European Union Risk Assessment Report

2,2-BIS(CHLOROMETHYL) TRIMETHYLENE BIS[BIS(2-CHLOROETHYL) PHOSPHATE] (V6)

CAS No: 38051-10-4

EINECS No: 253-760-2

RISK ASSESSMENT

FINAL APPROVED VERSION

LEGAL NOTICE

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RISK ASSESSMENT

May 2008

Ireland (lead) and United Kingdom

FINAL APPROVED VERSION

Rapporteur for the risk assessment of V6 is Ireland (lead) and United Kingdom

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Final report:	**2008**

Foreword

We are pleased to present this Risk Assessment Report which is the result of in-depth work carried out by experts in one Member State, working in co-operation with their counterparts in the other Member States, the Commission Services, Industry and public interest groups.
The Risk Assessment was carried out in accordance with Council Regulation (EEC) 793/93[1] on the evaluation and control of the risks of "existing" substances. "Existing" substances are chemical substances in use within the European Community before September 1981 and listed in the European Inventory of Existing Commercial Chemical Substances. Regulation 793/93 provides a systematic framework for the evaluation of the risks to human health and the environment of these substances if they are produced or imported into the Community in volumes above 10 tonnes per year.
There are four overall stages in the Regulation for reducing the risks: data collection, priority setting, risk assessment and risk reduction. Data provided by Industry are used by Member States and the Commission services to determine the priority of the substances which need to be assessed. For each substance on a priority list, a Member State volunteers to act as "Rapporteur", undertaking the in-depth Risk Assessment and recommending a strategy to limit the risks of exposure to the substance, if necessary.
The methods for carrying out an in-depth Risk Assessment at Community level are laid down in Commission Regulation (EC) 1488/94[2], which is supported by a technical guidance document[3]. Normally, the "Rapporteur" and individual companies producing, importing and/or using the chemicals work closely together to develop a draft Risk Assessment Report, which is then presented at a meeting of Member State technical experts for endorsement. The Risk Assessment Report is then peer-reviewed by the Scientific Committee on Health and Environmental Risks (SCHER) which gives its opinion to the European Commission on the quality of the risk assessment.
If a Risk Assessment Report concludes that measures to reduce the risks of exposure to the substances are needed, beyond any measures which may already be in place, the next step in the process is for the "Rapporteur" to develop a proposal for a strategy to limit those risks.
The Risk Assessment Report is also presented to the Organisation for Economic Co-operation and Development as a contribution to the Chapter 19, Agenda 21 goals for evaluating chemicals, agreed at the United Nations Conference on Environment and Development, held in Rio de Janeiro in 1992 and confirmed in the Johannesburg Declaration on Sustainable Development at the World Summit on Sustainable Development, held in Johannesburg, South Africa in 2002.
This Risk Assessment improves our knowledge about the risks to human health and the environment from exposure to chemicals. We hope you will agree that the results of this in-depth study and intensive co-operation will make a worthwhile contribution to the Community objective of reducing the overall risks from exposure to chemicals.

[1] O.J. No L 084, 05/04/199 p.0001 – 0075

[2] O.J. No L 161, 29/06/1994 p. 0003 – 0011

[3] Technical Guidance Document, Part I – V, ISBN 92-827-801 [1234]

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Note regarding EU enlargement

Work on this risk assessment began before enlargement of the EU to 27 member states in 2006. All tonnage data, and references to the 'EU' in this risk assessment report, therefore refer to the former EU of 15 Member States.

Reasons for prioritisation for risk assessment

Chlorinated alkyl phosphate esters (particularly TCPP) were identified as possible substitutes for pentabromodiphenyl ether (pentaBDE) in the risk reduction strategy for that substance (EC 2001). A risk assessment of this group is therefore important as that substance has now been banned from the EU market. It has since become clear, from discussion with the industry, that in the EU these chemicals are not direct replacements for pentaBDE, and that changes in TCPP consumption are linked mostly with the decline in TCEP use and increase in the market for polyurethane (PUR) generally (pers. comm., 1st March 2004). They appear to be relatively persistent substances, and there is some human health concern (it was agreed to classify TDCP as Carc. Cat 3, R40 in 2005[4]).

Four substances in this group are listed in IUCLID, and were ranked according to the EURAM method (EU Risk Ranking Method); their priority scores (PS) are shown in **Table i**.

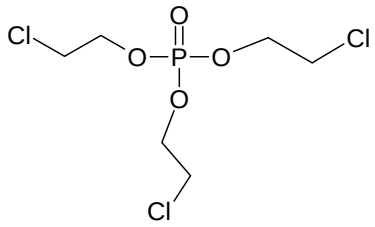
Table i Priority Scores of chlorinated alkyl phosphate esters

Name	CAS No.	Aquatic PS	Health PS
tris(2-chloroethyl) phosphate (TCEP)	115-96-8	15.3	61.2
tris(2-chloro-1-methylethyl) phosphate (TCPP)	13674-84-5	10.5	58.1
tris[2-chloro-1-(chloromethyl)ethyl] phosphate (TDCP)	13674-87-8	42.6	39.8
2,2-bis(chloromethyl)trimethylene bis(bis(2-chloroethyl)phosphate) (V6)	38051-10-4	34.2	39.8

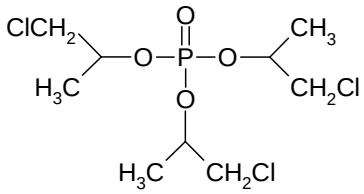
Note: A priority score of 100 is the highest priority.

The substance structures are shown below.

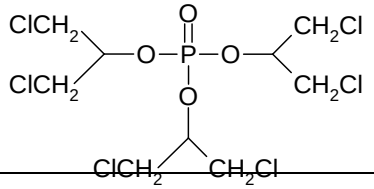
Tris(2-chloroethyl) phosphate (TCEP)



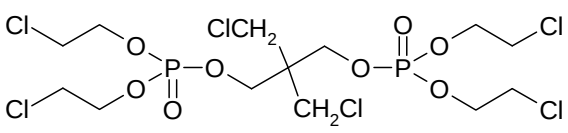
Tris(2-chloro-1-methylethyl) phosphate (TCPP)[5]



Tris[2-chloro-1-(chloromethyl)ethyl] phosphate (TDCP)



2,2-Bis(chloromethyl)trimethylene bis(bis(2-chloroethyl)phosphate) (V6)



[4] Commission Working Group on Classification and Labelling of Dangerous Substances Meeting on the Health Effects of Pesticides, Existing Chemicals & New Chemicals, November 14-18, 2005

[5] Structure shown is the main isomer present

A previous assessment in 1995 concluded that there was insufficient exposure and hazard information to perform a risk assessment for some of these substances ("The Flame Retardants Project Final Report, KEMI Report No. 5/96"). V6 in particular was data poor. A 1998 OECD SIDS assessment concluded that TCPP was a low priority for further work (the environmental exposure was said to be 'minimal') (UNEP, 1999). Nevertheless, the pentabromodiphenyl ether risk reduction strategy indicated that TCPP use is increasing owing to new technologies in both rigid and flexible foam systems. An in depth ESR assessment is a useful check of OECD conclusions.

The substances TDCP, TCPP and V6 are therefore good candidates for a concurrent assessment in view of their similar use pattern and structures. Other flame retardant substances (from Environmental Health Criteria document (WHO, 1998) or UK review) within this group that do not appear to be EU HPV substances are shown in **Table ii**. The substance with CAS number 6145-73-9 is an isomer of TCPP and is present in the commercial substance. The substance with CAS number 78-43-3 is an isomer of TDCP. Both of these CAS numbers may have in the past been erroneously applied to the respective substances.

Table ii Chlorinated alkyl phosphate esters which are not EU HPV substances

Name	CAS No.	Status	Data availability (according to EHC)	Use
tris(2-chloro-1-propyl) phosphate	6145-73-9	LPV	poor	rigid urethane foams
tetrakis(2-(chloroethyl)ethylene-diphosphate	33125-86-9	Believed not to be available[1]	poor	"plastics"
tris(2,3-dichloro-1-propyl) phosphate	78-43-3	Believed not to be available[1]	poor	"plastics"

Note: None of these substances are commercially available as such, or produced as isolated products, by EU manufacturers. These substances are not listed as either HPV or LPV substances by the ECB.

TCPP, TDCP and V6 all appear on the 4th ESR Priority List and their risk assessments have been completed by Ireland (leading the work and assessing human health) and the UK (leading on the environmental assessment). See HSA/EA 2008a and b for the other assessments. TCEP, from the 2nd ESR Priority List, has been assessed by Germany. There is some overlap between the substances in both properties and use pattern, and hence this risk assessment report contains references to the assessments of these other substances.

Physicochemical, environmental and ecotoxicological data for all four substances are presented together for comparison in Appendix C to this risk assessment.

0 OVERALL RESULTS OF THE RISK ASSESSMENT[6]

CAS Number: 38051-10-4
EINECS Number: 253-760-2
IUPAC Name: 2,2-Bis(chloromethyl) trimethylene bis[bis(2-chloroethyl) phosphate]

Environment

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all compartments for all local life cycle stages, and at the regional scale in all compartments.

V6 does not meet all of the PBT criteria (it meets the screening criteria for P or vP).

Human health

Human health (toxicity)

Workers

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all worker exposure scenarios in relation to all toxicological endpoints

Consumers

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all consumer exposure scenarios in relation to all toxicological endpoints.

Humans exposed via the environment

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

6 Conclusion (i) There is a need for further information and/or testing.
Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

Conclusion (ii) applies to both regional and local exposures in relation to all toxicological endpoints.

Combined exposure

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to combined exposure in relation to all toxicological endpoints.

Human health (physico-chemical properties)

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all endpoints.

CONTENTS

EUSES Calculations can be viewed as part of the report at the website of the European Chemicals Bureau: http://ecb.jrc.it

TABLES & FIGURES

Note: There are two further Annexes to this risk assessment report:

Confidential use pattern and exposure annex: this annex presents confidential details of the release scenarios for production and uses of V6 used in the risk assessment. It is available to competent authorities as part of the ESR review process, on request from the Rapporteur. This is referred to in the text as the 'Confidential Annex'.

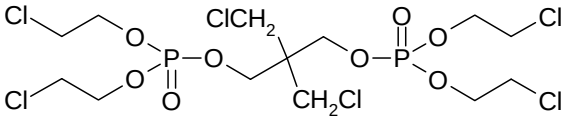
Confidential analytical data annex: this presents confidential details of the purity and impurities of commercially available V6 together with various spectra. It is available to competent authorities as part of the ESR review process, on request from the Rapporteur. This is referred to in the text as the 'confidential annex of compositional data'.

The Rapporteur can provide the confidential annexes on request, as appropriate.

1 GENERAL SUBSTANCE INFORMATION

1.1 IDENTIFICATION OF THE SUBSTANCE

CAS Number: 38051-10-4
EINECS Number: 253-760-2
IUPAC Name: 2,2-bis(chloromethyl) trimethylene bis[bis(2-chloroethyl) phosphate]
Molecular formula: $C_{13}H_{24}Cl_6O_8P_2$
Structural formula:



Molecular weight: 583.00
Synonyms: 2,2-Bis(chloromethyl)-1,3propanediyl bis[bis(2chloroethyl)phosphate
Tetrakis(2-chloroethyl) dichloroisopentyldiphosphate
Phosphoric acid, 2,2-bis(chloromethyl)-1,3-propanediol tetrakis (2-chloroethyl) ester
Phosphoric acid, 2,2-bis(chloromethyl)-1,3-propanediyl tetrakis (2-chloroethyl) ester
1,3-Propanediol, bis(2 chloromethyl) and bis(2 chloroethyl), phosphate (1:2)
Amgard V6 (trade name)
V6: this trade name is used throughout this report

Smiles notation: O=P(OCCCl)(OCCCl)OCC(CCl)(CCl)COP(=O)(OCCCl)OCCCl

1.2 PURITY/IMPURITIES, ADDITIVES

Purity

V6 is >90% pure (w/w).

Impurities:

Name	EINECS number	CAS number	% (w/w)
Tris(2-chloroethyl) phosphate (TCEP)	204-118-5	115-96-8	4.5 – 7.5

The full impurity profile of the commercial product V6 is confidential. Details are given in the confidential annex of compositional data.

It is known that TCEP is a hazardous substance, as assessed under the second Priority List. The environmental burden for TCEP associated with the production and use of V6 is assessed in the Risk Assessment Report for TCEP (BAUA, 2006).

