternal toxicity was 1000 mg/kg/day, based on the absence of statistically significant effects in dams, and the NOAEL for developmental toxicity was 400 mg/kg/day, based on a statistically significant and dose-related incidence of skeletal variations in foetuses. However, it appeared from the EU and NTP reports on DIDP that further details on the study may have been provided later in the published literature. The conclusions presented here are based on information provided in the screening study. Similar developmental toxicity was observed in later studies after DIDP administration.

Based on a larger toxicology database, both the EU and NTP reports concluded that DIDP was a developmental toxicant. In the NTP report, the NOAEL for developmental toxicity in the two prenatal developmental studies in rats was 40-100 mg/kg/day based on the effects on the developing skeletal system. In the two oral two-generation reproductive toxicity studies in rats, adverse effects on pup survival and growth were observed, the NOAELs being 38-44 mg/kg/day during pregnancy and 52-114 mg/kg/day during lactation. In their risk assessment, the EU used NOAELs of 500 mg/kg/day, for skeletal variations, and 253 mg/kg/day, for body weight decrease in offspring. No fertility effects were observed in any studies.

In the EU report, the effects observed were not considered severe enough to warrant classification against the EU criteria.

The developmental effects of several phthalates are exerted via alternations in testosterone-synthesizing ability of the foetal testes. The mode of action of the testicular toxicity is via the monoester with the target cell in the testis being the Sertoli cell, although the precise biochemical interaction has yet to be identified. Attention has also been focused on the endocrine-active effects of phthalates including interactions with both oestrogen and androgen action. The experimental results indicate that only selected phthalates esters exhibit weak oestrogen receptor-mediated activity in some *in vitro* assays at high concentrations (IPCS, 2002).

No overt effect related to endocrine disruption of the reproductive system was observed in any of the studies considered in the EU report on DIDP.

Genotoxicity
An Ames test on DIDP submitted to NICNAS for assessment was negative. From a larger database, the EU report concluded that DIDP was not genotoxic. It is not mutagenic *in vitro* in bacterial mutation assays with and without metabolic activation, and is negative in a mouse lymphoma assay. It was not clastogenic in a mouse micronucleus assay *in vivo*.

Carcinogenicity
The EU report on DIDP concluded that there is long-term concern for carcinogenicity.

Hazard classification
Based on toxicological data available for the notified chemical and the close analogue, DIDP, the notified chemical is not a hazardous substance according to the NOHSC Approved Criteria for Classifying Hazardous Substances (NOHSC, 1999).

Comments
Some phthalates have been designated as hazardous substances in Europe and Australia, for example, .phthalates have been linked to endocrine disrupting effects, particularly on the male reproductive system. This is based on their effects at high doses in laboratory animals.

The National Drugs and Poisons Schedule Committee (NDPSC) has included diethyl phthalate (DEP) and dimethyl phthalate (DMP) in Appendix C of the Standard for the Uniform Scheduling of Drugs and Poisons (SUSDP), that is, substances recommended for prohibition of sale, supply or use on the basis of health concerns. This decision was made on the grounds of concerns about developmental toxicity of the phthalates in unborn and pre-pubertal children and consideration of use patterns.

Phthalates (as a class) are on the NICNAS candidate list of priority existing chemicals.

9.2.4. Occupational health and safety – risk characterisation

Based on the assessment of health effects, the following NOAELs are used in the risk characterisation:
- 39 mg/kg/day for liver and thyroid effects (X)
- 400 mg/kg/day for skeletal variations (Y), and
- 253 mg/kg/day for effects on offspring.(Z).

From the exposure estimates, the following margins of exposure (MOEs) are calculated for the various scenarios (MOE = NOAEL/internal dose).

	X	Y	Z
Workers – all scenarios	35.5	364	230

Taking into account that exposure estimates were worst-case, the risk of adverse health effects in workers exposed to the notified chemical is low.

9.2.5. Public health – risk characterisation

From the exposure estimates, the following MOEs are calculated for the various scenarios.

	X	Y	Z
Consumers - adult	6840	70 200	44 400
Consumers - children	1680	-	-

Taking into account that exposure estimates were worst-case, the risk of adverse health effects in consumers, including children, is very low. Due to doubts about the applicability of the

NOAELs for reproductive effects to children, these MOEs were not calculated.

10. CONCLUSIONS – ASSESSMENT LEVEL OF CONCERN FOR THE ENVIRONMENT AND HUMANS

10.1. Hazard classification

Based on the available data, the notified chemical is not classified as a hazardous substance under the NOHSC *Approved Criteria for Classifying Hazardous Substances* (NOHSC, 1999).

10.2. Environmental risk assessment

The chemical is not considered to pose a risk to the environment based on its reported use pattern.

10.3. Human health risk assessment

10.3.1. Occupational health and safety

There is Low Concern to occupational health and safety under the conditions of the occupational settings described.

10.3.2. Public health

There is No Significant Concern to public health under the end-use conditions described.

11. MATERIAL SAFETY DATA SHEET

11.1. Material Safety Data Sheet

The MSDS of the notified chemical provided by the notifiers were in accordance with the NOHSC *National Code of Practice for the Preparation of Material Safety Data Sheets* (NOHSC, 1994a). They are published here as a matter of public record. The accuracy of the information on the MSDS remains the responsibility of the applicant.

11.2. Label

The labels for the notified chemical provided by the notifiers were in accordance with the NOHSC *National Code of Practice for the Labelling of Workplace Substances* (NOHSC, 1994b). The accuracy of the information on the label remains the responsibility of the applicant.

12. RECOMMENDATIONS

REGULATORY CONTROLS

Use

- The notified chemical is not to be used in toys or food and medical contact materials.

CONTROL MEASURES

Occupational Health and Safety

- Employers should implement the following engineering controls to minimise occupational exposure to the notified chemical:
  - Enclosure of formulation processes as much as possible
  - Local exhaust ventilation where process not enclosed

- Employers should implement the following safe work practices to minimise occupational exposure during handling of the notified chemical:
  - Avoid generation of vapours and aerosols during transfer and mixing operations

- Employers should ensure that the following personal protective equipment is used by workers to minimise occupational exposure to the notified chemical:

- Overalls
- Chemical-resistant gloves (nitrile rubber or neoprene)
- Goggles or safety spectacles

Guidance in selection of personal protective equipment can be obtained from Australian, Australian/New Zealand or other approved standards.

- A copy of the MSDS should be easily accessible to employees.

- If products and mixtures containing the notified chemical are classified as hazardous to health in accordance with the NOHSC *Approved Criteria for Classifying Hazardous Substances*, workplace practices and control procedures consistent with provisions of State and Territory hazardous substances legislation must be in operation.

Environment

- The following control measures should be implemented by end users to minimise environmental exposure during use of the notified chemical:
    - Do not allow material or contaminated packaging to enter drains, sewers or water courses.

Disposal

- The notified chemical should be disposed of by either incinerating liquid wastes containing the notified chemical or landfill for PVC articles containing the notified chemical.

Emergency procedures

- Spills/release of the notified chemical should be handled by containment to prevent run-off sorbed onto a absorbent material (soil, sand or other inert material). Collect and seal in properly labelled containers for disposal.

12.1. Secondary notification

The Director of Chemicals Notification and Assessment must be notified in writing within 28 days by the notifier, other importer or manufacturer:

(1) Under Subsection 64(2) of the Act:
- if any of the circumstances listed in the subsection arise.

The Director will then decide whether secondary notification is required.

No additional secondary notification conditions are stipulated.

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