It has been indicated (EUROPUR, 2005a) that V6 is now available with no TCEP impurity. It should be noted that no measured data relating to this new V6 product have been provided. The risk assessment therefore reflects the TCEP-containing substance. The possible significance of the presence of this impurity is assessed in the relevant sections (see section 3.3). Industry has recently indicated that purer forms of V6 (known as V66 and TL10) are now being produced and that these will replace the V6 currently marketed (pers. comm. 21st December 2006). The data presented in Chapters 1 to 4 refers to V6 of >90% purity as described above and not V66 or TL10.

Additives

A stabiliser is used. The Rapporteur considers that the additive would be insignificant in respect of the risk assessment of V6.

1.3 PHYSICO-CHEMICAL PROPERTIES

1.3.1 Summary of physico-chemical properties

The physico-chemical property values of V6 that have been reviewed and selected for use in the risk assessment are summarised in Table 1.1, and are justified below. The presence of TCEP will have an influence on the whole substance properties. Properties such as solubility, which are important for environmental modelling purposes, will relate to the main component only.

Melting / freezing

A modern GLP-compliant study (A1, 92/69/EEC) has been carried out (Paradis, 2002a). In full compliance with the test guideline, V6 was shown to have a freezing point <-50.5°C.

Boiling

An internal study gave a decomposition temperature of 252.29ºC (Regius, 2000).

A value of >200°C is reported in IUCLID, but there are no details available to substantiate this value.

The Syracuse Research corporation program MPBPVP, version 1.40, gives the result 480°C. This is above the realistic limit of atmospheric pressure measurements, of around 400°C, but is indicative of the approximate value that might be expected in the absence of decomposition. The relevant parts of the output of the program are:

```
Experimental Database Structure Match:  no data

SMILES : O=P(OCCCL)(OCCCL)OCC(CCL)(CCL)COP(=O)(OCCCL)OCCCL
CHEM   : Phosphoric acid, 2,2-bis(chloromethyl)-1,3-propanediyl tetrakis(2-
chloroethyl) ester
MOL FOR: C13 H24 CL6 O8 P2
MOL WT : 583.00
----------------------- SUMMARY MPBPWIN v1.40 --------------------

Boiling Point:  480.00 deg C (Adapted Stein and Brown Method)

-------+-----+--------------------+----------+---------
 TYPE  | NUM |  BOIL DESCRIPTION  |  COEFF   |  VALUE
-------+-----+--------------------+----------+---------
 Group | 12  |  -CH2-             |   24.22  |  290.64
 Group |  1  |  >C<               |    4.50  |    4.50
 Group |  6  |  -O- (nonring)     |   25.16  |  150.96
 Group |  2  |  O=P<              |  107.23  |  214.46
 Group |  6  |  -Cl (primary)     |   62.63  |  375.78
   *   |     |  Equation Constant |          |  198.18
=============+====================+==========+=========
RESULT-uncorr|  BOILING POINT in deg Kelvin  | 1234.52
RESULT- corr |  BOILING POINT in deg Kelvin  |  874.16
Special-Limit|  BOILING POINT in deg Kelvin  |  753.16
             |  BOILING POINT in deg C       |  480.00
-----------------------------------------------------
```

Density at 20°C

A modern GLP study according to the pycnometer method (A3, 92/69/EEC) has been carried out (Paradis, 2002b). In full compliance with the test guideline, V6 was shown to have a relative density of 1.473 ± 0.001.

An internal memorandum from the producer shows a relative density value of typical production V6 of 1.48 at 25.4°C.

Vapour pressure

A GLP vapour pressure study was submitted for review (Tremain, 2003). The test report states that an attempt to measure the vapour pressure using the vapour balance method was made, but the apparatus was glued up by test substance, preventing its correct operation. A QSAR estimation was performed using EPIWIN Version 3.05, modified Grain method, and is reported as 2.75×10^{-6} Pa at 25°C.

Measured data for TCPP and TDCP were used to validate the estimation. There was sufficiently close agreement between the measured vapour pressures for these two substances and the values estimated by the above method and the estimation was therefore considered to be acceptable.

It should be noted that the TCEP impurity present within V6 is expected to give rise to a higher 'bulk' vapour pressure than that of the pure V6 component. The 'bulk' value is relevant to certain occupational safety considerations, and the 'true' value is relevant to environmental risk assessment.

Surface tension

A modern GLP study (A5, 92/69/EEC) has been carried out (Paradis, 2002c). In full compliance with the test guideline, V6 was shown to have a surface tension of 53.9 ± 1.0 mN/m at 20°C (V6 at 209 mg/l).

This suggests that V6 has weak surface activity at the air-water interface, but not enough to indicate that an octanol-water partition study would be compromised by the formation of emulsions or microemulsions during the test.

Water solubility

A modern GLP study according to the shake-flask method (A6, 92/69/EEC) has been carried out (Groult, 2002a). In full compliance with the test guideline, V6 was shown to have a water solubility of 232 ± 4 mg/l at 20°C. The ± value is the standard deviation.

Octanol-water partition coefficient

A modern GLP study according to the shake-flask method (A8, 92/69/EEC) has been carried out (Groult, 2002b). In full compliance with the test guideline, V6 was shown to have a K_{ow} value of 676 ± 80 and a log K_{ow} of 2.83 ± 0.05 at 20°C. The ± values are the standard deviations.

Flash point (closed cup)

A reliable value of 191°C in accordance with method A9 of 92/69/EEC is available (Tremain and Bartlett, 1995), although information about the composition of the sample used was absent from the study report.

Flammability

The chemical substance of concern V6 has use as a flame retardant, it does not support combustion. In a fire, the mechanism of action of the flame retardant is primarily one by which phosphorus interferes with the combustion process, in the solid and gas phases, to produce a 'char' via formation of phosphoric acid. This char acts as a barrier and in turn prevents further oxygen reaching the site of combustion and the fire is 'starved' of fuel. The presence of the halogen – chlorine atoms – also aids this process in that they scavenge free radicals formed in the gaseous phase of the fire and consequently decreases the release of flammable volatiles.

The substance is not "extremely flammable" or "flammable" as referenced by the flash point (Method A9) and auto ignition temperature (Method A15).

Flammability (contact with water)

Based on the known chemical and physical properties of the substance V6 and its chemical structure, negative results are predicted for the following flammability test of Commission directive 84/449/EEC, hence it is considered justified to omit; Method A12 flammability in contact with moisture.

In contact with water or damp air, this substance will not react to produce hazardous gases.

A derogation in respect of this test was requested by industry and accepted by the TCNES.

Pyrophoric properties

The chemical substance of concern V6 has use as a flame retardant, it does not support combustion.

In a fire, the mechanism of action of the flame retardant is primarily one by which phosphorus interferes with the combustion process, in the solid and gas phases, to produce a 'char' via formation of phosphoric acid. This char acts as a barrier and in turn prevents further oxygen reaching the site of combustion and the fire is 'starved' of fuel. The presence of the halogen – chlorine atoms – also aids this process in that they scavenge 'free radicals' formed in the gaseous phase of the fire and consequently decreases the release of flammable volatiles.

The substance is not "extremely flammable" or "flammable" as referenced by the flash point (Method A9) and auto ignition temperature (Method A15).

A derogation in respect of this test was requested by industry and accepted by the TCNES.

Explosivity

Based upon the chemical structure of the substance V6 and the known synthetic route of manufacture via an exothermic chemical reaction, there is no indication that this substance is thermodynamically unstable.

The structure does not contain any of the more commonly known endothermic groups such as: azides, cyano-, dienes, acetylenic, peroxide or chlorate groups.

It is industry's opinion that this plus oxygen balance calculation supports the contention that this substance is unlikely to possess explosive properties.

A derogation in respect of this test was requested by industry and accepted by the TCNES.

Autoignition temperature

A reliable value of >400°C in accordance with method A15 of 92/69/EEC is available (Tremain and Bartlett, 1995), although information about the composition of the sample used was absent from the study report.

Oxidising properties

By reference to the structural formula, it can be seen that V6 contains highly electronegative atoms of chlorine, however the fact that these elements are only bonded to carbon and/or hydrogen renders it unlikely that this will confer oxidising properties on the substance. Furthermore, in order for a substance to have oxidising properties, a stable reduced form of the substance would need to exist, which is considered to be unlikely for V6.

Based upon information submitted in relation to A1 and A14 of Commission Directive 84/449/EEC and by analogy with similar existing chemicals, it is industry's opinion that the evidence supports the contention that the substance is unlikely to possess oxidising properties.

A derogation in respect of this test was requested by industry and accepted by the TCNES.

Henry's Law Constant

The Henry's Law constant has been derived from the values of vapour pressure and water solubility.

$$H = \frac{\text{Molecular weight} * \text{Vapour pressure}}{\text{Water solubility}}$$

A value of 6.45 x 10^{-6} Pa.m^3/mol is used in the risk assessment, based on EUSES adjustments of the properties for temperature dependence.

Table 1.1 Summary of physico-chemical properties chosen for use in the risk assessment

Property	**Value**	**Reliability**[1]	
Physical state	Liquid		
Freezing point	<-50.5	(1) valid without restriction	Paradis, 2002a
Boiling point	**252°C, (decomp.)** >200°C 480°C (estimated)	(2) valid with restrictions (4) not assignable	Submission made by industry.
Relative density	**1.473 at 20°C** 1.48 at 25.4°C	(1) valid without restriction (4) not assignable	Paradis, 2002b Industry internal memo
Vapour pressure	**2.75 x 10^{-06} Pa** at 25°C (estimated)	(2) valid with restrictions	Tremain, 2003
Surface tension	53.9 mN/m at 20°C	(1) valid without restriction	Paradis, 2002c
Water solubility	**232 mg/l at 20°C**	(1) valid without restriction	Groult, 2002a
Partition coefficient n-octanol/water (log value)	**log K_{ow} = 2.83**	(1) valid without restriction	Groult, 2002b
Granulometry	Not applicable		
Flash point	191°C	(2) valid with restrictions	Tremain and Bartlett, 1995
Autoflammability	>400°C	(2) valid with restrictions	Tremain and Bartlett, 1995
Flammability	No data; no test required		Not expected to be flammable. Derogation accepted by TC NES
Explosive properties	No data; no test required		Not expected to be explosive. Derogation accepted by TC NES
Oxidizing properties	No data; no test required		Not expected to be oxidising. Derogation accepted by TC NES
Viscosity	2600 cps at 25.4°C	(4) not assignable	Internal producer memorandum
Henry's Law constant	6.45 x 10^{-06} Pa.m^3/mol at 25 deg C	(2) valid with restrictions	By calculation from VP (calculated) and WS results

[1] Klimisch code

1.4 CLASSIFICATION

1.4.1 Current classification

Classification as not dangerous for the environment (not classified) was agreed at EU level in 2005[7].

1.4.1.1 Basis of classification for the environment

Data presented in this report are consistent with no classification for the environment. The fish, *Daphnia* and algae acute E(L)C_{50} values all fall in the range 10 to 100 mg/l, and there is no evidence of ready degradability in standard tests. However, R52-53 is not applicable for V6 for the reasons outlined below:

- The measured acute data show a similar level of sensitivity across the three taxonomic groups.
- Reliable chronic NOECs are available for invertebrates and algae and both are above 1 mg/l (>3.7 and 10 mg/l respectively). The acute-to-chronic ratios are ≤11.4 and 3.5 respectively.
- The tests have been conducted well below the water solubility limit (232 mg/l), and the low log K_{ow} (2.83) does not suggest that the substance will accumulate over long periods (in line with measured BCF data for analogous substances). The acute toxicity therefore probably reflects the effect of uptake at steady state (i.e. not just partial uptake).
- There is reasonable agreement between the measured acute fish LC_{50} (52 mg/l) and QSAR predictions (17-32 mg/l, using SRC ECOSAR with measured physicochemical data entered). The substance therefore appears to be behaving in a predictable way.
- There is no indication of neurotoxicity in this chemical class from mammalian and avian studies.
- There is therefore no reason to suppose that there will be a significant difference in chronic effects in fish compared to the other taxa.
- Applying the worst-case acute-to-chronic ratio for *Daphnia* to fish would give a NOEC of approximately 4.5 mg/l. This is very similar to the QSAR estimate of 7.0 mg/l (using SRC ECOSAR with measured physicochemical data entered).
- The acute-to-chronic ratio would be above 50 if the fish NOEC were below 1 mg/l, which is clearly out of line with the observations for *Daphnia* and algae.

Given these considerations it is unlikely that V6 would be chronically toxic to fish at <1 mg/l and testing to confirm this assertion could not be justified on animal welfare grounds. V6 should not therefore be classified.

[7] Commission Working Group on the Classification and Labelling of Dangerous Substances Meeting on Environmental Effects of Existing Chemicals, Pesticides & New Chemicals September 28-30, 2005

1.4.2 Proposed classification

Based on the data presented in this risk assessment report, it is proposed not to classify V6 for human health effects.

V6 that is currently placed on the market contains 4.5 – 7.5% TCEP as an impurity. The human health classification for TCEP was agreed at EU level in 2005 as T; Repro. Cat 2 R60; Carc Cat 3 R40; R22[8]. Therefore, marketed V6 will also have to be classified as Category 3 carcinogen, R40 and Category 2 for fertility, R60, if its TCEP content exceeds 1.0% and 0.5%, respectively. Industry has indicated that purer V6 (known as V66 and TL10) are now being produced and that these will replace the V6 currently marketed (pers. comm. 21st December 2006).

[8] Commission Working Group on the Classification and Labelling of Dangerous Substances Meeting on the Health Effects of Pesticides, Existing Chemicals & New Chemicals November 14-18, 2005.

2 GENERAL INFORMATION ON EXPOSURE

It should be noted that there is just one EU producer of V6. Therefore, only very limited information on the life cycle in the EU has been included in this assessment report on the grounds of confidentiality. Further information on the life cycle is given in a Confidential Annex, which also describes how research into the life cycle was carried out.

Tonnages and environmental concentrations derived from them have not been corrected for purity of the substance.

The producer has participated in the industry consortia working on the risk assessments for TCPP and TDCP. The consortia assisted in the early stages of this assessment by sending out a questionnaire to users of V6. The results were collated confidentially by the Rapporteur. More recently, the consortia have assisted with further consultation with the confidential downstream users.

Relationship between TCPP, TDCP and V6

As noted in the Foreword, the substances TDCP, TCPP and V6 are good candidates for a concurrent assessment in view of their similar use pattern and chemical similarity. All three substances are used predominantly in various types of polyurethane foam applications in the EU (>97.5% of TCPP; >85% of TDCP and >95% of V6). Chlorinated alkyl phosphate esters (particularly TCPP) were identified as possible substitutes for pentabromodiphenyl ether (pentaBDE) in the risk reduction strategy for that substance (EC 2001). However it has since become clear, from discussion with the industry, that in the EU these chemicals are not direct replacements for pentaBDE, and that changes in TCPP consumption are linked mostly with the decline in TCEP use and increase in the market for polyurethane (PUR) generally (pers. comm., 1st March 2004). As discussed in section 2.1.2, consumption levels appear to have stabilised in recent years; this risk assessment represents a realistic upper limit of EU production and consumption and significant increases are not anticipated in the near future.

2.1 PRODUCTION

2.1.1 Production processes

V6 is produced from pentaerythritol, phosphorus trichloride, chlorine and ethylene oxide (Marcenac 2002).

The process is carried out by adding a polyhydric alcohol to phosphorus trichloride in a carrier solvent in the presence of a catalyst. The crude product is then washed to remove acidic impurities, dehydrated and filtered. The product is stabilised before it is packed into drums or transferred to road tanker (pers. comm. 30th April 2001, Rhodia).

2.1.2 Production capacity

There is only one producer of V6 in the EU (Albemarle (whose V6 business was owned earlier in the ESR process by Rhodia and previously Albright and Wilson)). Total EU production in 2000 was less than 5,000 tonnes, with production taking place at one site in the UK (pers. comm. 30th April 2001, Rhodia). Some of the V6 produced in the EU is exported

(pers. comm. 22nd August 2002, Rhodia). Between 1999 and 2003, production has fluctuated slightly but the total EU sales tonnage has remained reasonably stable within approximately 10%. The EU consumption used in the risk assessment represents the upper limit of sales in the five year period for which data are available. The Rapporteur has no reason to anticipate significant tonnage increases in the near future, based on industry information and general research.

There are understood to be no imports of V6 into the EU. In respect of automotive and furniture use, by far the most significant applications of V6, it is known that there is some import/export of finished articles, but overall the EU is a net exporter. There is no specific information regarding the movements of V6-containing furniture and vehicles. It is possible that finished goods containing V6 in rebonded foam may be imported into the EU. This is not accounted for in the assessment as there is too little information, although it is not likely to be significant.

The production of V6 is increasing by around 10% per annum. However, most of this increase is accounted for by markets outside the EU (pers. comm. 22nd August 2002, Rhodia), and therefore the EU consumption is stable.

2.2 USES

2.2.1 Introduction

V6 is an additive flame retardant, i.e. it is physically combined with the substrate being treated rather than chemically combined. The amount of flame retardant used in any given application depends on a number of factors, such as the flame retardancy required for a given product, the effectiveness of the flame retardant and any synergist within a given polymer system, the physical characteristics of the end product (e.g. colour, density, stability, etc.), and the use to which the end product will be put.

Less than 2,500 tonnes of V6 were consumed in the EU in the year 2000. Over 95% was used in the production of flexible polyurethane (PUR) foam, mainly for use in the automotive industry. V6 is not used in rigid foams owing to cost considerations (Pers. comm. 16th October 2001).

V6 is a speciality product for use in the same market as the flame retardants TCPP and TDCP. Owing to the price differential between these products, V6 is only used in those applications where a more efficient flame retardant is required to meet specific standards (pers. comm. 19th March 2002). V6 is particularly suited to automotive and furniture applications where resistance to migration upon ageing is a requirement of the flammability standards used (Rhodia, 2000).

The life cycle stages considered in this assessment are reported in **Table 2.1** and shown in **Figure 2.1**. Further information including information on the confidential life cycle stages is given in the Confidential Annex. Given that the only producer has provided a detailed breakdown of tonnage, the life cycle is well defined.

Table 2.1 Use pattern for V6

Ref. Env[1]	Ref. HH[2]	Industry Category	Use category	Description	Percentage of total use
A	5	11	22	PUR foam for use in automotive applications	50% to 75%
B	2, 3	11	22	PUR foam for use in furniture	25% to 50%
C	-	Confidential	22	Confidential	<5%
D	-	Confidential	22	Confidential	<5%
E	-	Confidential	22	Confidential	<5%
F[3]	-	Confidential	22	Confidential	<5%
G	4	11	22	Rebonding of flexible foam	This is a form of recycling
H	-	11	22	Recycling as loose crumb	This is a form of recycling
Total					100%

Industry Category 11 = polymers industry Use category 22 = flame retardants and fire preventing agents

Notes:

1 – Reference letter used in the Environmental risk assessment

2 – Reference number used in the Human Health risk assessment

3 – Note that for application F the producer company has confirmed that this application of V6 is not applicable in Europe (pers. comm., 11th October 2005). The information about this application obtained in the original survey probably related to customer trials.

Product Register Data

Data from product registers have been provided by Denmark, Sweden and Switzerland. This information is summarised in **Table 2.2**, together with data from the SPIN database (data about the use of substances in Norway, Sweden, Denmark and Finland). The product register data do not provide any new information concerning uses of V6.

Table 2.2 Product register and SPIN data

Country	Year	Tonnage	Number of Products	Concentration*	Description
Denmark	-	Confidential	1	60% to 100%	Industry group: manufacture of rubber and plastic products. Product types: Foaming agents
Sweden	1999	<10	2	-	-
	2000	0	3	-	Use: raw material (fire prevention additive in plastics). Trade code: Industry for plastic products. No consumer products.
Switzerland	-	-	1	90%	Commercial product

* Intervals used in the Danish Product Register are 0-1%, 1-5%, 5-10%, 10-20%, 20-50%, 50-80% and 80-100%. If limited data indicate confidential information, broader intervals are used.

A life cycle assessment study by Simonson *et al* (undated) investigated emission of pollutants associated with different life cycle stages of sofas. Three sofas were tested. The purpose was to assess pollutant emissions at all stages of the sofas' life cycle, including in the event of fire. Emissions of the flame retardant (FR) itself were not investigated. The information and assumptions regarding the life cycle are useful for comparison with the assessment made in

the current risk assessment. A schematic representation shows the life cycle stages of relevance for the flame retardant as:

- flame retardant production
- material (i.e. foam) production
- production of primary product (i.e. item of furniture)
- use of primary product (i.e. in-service)
- recycling processes (see note below)
- incineration
- landfill/landfill fire
- fire of primary products.

Service lives of ten and fifteen years were used in the LCA, though this appears to have been used as a half-life in the assessment. The mode of recycling is interesting; the schematic indicates mechanical/feedstock recycling but elsewhere in the report the only route of 'recycling' investigated for releases is for heat recovery (i.e. incineration).. Mechanical/feedstock recycling is not believed by the Rapporteur to be a valid route and is not assessed in this RAR.

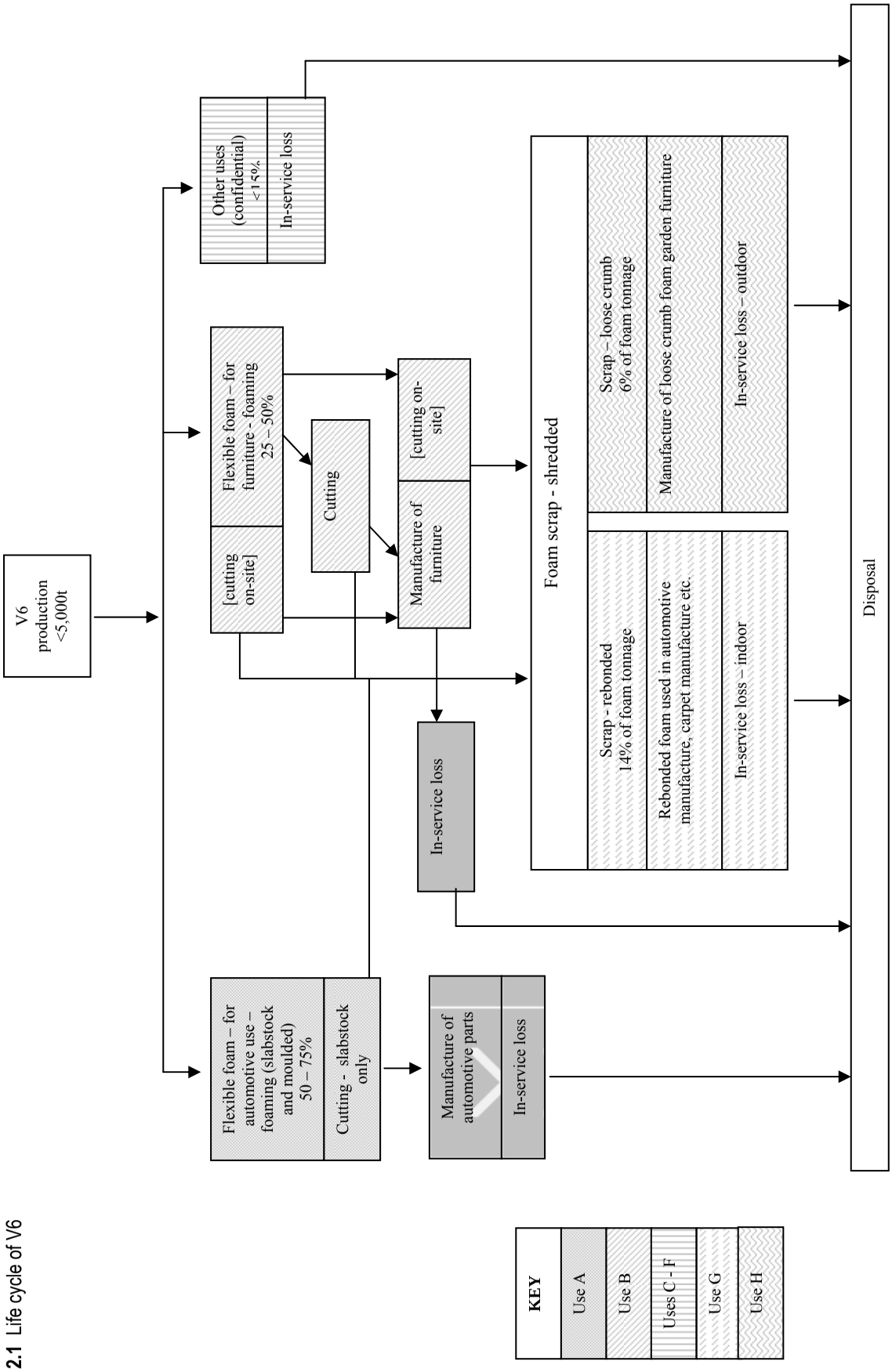


Figure 2.1 Life cycle of V6

2.2.2 Scenarios

A longer, more general, discussion of relevant industries is provided in Appendix A.

2.2.2.1 Flexible foam

2.2.2.1.1 Flexible foam production

Flexible foams are produced by pouring the blend of the two raw materials (polyol containing additives including flame retardants such as V6, and di-isocyanate) onto a rolling conveyor belt (slabstock foam) or into a mould (moulded foam). Moulded foam is mainly used in the automotive industry (seat cushions, headrests), with some use for office furniture. Slabstock foam is cut in accordance with the specifications demanded by customers, the main application being for furniture (EC, 1997). Slabstock foams are also used for rear car seats and fabric lining for seat covers and roofing in cars. The market for slabstock foams is around seven times larger than the market for moulded foams for car seats (Mark and Kamprath 2000).

Note that the PUR industry uses the term "conversion" to describe the cutting of foam. In the Emission Scenario Document (ESD) for Additives used in the Plastics Industry (OECD, 2004), however, the term "conversion" is used to describe manufacture of products (i.e. foaming). For the purposes of clarity in this assessment the term "conversion" is used only as defined in the ESD.

V6 is used in flexible slabstock polyether and moulded foams (Rhodia 2000).

For further information on slabstock foams, moulded foams and polyether versus polyester foams, refer to section 1 of the Life Cycle Annex. The majority of the description of foam production presented in this section is taken from the ESR risk assessment for Pentabromodiphenyl ether (EC, 2000).

2.2.2.1.2 Cutting

Blocks of PUR foam generally have to be cut into the required size/shape of the final product. This operation usually occurs after the blocks have cured and cooled. For some applications (e.g. seats for office furniture), PUR foam can be produced in a mould of the desired shape and so cutting is not required.

When fabricating a block, the first stage is usually to trim the sides and top of each block to give a block with uniform faces. This is carried out using vertical and horizontal band knives. The amount of scrap foam removed from the block depends on the size of the block and the type of machine used to produce it. For instance, it has been estimated for a block of foam of density 22 kg/m ^{3} and having dimensions 2 m x 1.5 m x 1 m, the scrap foam generated from trimming will vary from around 15% to <5%, depending on the machine used. The highest wastage figures are from "domed-topped" blocks made in machines with unrestrained tops, with lower figures being obtained from machines/processes designed to minimise the formation of a domed top (Woods, 1982).

Blocks are sold to "converters" (hereinafter called "cutters") who cut these into the required size and shape. Foam producers operate their own cutting facilities, but also sell to a large number of other cutters, most of which (in the UK at least) are small, privately owned companies. In the UK alone there are hundreds of foam cutters (pers. comm.[9]). Cutting is carried out using band saws. Dusts are collected at the point of cutting by extractors attached to the blade. Hot wire cutting methods are not used any more in this industry (pers. comm., 2nd July 2004).

Overall, for any flexible slabstock foam, scrap foam from cutting totals around 20% of the final product (pers. comm., not attributable):

- half (10%) is lost in terms of skins when the block is first cut (when a block is made it has a skin like a loaf of bread which needs to be removed)
- the other half (10%) comes from cutters for example when cushions are cut. In this regard not all are cushions are squares, for example some are circles, and therefore generate more scrap.

The collection rate for scrap produced by cutters is "very high" as rebonding facilities pay for the scrap foam, the alternative being for the cutter to pay for disposal of the foam (pers. comm., not attributable). Scrap foam may be sold as second quality foam, or will be granulated (to form 'crumb') and made into rebonded foam.

2.2.2.1.3 Furniture manufacture

Cutters sell foam of the required size and shape to furniture makers, i.e. furniture makers do not need to re-cut the foam. That said, some foam is sold directly to furniture makers who cut their own foam. In this regard end product manufacturers may carry out cutting of polyurethane foam (EC 2000). In contrast some cushions arrive at the furniture manufacturer pre-covered with polyester fibre (pers. comm., not attributable).

Flame bonding is a method for laminating polyurethane foam sheet to materials such as textiles. The foam sheet is passed across a propane/air flame and the foam is then brought together with the textile material between pressure rolls. The flame treatment generates a chemically active surface which facilitates bonding to the textile substrate (HMIP, 1995). The high temperature used in flame bonding leads to emission of volatile organic compounds (VOCs), including benzene, together with hydrogen cyanide and particulate matter as a result of pyrolysis. Free di-isocyanates including toluene di-isocyanate (TDI), are also present in the fumes which are given off in the process, as a result of oxidation and chain scission (HMIP, 1995). Flame lamination companies within the EU have to comply with national emission regulations and most facilities achieve these requirements by the use of appropriate attenuation techniques. Activated carbon scrubbing techniques are often used to meet the more stringent national emission legislation (pers. comm. 22nd January 2007).

[9] In all cases of a non-attributed pers. comm. it is not possible to reveal the source of the data. The information was provided by industry during the consultation process.

2.2.2.1.4 Recycling of PUR foams

Rebonding

In a typical process, foam scrap is fed through a shredding machine and then into a granulator. The granules are screw conveyed into a vessel where the material is sprayed with pre-polymer and mixed to ensure a thorough coating. The coating granules are then screw conveyed into a rectangular or circular moulding press where the mix is compressed and consolidated as the pre-polymer cures. Curing is facilitated by steam injection (HMIP 1995). The condensate is ultimately removed under vacuum and vented to the air (pers. comm. 29th April 2004). The rebonded blocks are removed and allowed to stand in order to cool (HMIP, 1995). The foam product is then either cut (converted) in the usual way (EUROPUR, 2005a), or can be "peeled" from the block at the desired thickness and a suitable backing is then applied (EC, 2000).

It has been reported that V6 is used as flame retardant for virgin and bonded flexible urethane foam (Ash 1997). While V6 will be present in off-cuts of slabstock foam which undergo re-bonding, owing to cost considerations it is believed that V6 would not be added directly to the re-bonding process.

A survey carried out by EUROPUR (pers. comm. 7th December 2005) accounted for approximately 45 kilotonnes of rebonded foam produced in the EU, and it was estimated that approximately 60 kilotonnes are rebonded in total. A high proportion of this is produced in the UK (approximately 22 kilotonnes). Across the EU, only a low proportion of this will contain flame retardants. Cheaper non-FR foam trim can be obtained exclusively but it is likely that a site rebonding FR-PUR will also be handling non-FR foam. It has been estimated that a typical site might rebond 3-5 kilotonnes of foam per year in total (pers. comm. 29th April 2004).

Use of Rebonded Foam

The relative high density and resilience of rebond make it suitable for applications including vibration sound dampening, sport mats, cushioning, packaging and carpet underlay and new applications are constantly being developed (ISOPA 2001a). In cars, rebond can be used for sound insulation, for example under the carpet in the boot. In cushioning, a strip of re-bonded foam is used along the front of some cushions on the basis that it is more hard wearing. There is also some use in office furniture (ISOPA 2003).

Re-bonders in mainland Europe now handle the two lines of scrap together (the flame retarded foam from the UK, and foam produced elsewhere in Europe, a smaller proportion of which contains flame retardants), avoiding the need to clean out the machines in between a run of each type (pers. comm., not attributable).

In the risk assessment of pentabromodiphenyl ether (EC 2000), losses from re-use or disposal of scrap foam were not separated from losses during use and disposal of finished articles. In this risk assessment, the rates of release from the two types of foam will be evaluated in the same way.

Loose crumb

Shredded scrap foam is used directly for some applications. This is referred to as 'loose crumb' and is used in deep-buttoned soft-cushions for garden furniture and in some low-grade

furniture applications. In Europe, the major use of loose crumb is reported to be in garden furniture. The foam industry has indicated that the market for reuse of scrap foam in this way is small and is deteriorating (Bürgi, 2002). To give a realistic worst case, and in the absence of firm information, it is assumed in this assessment that 70% of the scrap foam remaining in the EU will be rebonded and 30% will be recycled as loose crumb[10].

While all such furniture previously was returned to the UK to meet the demand generated by UK regulations, 50% now stays in mainland Europe. For the purposes of this risk assessment it is assumed that 75% of scrap foam generated in the EU remains here, with the remaining 25% being exported to the US. Thus it is assumed that 75% of the V6 in scrap foam remains in the EU. The risk assessment is not very sensitive to this assumption, because daily use rate at the main site is not affected by the total. To assess the reasonable worst case (since the rate of loss is higher from outdoor service), it is assumed that all loose crumb is used in garden furniture.

For a full summary of recycling options for PUR foams, including further details on the rebonding process and use of rebonded foam, refer to section 2 of the Life Cycle Annex.

2.2.2.1.5 Automotive use: Use A

Production and use

Data have been provided by the producer of V6 and by companies using V6 in the production of foams for automotive applications. The number of sites using V6 is known.

Data provided by a foam producer indicates that V6 is used in the production of foams for use with textiles in the manufacture of car seat, door panels, soundproofing, head liners and cushions. In this regard, most front car seats are made from cold cure moulded foams that (as indicated in section 1 of the Life Cycle Annex) do not contain flame retardants. To provide the required level of flame retardancy, the textile covering of such seats are treated with flame retardants (pers. comm. 31st July 2002, producers and downstream users). Head liners used in the roofs of cars are made from slabstock foam.

In the absence of any specific information it is assumed that half of the V6 used in automotive applications is associated with slabstock foams, and that the remainder is used in moulded foams. Hence, only half of the automotive foam containing V6 is subject to cutting, with associated scrap proceeding into rebonding and loose crumb applications.

For further information on use of V6 in automotive applications, refer to section 3 of the Life Cycle Annex.

Rebonding and loose crumb

As discussed in section 2.2.2.1.4, the vast majority of scrap slabstock foam produced during cutting is rebonded or recycled as loose crumb. On average 20% of foam produced will end up as scrap. It is assumed that 75% of the scrap foam generated in the EU remains within the

[10] Note: industry (EUROPUR) has indicated that 30% recycling in the form of loose crumb may be an overestimate (pers. comm., 27th March 2006). Therefore it is possible that a higher proportion may be rebonded. However, due to the similarities between the release levels from loose crumb and rebonding processes, and the similarity of site distribution (information provided in the EUROPUR survey) (pers. comm. 7th December 2005), this has no significant implications for the risk assessment at the processing stage.

EU (and therefore is relevant to recycling in the risk assessment); the remainder is assumed to be exported.

As V6 is used in some slabstock foams for automotive applications, some of the scrap foam from the cutting operations will be rebonded or recycled as loose crumb. Thus it is assumed that 7.5% of V6 will be recycled in these ways (i.e. 50% use in slabstock x 20% waste x 75% remaining in the EU). In the absence of firm information, it is assumed that 70% of such scrap will be rebonded and 30% recycled as loose crumb[9].

Imports and exports of motor vehicles and parts

The level of automotive imports and exports into the EU were examined to indicate whether additional V6 could be entering via this route. European Commission data (EC 2002) indicate that in 1999, EU imports of cars, light commercial vehicles and components were worth EUR 46.58 billion. During the same period, the EU exported the equivalent of EUR 61.35 billion. Thus there was a net trade surplus for the EU with the rest of the world amounting to EUR 14.8 billion in 1999. On this basis it could be argued that there is likely to be a net export from the EU of V6 in automotive goods. To be conservative, no attempt has been made to account for this trade in the assessment.

End of Life

The risk assessment allows for some landfilling of end-of-life automotive foam. Some will be incinerated for energy recovery, though the proportions are not clear.

For further information on end-of-life, the current and future situations for automotive plastics, refer to section 3 of the Life Cycle Annex.

2.2.2.1.6 Furniture foams: Use B

Production and Use

V6 is used in the manufacture of furniture in those applications where the less expensive and more volatile flame retardants TCPP and TDCP alone cannot meet the required standards, which vary globally. In this regard the producer reports that V6 offers "unrivalled resistance to migration on ageing providing the opportunity for foams to be developed which meet California Bulletin 117 and UL94 HF1 requirements" (Rhodia, 2000). V6 can be combined with either TDCP or TCPP in order to reduce formulation cost (Rhodia, 2002).

California Bulletin of Home Furnishings 117 is a US standard applying to public buildings and to domestic situations. Some companies operating in Europe choose to adopt this standard (e.g. US hotel chains). The standard requires that foam is heat aged at 104^{o}C for 24 hours. TCPP cannot meet this heat-ageing requirement owing to its volatility. TDCP can meet the standard in some circumstances, but in others V6 is required (pers. comm. 19th March 2002, Rhodia). These observations support the view that losses from foam must be related to volatility.

ISOPA data (undated) indicates that 400 foamers/moulders are involved in the production of furniture and bedding from PUR foam in Europe each year, consuming 530,000 tonnes of polyurethane. Given the price and specialist nature of V6, only a small number of foamers

will use this flame retardant. Data have been provided by the producer of V6. The number of sites using V6 is known.

Rebonding and loose crumb

As discussed in Section 2.2.2.1.4, the vast majority of scrap foam from foam cutting and furniture production is rebonded or recycled as loose crumb. On average 20% of foam produced will end up as scrap. It is assumed that 75% of the scrap foam generated in the EU remains within the EU (and therefore is relevant to recycling in the risk assessment); the remainder is assumed to be exported.

It is thus assumed that 15% of V6 will be recycled in these ways in the EU (i.e. 20% scrap x 75% remaining in the EU). In the absence of firm information, it is assumed that 70% of this scrap foam is rebonded and 30% recycled as loose crumb[9].

Imports and Exports of Furniture into the EU

Imports of furniture into the EU were examined to identify whether additional V6 may be entering the EU via this route. Imports of upholstered furniture from outside the EU-15 amounted to 848 million Euros in 1997. Most of these were sourced from Poland (more than 50%). Imports have been increasing continuously since 1993 to satisfy a growing internal demand. Extra-European exports of upholstered furniture stood at 1.17 billion Euro in 1997, an increase of 25% on the previous year. Two countries accounted for more than half of these exports: the United States (39%) and Switzerland (15%) (UEA, 2002). Thus there was a net trade surplus for the EU with the rest of the world amounting to 322 million Euro in 1997.

On this basis it could be argued that there is likely to be a net export from the EU of V6 in furniture products, especially as the main export market is the US and V6 is used to meet the US standard (California 117). To be conservative, no attempt has been made to account for this trade in the assessment.

End of Life

At the end of its useful life, furniture in the EU is sent to landfill or incinerated. Most furniture in the UK goes to landfill at the end of service life (pers. comm., not attributable). In this regard the Landfill Directive (1999/31/EC) calls for decreasing amounts of waste to be sent to landfill in all EU countries. As far as possible, waste is to be used for energy recovery with another potentially important route in the future being gasification of plastics including PUR (pers. comm. 31st July 2002).

2.3 TRENDS

The above discussion, and that described in the Life Cycle Annex, has identified the following trends:

- a trend away from exporting scrap foam to the US
- a trend towards increased recycling and recovery of PUR foams in general and towards automotive foams in particular, driven by the End of Life Vehicles Directive (ELV) (see the Life Cycle Annex)

The most important of these trends is the latter. The ELV Directive will necessitate large increases in recycling and recovery rates for automotive PUR.

2.4 LEGISLATIVE CONTROLS

The use of the flame retardant V6 in automotive and furniture applications is driven by fire safety standards. The key standards, applicable globally, are:

- the Federal Motor Vehicles Safety Standard No. 302 for automotive applications (see Section 2.2.2.1.5)
- the California Bulletin of Home Furnishings 117 for furniture applications (see section 2.2.2.1.6).

In the UK there are The Furniture and Furnishings (Fire) (Safety) Regulations 1988 (SI 1988 No. 1324) as amended by The Furniture and Furnishings (Fire) (Safety) (Amendment) Regulations 1989 (SI 1989 No. 2538). The equivalent legislation in Ireland is the Industrial Research and Standards (Fire Safety) (Domestic Furniture) Order 1995 (S.I. 316 of 1995).

While these regulations are important in driving the market for TCPP, they are not important for V6; V6 being too costly a flame retardant compared with TCPP. (Further information on the UK regulations can be found in the risk assessment for TCPP, see HSA/EA 2008a).

There is currently no harmonised set of standards for fire safety testing of furniture in the EU.

For the parts of the life cycle associated with polyurethane foaming, emissions of V6 will be restricted. All vapours produced in this reaction must be extracted, because potentially dangerous di-isocyanate vapours are produced in the course of the polymerisation. Release of di-isocyanate is highly controlled under a range of international and national regulations. More information is given in the risk assessment report for methylene di-isocyanate (Federal Public Service for Public Health, Safety of the Food Chain and the Environment, 2003).

In respect of flame retardants used in the manufacture of toys, European Standard EN 71-9 (Safety of Toys – Part 9: Organic Chemical Compounds – Requirements) states that certain specified flame retardants, including TCEP, which are used in textiles of toys and accessible components of toys intended for children under 3 years of age should not be found above the limit of quantification of the test method and therefore should not be detected in toys. More generally, Directive 88/319/EEC specifies that toys must not contain dangerous substances or preparations within the meaning of Directives 67/548/EEC and 88/379/EEC (repealed by 1999/45/EC) in amounts which may harm the health of children using them. V6 is not specifically covered by this legislation beyond this general aspect.

3 ENVIRONMENT

3.1 ENVIRONMENTAL EXPOSURE

Consultation with downstream users is complicated by the fact that V6 is only supplied by one producer and its market data are confidential. However, detailed consultation has not been necessary because the producing company co-operated fully with the Rapporteur and provided detailed information about the life cycle for the substance. This included information on the number and location of downstream users associated with each life cycle stage. Associations representing the downstream users have also been involved with the consultation.

In the assessment of some life cycle stages, it has been necessary to use appropriate defaults in order to characterise a reasonable worst-case release pattern. Site-specific data have been used, where available, to refine the exposure assessment. Defaults set out in this document originate in the A-tables of the Technical Guidance Document (TGD) (EC 2003), or the Emission Scenario Document (ESD) for Additives Used in the Plastics Industry (OECD, 2004). For plastics applications, the ESD defaults override those presented in the A-tables. The ESD gives rates of release only to air and wastewater. The TGD defaults also include rates of release to industrial soil. Exposure of industrial soil to V6 has not been evaluated in this risk assessment, since 1) the substance is subject to relatively high levels of control on industrial sites, and 2) a rate of release from handling is already calculated in accordance with the ESD. However, exposure of agricultural or grassland soil is foreseeable as a result of weathering and wear in service or at disposal, or by spreading of sewage sludge. This is described in section 3.1.5.1.

Most release rates for foam-related stages originate from new models, described in a report (Appendix B) which brings together theoretical modelling with the results of various published studies of releases of flame retardants (FRs) from foams.

EUROPUR has sponsored a study to investigate volatile losses of TCPP from small pieces of PUR foam at ambient temperature (Hall 2005). Pieces of foam were spread out on a tray under conditions of controlled air flow. The TCPP contents of the pieces were measured analytically over time. Three sizes of fragments of foam were studied in separate runs. Further details are available in Appendix B. A key finding from experimental data is that initial rapid losses occurred followed by approach to a consistent plateau at around 40% loss, suggesting that only 40% of TCPP in the matrix is available. Losses were fastest from the smallest pieces, but the plateau was the same in each case. Therefore, as a consequence of this study, percentage loss figures associated with possible overall volatile releases from foams or foam particles have been multiplied by a correction factor, representing that which is ‘available’ for release, i.e. is not very strongly bound. The available fraction is estimated to be 0.4 for TCPP, based on the experimental data. For V6, which is a more adsorbing, higher molecular weight molecule containing an additional phosphate group and proportionately more chlorine, it is realistic on grounds of structure and properties that a smaller proportion will be available for release. TCPP is not used in automotive applications due to a phenomenon called fogging where a film forms on the interior glass of the car (Patel, 2001). The phenomenon of fogging is not seen with TDCP and V6. V6 also has a much lower modelled level of volatility than TCPP, expressed as rate of loss. These factors have been

used to estimate that the available fraction for V6 is 10% at the most, although it could be lower than that[11].

The B-tables and ESD site-size methods are not used in most cases; sufficient information was available about specific aspects of the market to allow representative fractions in the main region and fractions of the main local source to be estimated. The number of days is then evaluated to give a reasonable operational rate given the size of the main site.

In this report and the Confidential Annex, 'R' refers to the fraction of total tonnage in the main region, and 'FMLS' is the fraction of the main local source, i.e. the fraction of the regional tonnage associated with the largest site. In accordance with the TGD definitions, a 'region' is a semi-industrialised European area with surface area 40,000 km^2, with standard default environmental properties and a population of 20 million people. All the figures are based on the most recent edition of the Technical Guidance Document (EC, 2003).

Note regarding environmental releases: There are no reasons to suspect these substances contribute directly to dioxin formation (e.g. there are no aromatic groups). Like all organohalogens the possibility exists that they could act in an indirect way as a source of halogen in high temperature processes. Since most incinerators should have measures in place to control halogenated dioxin emissions, this is mentioned for information only.

3.1.1 Properties of V6 in the context of the ESD (OECD, 2004)

The main desired activity of V6 is as a flame retardant. As V6 is an additive flame retardant, there is the possibility that it may diffuse out of the treated substrate to some extent. V6 is a liquid at room temperature. Its vapour pressure falls within the bracket identified as 'low' within the ESD (OECD, 2004).

The ESD envisages flame retardants as being either organic solids or inorganic solids. As stated above, V6 is a liquid, with a 'low' vapour pressure. For this reason it would be inappropriate to simply apply the organic flame retardants sections of the ESD, as the loss scenarios will be different:

- the potential for dust formation is removed
- process controls may be different.

These factors are thought to have a significant effect upon the handling and compounding stages, though once the additive is formulated, its original physical state is less relevant. However, it is noteworthy that ESD losses from the stage of conversion (e.g. foaming) are (for some additive types) dependent on the volatility of the additive.

[11] The models are based on data for similar substances obtained in static tests, but not V6 itself. Since V6 is particularly used in furniture (including car seats), which is frequently squeezed, it is possible that emissions from inner surfaces might not have been fully taken into account. However, although it may be possible to attempt to model the air exchange associated with squeezing in more detail with better experimental data, this could be complex and various other factors may play a role. Since these emissions are only relevant at the regional level (for which a rather high release rate is already assumed – see Section 3.1.2.5), the current approach is believed to be suitably precautionary.

Variation of loss rate based on volatility in the ESD

For conversion (i.e. foaming), the rates of loss given in the ESD conform to a pattern; a ratio of 1:5:25 between rates of loss of low: medium: high vapour pressure additives is well established. This relationship is applied in some cases here (e.g. for some in-service loss stages) in the derivation of 'correction factors' to derive default rates of loss for V6 (low volatility) based on corresponding known rates of loss for a medium-volatility additive.

Distinction between conversion at large and small sites in the ESD

The ESD, which sets out default rates of loss from all stages of the life cycle, also indicates that 'small' sites tend overall to have a higher rate of loss:

"*As is noted specifically for some of the processes, fume elimination equipment is commonly used to reduce emissions... All the* [release estimates from conversion] *relate to situations where fume elimination equipment is in operation, i.e. larger sites. For smaller sites (<…~750 tonnes of plastic) the emission factors should be increased by a factor of 10*".

It is notable that industry has consistently indicated that this assumption is overly conservative, since exposure to di-isocyanate fumes is always closely controlled. The evidence has been carefully considered and the factor of ten is not applied to life cycle stages of PUR foaming in this risk assessment.

3.1.2 Environmental releases

3.1.2.1 Release from production

3.1.2.1.1 Defaults

It is not considered necessary to seek default rates of loss, or fractions of the main local source. The manufacturing site within the EU has been identified and site-specific release data have been provided by the industry.

3.1.2.1.2 Extent of site-specific data

Site-specific data provided by the producer of V6 are set out in the Confidential Annex.

3.1.2.2 Release from flexible foams

For all life cycle stages following production, it could be considered that the releases associated with one life cycle stage should be subtracted from the tonnage taken forward to subsequent life cycle stages. However, it is considered that for this substance, such variations will be within the range of error in the risk assessment. Therefore, no such correction has been used in the risk assessment.

3.1.2.2.1 Foam production

Information on the number of sites is given in the Confidential Annex.

The ESD for plastics additives (OECD, 2004) has been consulted extensively in the course of preparation of this risk assessment. However, the magnitude of releases are based on a report (Appendix B), which brings together theoretical modelling with the results of various published studies of releases of FRs from foams.

The possible sources of environmental release during the manufacture of flexible polyurethane foam are likely to be associated with:

- the handling of the flame retardant prior to mixing with other ingredients (V6 is a liquid)
- volatilisation from the foam while at elevated temperatures (curing)
- volatilisation from the foam in storage.

Site visits and information received from the industry (see section 2 and the Life Cycle Annex) indicate that volatilisation in the foaming process and cleaning of equipment (both of which could theoretically be sources of release of a plastics additive) are not relevant in this case.

A mixing head immediately prior to feeding into the moulding system usually carries out mixing of the components required for the foam. The flame retardant additives can either be metered directly to the mixing head or may be premixed with the polyol component of the foam before feeding to the mixing head. Two main types of mixing head are commonly used: low pressure and high pressure. Low pressure mixing heads need to be cleaned out between cycles by flushing with a suitable solvent (e.g. methylene chloride) or may be flushed with further polyol which can then be reused if the formulation allows. High-pressure (impingement) mixing heads do not require solvent flushing between batches (HMIP, 1995).

Releases from curing and storage

The proposed rate of release in curing and storage, accounting for the finding that for V6 only 10% of the substance present is available for release, is 3E-05% to air and to wastewater. This is based on a model which brings together theoretical modelling with the findings of various published studies (Appendix B).

While some internal parts of the foam blocks reach a high temperature during curing, this is not expected to have a significant influence on the release rate. This is because the blocks are large and the exterior of the block soon cools.

An additional release of 0.01% to wastewater from handling of raw materials is included for small sites.

Releases to air:	3E-05%
Releases to wastewater**:**	3E-05% (large sites)
	0.01003% (small sites)

A discussion of the consequences of using ESD defaults is presented in the ESR RAR for TCPP (HSA/EA, 2008a).

3.1.2.2.2 Foam cutting and manufacture of end products

There may also be losses to the environment associated with the cutting of slabstock foams during cutting and trimming processes and manufacture of furniture and automotive furnishings.

Releases associated with the generation of foam dusts must be assessed, since modelling shows that FR contained in foam dusts will be volatilised very rapidly (Appendix B). While it is known from consultation that dusts are collected at the point of cutting by extractors attached to the blade, it could still be the case that a small proportion of dusts and small pieces of foam are exposed to air and hence that some FR could be released on a local scale. A study undertaken by EUROPUR (EUROPUR, 2005b) has established that up to 0.1% of foam is lost as dust and non-recycled offcut pieces. It is estimated that 1% of this material might not be collected by the extractor systems. These pieces of FR foam could then release FR into the workplace air and could reach the environment via air and also wastewater (via adsorption and cleaning). A release rate of 5E-05% to air and 5E-05% to water is proposed, accounting for the finding that for V6, only 10% of the substance present is available for release. This is based on a model which brings together theoretical modelling with the findings of various published studies (Appendix B).

Information on the number of sites is given in the Confidential Annex.

3.1.2.2.3 Rebonding and loose crumb

Rebonding

Elevated temperature processing applies to what is essentially an additional processing stage in the life cycle.

It is assumed that 5.25% of the V6 in automotive foams (see section 2.2.2.1.5) and 10.5% of the V6 in furniture foams (see section 2.2.2.1.6) will be rebonded in the EU (this is based on the combination of 20% of furniture foam and 10% of automotive foam being available for recycling; 75% remaining in EU for recycling; and 70% of recycling being in the form of rebonding[12]). Neither the quantity of V6-containing foam that is recycled, nor the concentration of V6 in the foam is relevant to this assessment as releases are estimated on the total amount of V6 present which depends on the levels of scrap foam.

The granulation and rebonding processes are contained within equipment, therefore rates of loss are anticipated to be much lower than the theoretical model might suggest. Granulating machines are fitted with dust extraction equipment. Taking the same approach as for cutting at furniture and automotive manufacturing sites, it could be estimated that up to 0.1% of foam is lost as dust, and that 1% of this material is not collected by the extractor systems and could be released to the local air compartment. Releases are therefore 1E-04% to air, accounting for the finding that for V6, only 10% of the substance present is available for release. There are no releases to wastewater (Appendix B).

[12] Note: industry (EUROPUR) has indicated that 30% recycling in the form of loose crumb may be an overestimate (pers. comm., 27th March 2006). Therefore it is possible that a higher proportion may be rebonded. However, due to the similarities between the release levels from loose crumb and rebonding processes, and the similarity of site distribution (information provided in the EUROPUR survey) (pers. comm. 7th December 2005), this has no significant implications for the risk assessment at the processing stage.

Information on the number of sites is given in the Confidential Annex. A survey carried out by EUROPUR has produced results in the form of numbers of sites and quantities of rebonded foam, associated with various EU15 countries (pers. comm. 7th December 2005). The survey data relate to total PUR, including non-FR foam. For V6, where there is no distinctive geographical concentration within Europe, the risk assessment parameters can be based directly on rebonding site size distribution. The following set of values are used in the risk assessment:

Fraction in the main region = 0.4
Fraction of the main local source = 0.55

Loose crumb

It is assumed that 2.25% of the V6 in automotive foams (see section 2.2.2.1.5) and 4.5% of the V6 in furniture foams (see section 2.2.2.1.6) will be recycled as loose crumb in the EU (this is based on the combination of 20% of furniture foam and 10% of automotive foam being available for recycling; 75% remaining in EU for recycling; and 30% of recycling being in the form of loose crumb[10]).

The granulation process is contained within equipment, therefore rates of loss are anticipated to be much lower than the theoretical model might suggest. Granulating machines are fitted with dust extraction equipment. Taking the same approach as for cutting at furniture manufacturing sites, it could be estimated that up to 0.1% of foam is lost as dust, and that 1% of this material is not collected by the extractor systems and could be released to the local air compartment. Releases are therefore 1E-04% to air, accounting for the finding that for V6, only 10% of the substance present is available for release. There are no releases to wastewater (Appendix B).

It has been indicated that granulation associated with loose crumb recycling generally does not take place at the same sites as rebonding (pers. comm., 27th March 2006). However, since both rebonding and loose crumb are dependent on the availability of scrap foam from the same sources, site distribution may be expected to follow the same distribution pattern. Information on the number of sites is given in the Confidential use pattern and exposure Annex.

3.1.2.2.4 In-service losses

Default rate of release

Based on measured releases, the ESD estimates loss to air and to water. It is known that all of the rates of loss used in the ESD were derived from measurements of medium-volatility additives, therefore it is appropriate to divide these rates by 5 (in accordance with the correction applied to rates of loss from conversion) to obtain the rate of loss of V6. Therefore the default release rates can be taken to be:

Indoor service:

Loss to air	0.01% over lifetime
Loss to wastewater	0.01% over lifetime

Outdoor service:

Loss to air	0.01% over lifetime

Loss to wastewater 0.03% per year

Values used in the risk assessment: Furniture and automotive foam

The ESD gives lifetimes for furniture of five to ten years. ISOPA (1997) gives PUR-specific lifetimes for furnishing/mattresses of greater than ten years. This is supported by reports that 50% of households change their upholstered furniture every eight to sixteen years (DTI undated). In the risk assessment, a lifetime of ten years is used.

All in-service losses are evaluated on a regional basis (over 365 days per year) because no specific local source can be identified for these releases. All service is taken to be indoors.

Given that the air surrounding the foam is likely to be slow moving, and the foam is covered in service by fabrics and upholstery, an annual rate of release of 1E-04% per year to air is proposed, accounting for the finding that for V6, only 10% of the substance present is available for release. This is based on a model which brings together theoretical modelling with the findings of various published studies (Appendix B). All in-service losses are evaluated on a regional basis because no specific local source can be identified for these releases.

Since V6 is an additive flame retardant it may be subject to volatilisation or leaching from the polymer matrix during the lifetime of the use of an article. Given that the parts are unlikely to be washed, the actual potential for leaching from the foam during use would appear to be minimal.

Rebond and loose crumb foams

The application of rebonded foam is assumed to be in indoor applications (such as furniture, mats, cushions and sound insulation, as described in section 2.2.2.1.4). The proportion in the main region is assumed to be 0.1 and a lifetime of ten years is used in the risk assessment.

Given that the air surrounding the foam is likely to be slow moving, and the foam is covered in service by fabrics and upholstery, an annual rate of release of 1E-04% per year to air is proposed, accounting for the finding that for V6, only 10% of the substance present is available for release. This is based on a model which brings together theoretical modelling with the findings of various published studies (Appendix B).

Loose crumb foam is assessed as outdoor service (garden furniture). A fraction of 10% in the main region is considered acceptable.

Given that the foam is covered in service by fabrics and upholstery, an annual rate of release of 1E-03% per year to air is proposed, accounting for the finding that for V6, only 10% of the substance present is available for release. This is based on a model which brings together theoretical modelling with the findings of various published studies (Appendix B). (Note: as described in Appendix B, the rate of release from loose crumb is ten times higher due than that from rebonded foam, due to its use in outdoor applications with higher air turnover).

Waste remaining in the environment

In keeping with the requirements of the TGD, some consideration of release through weathering and wear over the service life and at disposal is appropriate. A total of 2% release over the lifetime of the article is assumed for most life cycle stages. The release of V6 is

limited by the available fraction (for V6, only 10% of the substance present is available for release). Since modelling indicates immediate volatilisation from small particles (Appendix B), in this risk assessment the release is assessed as being entirely to air in the first instance. Hence the release rate used in the risk assessment is 0.2% to air. Redistribution of the substance via fugacity modelling is then dealt with by EUSES. These releases, which are associated with physical erosion of the polymer, are additional to 'in-service loss', which is associated with volatile releases from the article itself.

It is important to differentiate this route of release from the assessment of in-service loss. Waste remaining in the environment is associated with physical weathering and wear and hence release of FR from foam particles. In-service loss is simple volatilisation out of the foam article itself.

Not all life cycle stages will be subject to weathering and wear processes: these releases are assessed only for V6 used in flexible foams used for automotive and furniture applications, rebonded foam and 'loose crumb' furniture. The releases are evaluated on a regional scale, in keeping with the in-service distribution of the polymer between the regions for these applications.

In reality the potential for release of particulate waste from weathering, wear, etc., during the service life of furniture and automotive foams may be lower than this estimate, because the foam will have a protective covering. Furthermore, the scenario described above is theoretical only and it has not been possible to test its validity.

3.1.2.3 Release from other uses

Releases from other uses are discussed in the Confidential Annex.

3.1.2.4 Release from disposal

Disposal to landfill is considered likely to be the most significant route of disposal of flexible foam and other articles containing V6. Monitoring data for landfill leachate in England and Wales suggests that this is a significant exposure route for TCPP but not for TDCP. There are no monitoring data available on concentrations of V6 in landfill leachate. However, V6 has a lower volatility than both TDCP and TCPP and its water solubility and adsorption potential is intermediate between the two. It is therefore likely to be less mobile in landfills than TCPP. In addition, the tonnage of V6 in articles in service (and hence tonnages passing to landfill) per year, at the regional scale, is less than 5% of the equivalent tonnage of TCPP. Therefore the contribution of releases via landfill leachate to the PECregional values is considered to be negligible for the present risk assessment.

3.1.2.4.1 End of life for automotive foams

The ESD indicates that plastics constitute 6% of automotive wastes of which 3% is mechanically recovered, and the remaining 97% is landfilled or incinerated (without heat recovery).

Data from APME (2000) for 1998 indicate that of the 728,000 tonnes of plastic present in automotive wastes in Europe, 77% is landfilled, 10% mechanically recovered (and a further 0.14% exported for mechanical recovery) and 13% used for energy recovery.

Section 3 of the Confidential use pattern and exposure Annex reports on current levels of recovery and recycling for automotive PUR as stated in Mark and Kamprath (2000). There is reported to be 70,000 tonnes of PUR available for recovery each year, of which:

- 5% is recovered and recycled (3% in the Netherlands and an estimated 2% in Italy)
- 5% (present in ASR[13]) is used for energy recovery, i.e. incineration
- 92% (present in ASR) is sent to landfill.

These values are PUR-specific and are used in the risk assessment.

3.1.2.4.2 End of Life for furniture Foams

The ESD indicates that plastics constitute 72% of municipal solid waste arising. Of this waste stream:

- 20% is incinerated and the heat recovered
- 1% is mechanically recovered
- 79% is landfilled or incinerated (without heat recovery).

Data from ISOPA (1997) indicate the following for post-user plastics waste in Western Europe:

- 6% mechanical recycling
- 3% incineration without energy recovery
- 13% incineration with energy recovery
- 78% landfill.

Data from APME (2000) for 1998 indicate that of the 11,370,000 tonnes of plastic present in municipal waste in Europe:

- 4% is incinerated
- 66% landfilled
- 3% consumed in feedstock recycling
- 4% mechanically recovered (and a further 0.25% exported for mechanical recovery)
- 22% used for energy recovery.

Industry indicates that at end of life most furniture goes to landfill (see section 2.2.2.1.6).

[13] Automotive Shredder Residue

3.1.2.5 Regional and continental total releases

Total releases at the regional and continental scale include contributions both from local sites and from several life cycle stages evaluated only at the regional and continental scales. In total the releases rates to the various compartments are as shown in **Table 3.1**.

Table 3.1 Total releases to the regional and continental environmental compartments

Endpoint	Emission in kg/d
Total regional emission to air	0.71
Total regional emission to wastewater	0.094
Total regional emission to surface water	0.024
Total regional emission to industrial soil	2E-04
Total continental emission to air	6.33
Total continental emission to wastewater	0.20
Total continental emission to surface water	0.051
Total continental emission to industrial soil	0

3.1.3 Environmental fate

3.1.3.1 Degradation in the environment

3.1.3.1.1 Atmospheric degradation

No measured data are available. A half-life in air of 5.0 hours has been proposed based on an OH radical concentration of 5 x 10^5 molecules/ml, which is the default in the TGD (EC 2003).

As shown below, the Syracuse Research program AOPWIN gives a predicted reaction rate constant of 77.29 x 10^{-12} cm^3/molecule.sec. With the TGD model for photodegradation, this is equivalent to a half-life of 5.0 h

```
SMILES : O=P(OCCCL)(OCCCL)OCC(CCL)(CCL)COP(=O)(OCCCL)OCCCL
CHEM   : Phosphoric acid, 2,2-bis(chloromethyl)-1,3-propanediyl tetrakis(2-
chloroethyl) ester

MOL FOR: C13 H24 CL6 O8 P2
MOL WT : 583.00
---------------- SUMMARY (AOP v1.90): HYDROXYL RADICALS -----------------
Hydrogen Abstraction       =  77.2926 E-12 cm3/molecule-sec
Reaction with N, S and -OH =   0.0000 E-12 cm3/molecule-sec
Addition to Triple Bonds   =   0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds =   0.0000 E-12 cm3/molecule-sec
Addition to Aromatic Rings =   0.0000 E-12 cm3/molecule-sec
Addition to Fused Rings    =   0.0000 E-12 cm3/molecule-sec

   OVERALL OH Rate Constant =  77.2926 E-12 cm3/molecule-sec
```

3.1.3.1.2 Aquatic degradation

Abiotic degradation

A study of abiotic degradation (Groult, 2002c) according to the standard method (OECD 111, C7 of Commission directive 92/69/EEC) has shown no degradation in the preliminary test. This consisted of studying the stability of a solution of the substance at 50°C for 5 days in de-aerated test media at pH 4, 7 and 9. The result is interpreted as meaning that the hydrolytic half-life of V6 under ambient conditions in the environment is likely to be greater than one year. The study does not test the susceptibility of the substance to abiotic oxidation (i.e. by oxygen). However, there are no structural features of V6 which would suggest that oxidation is possible.

No relevant literature in the public domain has been found.

It is very unlikely that the rate of hydrolysis at environmentally-relevant pH values is fast enough to have any influence on predicted environmental concentrations.

Biodegradation studies

In a non-GLP study of ready biodegradability (SafePharm 1994f), sludge was sampled from wastewater treatment plant treating predominantly domestic sewage and used at a level of 1%. V6 was tested at a loading rate equivalent to 20 mg C/l (equivalent to 79.7 mg/l). The test substance was degraded by 5% over the 28-day period according to CO_2 evolution, and therefore is not readily biodegradable. Sodium benzoate was used as a reference substance, and its degradation met the required validity criteria. Tests were performed in duplicate. The study does not claim compliance with a guideline, although appears to be consistent with standard methods.

In a non-GLP study of inherent biodegradability (SafePharm 1996), performed according to the OECD 302C Modified MITI (II) procedure, sludge was sampled from 10 sites around the UK and was present in test vessels at a loading equivalent to 100 mg dry weight/l. The test substance (Amgard V6) was present at a level of 30 mg/l. Aniline was used as a reference substance, present at 100 mg/l. The observed cumulative percentage biodegradation of the test substance was very variable. The substance apparently degraded up to around 10% total, and then reverted to 0% degradation at day 9-10 (the reference substance degraded normally and fulfilled the required criteria). The test report suggests that the variability is "due to variations in the basal respiration rate of the inoculum". After 14 days a consistent increase in the extent of degradation started, and at the end of the 28-day test period the test substance was degraded by 37%, appearing to have reached a plateau in the final 7-8 days. The substance shows clear evidence of being biodegradable, although cannot be described as inherently biodegradable.

More information could have been obtained in a test with a longer exposure period, but the evidence from this summary-level report indicates that the substance is susceptible to partial degradation. It is possible that a definite degradation product, itself resistant to biodegradation, could have been formed.

For the purposes of modelling the rate constants for degradation in wastewater treatment and surface waters are set at 0 h^{-1}, in accordance with the TGD.

3.1.3.1.3 Degradation in soil

No studies of the degradation of V6 in soil are available. For the purposes of modelling the rate constants for degradation in soil are set at 0 h^{-1}.

3.1.3.1.4 Summary of environmental degradation

Key information is summarised in **Table 3.2**.

Table 3.2 Summary of degradation data for V6

Endpoint	Year test completed	Protocol cited	Results	Reliability	Study reference
Photodegradation	-	-	The rate constant for reaction with hydroxyl radicals is equivalent to an atmospheric half-life of 5.0 hours.	(2) valid with restrictions	-
Stability in water	2002	92/69/EEC C7	No hydrolysis was detected	(2) valid with restrictions	Groult, 2002c
Stability in soil	-	-	No data	-	-
Ready biodegradability 28d	1994	Modified Sturm test	5% degradation at the end of the study: not readily biodegradable	(2) valid with restrictions. Not GLP.	SafePharm, 1994
Inherent biodegradability 28d	1996	Modified MITI inherent test	37% degradation at the end of the study: not inherently biodegradable, although some susceptibility to degradation was demonstrated.	(2) valid with restrictions. Questionable analysis and interpretation	SafePharm, 1996

These data show that the rate constants in water, sediments, sewage sludge and soil can all be set to zero.

3.1.3.2 Distribution

A summary of studies related to the environmental distribution of V6 is given in **Table 3.3**.

Table 3.3 Studies related to environmental distribution of V6

Endpoint	Year test completed	Protocol cited	Results	Reliability	Study reference
Adsorption to soil	2002	Method C.19 of 2001/59/EC	Log K_{oc} = 4.04	(1) valid without restrictions[1]. GLP study	Cuthbert, J.E. and D.M. Mullee, 2002

Note 1 – It is important to note that while this result is of reliability (1), the results are not suitable in this case for application in risk assessment, for reasons expanded upon in the text (see Section 3.1.3.2.1). The method used is a screening study.

3.1.3.2.1 Adsorption

The understanding of the adsorption behaviour of V6, and the structurally-related substances TDCP and TCPP, is based on a number of items of data. These are:

- Measured adsorption coefficient in soils, sediment and sludge for TDCP, in accordance with OECD guideline 106
- Estimated adsorption coefficient by HPLC measured with all three substances, in accordance with OECD guideline 121
- Prediction by standard QSAR methods, from the TGD.

Application of findings of OECD 106 study for a structurally-related substance

The K_{oc} of the structurally-related substance TDCP has been determined to be 1780 in a reliable study (Schaefer and Ponizovsky, 2006).

The K_{oc} of TDCP predicted using the TGD equation for phosphates is 950 and using the 'hydrophobics' equation is 1230. These are somewhat lower than the measured value, suggesting that TDCP is adsorbing to organic matter more strongly than predicted by these equations. The TGD methods are discussed in more detail below.

From the OECD 106 study on TDCP, a regression equation was derived from a plot of log K_d versus log OC (organic carbon concentration), in order to derive a K_{oc} from the whole data set. Further details are reported in the TDCP risk assessment report. The log K_{ow} of TDCP is 3.69. Based on the measured log K_{ow} of 3.69 and the measured log K_{oc} of 3.25 from the OECD 106 study, the following empirical relationship can be derived: log K_{oc} = -0.44 + log K_{ow}. It is assumed that this same relationship can be applied to V6. Applying the same relationship for V6 (Log K_{ow} = 2.83) gives the result log K_{oc} = 2.39, K_{oc} = 245. The basis of such an approach is the structural analogy between the substances, and is justified because the most reliable information in the whole data set is the measured K_{oc} of TDCP. The robustness of this approach is reviewed below.

For the substance TDCP it was found that the HPLC test resulted in a 7-fold higher K_{oc} than was found in the OECD 106 study. This suggests that some specific interaction with the HPLC column, possibly involving the phosphate group, had occurred; binding to the natural substrates in the OECD 106 test system was much lower than to the HPLC column substrate. This interpretation is further supported in that V6, which has two phosphate groups, is the substance for which the HPLC estimate is most out of line, relative to the K_{ow}. Adsorption behaviour in the OECD 106 study was proportional to organic carbon content as expected suggesting that adsorption to components other than organic carbon was not significant.

HPLC estimation method

A reliable modern measurement of the soil adsorption coefficient K_{oc} for V6 obtained by the HPLC estimation method in accordance with OECD guidelines and EU method C19 is available (Cuthbert and Mullee, 2002). The result is $K_{oc} = 1.1 \times 10^4$, log K_{oc} = 4.04. This value applies to the main component and would not have been affected by the impurities present. It should be noted that the calibration substances were general substances, not related structurally to V6, there being insufficient reliable calibration substances containing the phosphate group. For this reason, estimates of K_{oc} from the EPIWIN program are not considered to be reliable enough for phosphates and are not included here.

QSAR methods from the TGD

The TGD gives a method for estimating the value of K_{oc} based on log K_{ow}. The most appropriate equation is that for phosphates:

Log K_{oc} = 0.49 log K_{ow} + 1.17 (n = 41, r^2 = 0.73, s.e. = 0.45)

The log K_{ow} for V6 is 2.83 ± 0.05. On the basis of the uncertainty on this value, a range of log K_{oc} can be estimated. From the above equation, K_{oc} = 360.3 (340.6 – 381.2).

The HPLC-estimated K_{oc} value is somewhat higher than the predicted value from the TGD method. This is consistently true for this group of substances. Within the ESR assessment of other chloroalkyl phosphates (4th priority list; Rapporteur UK/Ireland and 2nd priority list; Rapporteur Germany) measured K_{oc} values exceed K_{oc} values calculated, in accordance with the TGD, on the basis of log K_{ow}, using the QSAR for phosphates. Available data are summarised in **Table 3.4**. Estimates made using the hydrophobics equation are also provided for reference.

Table 3.4 Comparison of measured and estimated K_{oc} for chloroalkylphosphates in the ESR process

Substance (CAS)	K_{oc} derived from OECD 106 result for TDCP	K_{oc} measured [l/kg] by HPLC estimation	K_{oc} estimated [l/kg] from log K_{ow} (Phosphates)	K_{oc} estimated [l/kg] from log K_{ow} (Hydrophobics)
TCPP (13674-84-5)	174	576	304	187
TDCP (13674-87-8)	1780	12300	951	1230
V6 (38051-10-4)	**245**	11000	360	247
TCEP (115-96-8)	-	-	110	-

Conclusions

The estimates from HPLC are consistently out of line with other approaches. Both the phosphates and hydrophobics equations predict statistically similar K_{oc} values for V6 to the value derived using the OECD 106 measured value for TDCP. It is considered that the uncertainty in reading across from TDCP to V6 is less than or similar to the uncertainty in applying the QSAR methods, especially given the relatively low value of r^2 for the phosphates equation.

The value of K_{oc} = 245 is used in the risk assessment of V6.

The coefficients in **Table 3.5** are derived from this value, using default conversion factors.

Table 3.5 Adsorption coefficients used in the environmental risk assessment

Partition coefficient	Symbol	Values used
Organic carbon - water partition coefficient	K_{oc}	245 l/kg
Solids - water partition coefficient for soil	Kp_{soil}	4.9 l/kg
Solids - water partition coefficient for sediment	Kp_{sed}	12.2 l/kg
Solid - water partition coefficient for suspended matter	Kp_{susp}	24.5 l/kg
Soil - water partition coefficient	$K_{soil\text{-}water}$	7.55 m^3/m^3
Sediment - water partition coefficient	$K_{sed\text{-}water}$	6.93 m^3/m^3
Suspended matter - water partition coefficient	$K_{susp\text{-}water}$	7.03 m^3/m^3

3.1.3.2.2 Precipitation

The low volatility and moderate solubility and adsorption coefficient suggest that most V6 found in the atmosphere will adsorb to particulate matter, which may then be washed out by rainfall. The TGD estimates this from vapour pressure, leading to a similar conclusion.

3.1.3.2.3 Volatilisation

A Henry's Law constant of 6.45 x 10^{-06} Pa.m^3/mol can be calculated from the vapour pressure (calculated) and water solubility. This indicates a preference for water compared to air, and hence a low rate of volatilisation from surface water to air.

3.1.3.2.4 Distribution in wastewater treatment plants

It is assumed that no biodegradation occurs during wastewater treatment.

Based on the physico-chemical properties of V6 (vapour pressure = 5.6 × 10^{-6} Pa, water solubility = 232 mg/l, Henry's law constant = 6.45 x 10^{-6} Pa m^3/mole and K_{oc} = 245 l/kg) the predicted behaviour of the substance during wastewater treatment (as estimated by the SIMPLETREAT program within EUSES) is:

Fraction to air	0%
Fraction to surface water	97.0%
Fraction to sludge	2.97%
Fraction degraded	0%

3.1.3.2.5 Distribution in the environment according to fugacity modelling

The approach to distribution modelling is described below. Two models have been used:

- The 1997 EQC model, at Level I, with equal emissions to air, water, and soil
- The 1999 Level III model, using the EU default parameters, initially with equal emissions to air, water and soil and then with a variety of scenarios.

The physicochemical properties entered were as given in section 1; K_{oc} is estimated by the fugacity modelling program itself from K_{ow} as 277, which is sufficiently close to the selected K_{oc} value that no adjustment is required to the input value of log K_{ow}.

The reaction half-lives have been set at negligible reaction in all compartments. For purposes of examining the importance of the value of K_{ow} and K_{oc}, the emissions were to air, water and soil.

For equal inputs into each compartment, the results obtained are presented in **Table 3.6**.

Table 3.6 Outputs of two fugacity models

	EQC Level I	Level III
% in air	0	0
% in soil	37.1	89.8
% in water	62.0	10.1
% in sediment	0.83	0.048

The results for EQC Level I (the simplest model) indicate that water, soil and sediment are all significant should V6 be stable in the environment. The Level III result shows less substance in water because it accounts for mass flow of water out of the region being modelled.

The Level III model has been used to indicate the fate modelled for separate releases into different compartments. No inflow from outside the modelled area (the whole EU) has been included. The results are presented in **Table 3.7**.

Table 3.7 Output of fugacity model for various release scenarios

	To air, water and soil	To air	To water	To soil
% in air	0	0.002	0	0
% in soil	89.8	93.0	0	93.2
% in water	10.1	7.0	99.5	6.72
% in sediment	0.05	0.03	0.48	0.03

The results reflect that most V6 found in air would be precipitated to soil, and that there is very little movement between soil and water, because transfer via the air compartment is very slow. In water, the modelled adsorption to sediment is very low.

3.1.3.3 Accumulation and metabolism

3.1.3.3.1 Aquatic organisms

The TGD gives a method for estimating the value of BCF in fish based on log K_{ow}. The appropriate equation is the linear equation for substances with log K_{ow} <6:

Log BCF_{fish} = 0.85 log K_{ow} – 0.70

The log K_{ow} for V6 is 2.83 ± 0.05. On the basis of the uncertainty on this value, a range of log BCF can be estimated. From the above equation, BCF_{fish} = 50.8 (range 46.0 – 56.0).

The measured BCFs for TDCP and TCPP are relatively low in comparison with the predictions and with other substances of similar log K_{ow} values. There could be various causes for such a result, including the possibility of rapid metabolism in the organism. There is evidence for metabolism of both TCPP and TDCP. TCEP has a similarly low measured BCF value and metabolism occurred in both *in vivo* toxicokinetics and *in vitro* studies. While no toxicokinetics data are available for V6, there is evidence for metabolism from an *in vitro* study using mammalian cells.

In the absence of firm bioaccumulation or metabolic data, the estimated BCF_{fish} value of 50.8 has been used in the risk assessment for V6, though the evidence from similar substances suggests that this may be a conservative estimate.

3.1.3.3.2 Terrestrial organisms

The revised TGD gives a new method for estimating the value of BCF in earthworms based on log K_{ow}, using the method of Jager (1998):

$$BCF_{earthworm} = \frac{(0.84 + 0.012.K_{ow})}{RHO_{earthworm}}$$

For $RHO_{earthworm}$ by default a value of 1 kgwwt.L^{-1} can be assumed. The log K_{ow} for V6 is 2.83 ± 0.05. On the basis of the uncertainty on this value, a range of log BCF can be estimated. From the above equation, $BCF_{earthworm}$ = 8.95 (range 8.07 – 9.94).

3.1.4 Aquatic compartment (including sediment)

$PEC_{sediment}$ is calculated using the equilibrium partitioning approach.

The value $Clocal_{effluent}$ for wastewater treatment plants is used as the value of PEC for WWTP micro-organisms.

3.1.4.1 Calculation of predicted environmental concentrations (PEC_{local})

The PECs for V6 are calculated using the methods given in the latest version of the Technical Guidance Document (EC, 2003), except where site-specific assessment is appropriate and suitable acceptable data have been provided (more information is given in the Confidential Annex). Where a default local assessment applies, the usual models, equations and assumptions apply.

Some notes on the basis of PEC are given in **Table 3.8**.

Table 3.8 Notes on the basis of PECs for specific life cycle stages

		Basis of release rates to the environment
1	Producer	Site specific data
A1a	Flexible foam - automotive - foaming large site	Appendix B
A1b	Flexible foam - automotive – foaming	Appendix B
A2	Flexible foam - automotive – cutting	Appendix B
B1	Flexible foam - furniture – foaming	Appendix B
B2	Flexible foam - furniture cutting	Appendix B
C1	CONFIDENTIAL	Estimates from relevant ESDs; read across from relevant previous published risk assessments; site specific info and WWTP details in some instances Note that for application F (life cycle stages F1 and F2) the producer company has confirmed that this application of V6 is not applicable in Europe (pers. comm., 11th October 2005). The information about this application obtained in the original survey probably related to customer trials.
C2	CONFIDENTIAL	
D1	CONFIDENTIAL	
F1	CONFIDENTIAL	
F2	CONFIDENTIAL	
G1	Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	Appendix B
H1	Loose Crumb	Appendix B

3.1.4.1.1 Calculation of PEC_{local} for production

PEC_{local} for production is based on site specific, confidential details of effluent concentration and wastewater treatment plant size and function. Calculated PECs are summarised in **Table 3.9**.

Table 3.9 PEC_{local} for industrial and professional use

	$C local_{effluent}$ [mg/l]	$C local_{water}$ [mg/l]	PEC_{water} [mg/l]	$PEC_{sediment}$ [mg/kg wwt]
Production	5.8E-05	5.8E-07	6.01E-06	3.67E-05

3.1.4.1.2 Calculation of PEC_{local} for formulation

Formulation is not a relevant life cycle stage for V6.

3.1.4.1.3 Calculation of PEC_{local} for industrial/professional use

PEC_{local} values for industrial and professional use are calculated for all life cycle stages. Calculated PECs are summarised in **Table 3.10**.

Table 3.10 PEC_{local} for industrial and professional use

	$C local_{effluent}$ [mg/l]	$C local_{water}$ [mg/l]	PEC_{water} [mg/l]	$PEC_{sediment}$ [mg/kg wwt]
A1a: Flexible foam - automotive - foaming large site	1.75E-04	1.75E-05	2.29E-05	1.40E-04
A1b: Flexible foam - automotive - foaming	7.29E-03	7.29E-04	7.34E-04	4.48E-03
A2: Foam cutting	2.97E-05	2.97E-06	8.40E-06	5.13E-05
B1: Flexible foam - furniture - foaming	0.0581	5.81E-03	5.81E-03	0.0355
B2: Foam cutting	3.64E-05	3.64E-06	9.07E-06	5.54E-05
C1: CONFIDENTIAL	0.032	3.20E-03	3.21E-03	0.0196
C2: CONFIDENTIAL	5.84E-03	5.84E-04	5.89E-04	3.60E-03
D1: CONFIDENTIAL	8.27E-03	8.27E-04	8.32E-04	5.08E-03
F1: CONFIDENTIAL	0.0566	5.66E-03	5.66E-03	0.0346
F2: CONFIDENTIAL	0.463	0.0463	0.0463	0.283
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	0	0	5.43E-06	3.32E-05
H1: Loose Crumb	0	0	5.43E-06	3.32E-05

3.1.4.1.4 Calculation of PEC_{local} for private use

This scenario is not applicable. In-service loss and waste remaining in the environment are characterised on a regional scale.

3.1.4.1.5 Calculation of PEC_{local} for disposal

This scenario is not included in the assessment. Emissions from landfills are covered by discharge consents.

3.1.4.2 Measured levels

No data are available for review.

3.1.4.3 Comparison between predicted and measured levels

No measured environmental concentrations are available.

3.1.5 Terrestrial compartment

3.1.5.1 Calculation of PEC_{local}

The most significant contribution to PEClocal soil comes from spreading of WWTP sludge onto agricultural land. The PECs for V6 are calculated using the methods given in the Technical Guidance Document, except where site-specific assessment is appropriate and suitable acceptable data have been provided (more information is given in the Confidential Annex). Where a default local assessment applies, the usual models, equations and assumptions apply.

3.1.5.1.1 Calculation of PEClocal for production

PEC_{local} for production is based on site specific details of effluent concentration and wastewater treatment plant size and function. Calculated PECs are summarised in **Table 3.11**.

Table 3.11 PEC_{soil} for industrial and professional use

	Agric. soil 30 day average (mg/kg wet w t.)	Agric. soil 180 day average (mg/kg wet wt.)	Grassland 180 days average (mg/kg wet wt.)
Production	1.04E-04	1.03E-04	7.40E-05

3.1.5.1.2 Calculation of PEC_{local} for formulation

Formulation is not a relevant life cycle stage for V6.

3.1.5.1.3 Calculation of PEC_{local} for industrial/professional use

PEC_{local} values for industrial and professional use are calculated for all life cycle stages. Calculated PECs are summarised in **Table 3.12**.

Table 3.12 PEC_{soil} for industrial and professional use

	Agric. soil 30 day average (mg/kg wet w t.)	Agric. soil 180 day average (mg/kg wet wt.)	Grassland 180 days average (mg/kg wet wt.)
A1a: Flexible foam - automotive - foaming large site	1.96E-04	1.93E-04	1.08E-04
A1b: Flexible foam - automotive - foaming	5.24E-03	5.12E-03	1.43E-03
A2: Foam cutting	8.73E-05	8.68E-05	7.28E-05
B1: Flexible foam - furniture - foaming	0.0413	0.0403	0.011
B2: Foam cutting	9.10E-05	9.04E-05	7.26E-05
C1: CONFIDENTIAL	0.0228	0.0223	6.06E-03
C2: CONFIDENTIAL	4.21E-03	4.11E-03	1.16E-03
D1: CONFIDENTIAL	5.95E-03	5.82E-03	1.64E-03
F1: CONFIDENTIAL	0.0405	0.0396	0.0111
F2: CONFIDENTIAL	0.329	0.321	0.0868
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	6.65E-05	6.65E-05	6.75E-05
H1: Loose Crumb	6.45E-05	6.46E-05	6.50E-05

3.1.5.1.4 Calculation of PEC_{local} for private use

This scenario is not applicable. In-service loss and waste remaining in the environment are characterised on a regional scale.

3.1.5.1.5 Calculation of PEC_{local} for disposal

This scenario is not included in the assessment. This scenario is not included in the assessment. Emissions from landfills are covered by discharge consents.

3.1.5.2 Measured levels

No data are available for review.

3.1.5.3 Comparison between predicted and measured levels

No data are available for review.

3.1.6 Atmosphere

Given the low levels of releases, the low volatility and moderate solubility and adsorption coefficient of V6, together with its short predicted atmospheric half-life for degradation by hydroxyl radicals, it is not expected that exposure via the atmosphere will be significant.

The concentrations of V6 in the atmosphere have been estimated using EUSES 2.0.3. The predicted local and regional atmospheric concentrations are shown in **Table 3.13**.

Table 3.13 Estimated air concentrations of V6

Scenario	Air concentrations (C_{local}) (mg/m³)		$PEC_{local(air),\ ann}$ (mg/m³)
	Emission episode	Annual average	
Production	3.68E-13	2.81E-13	8.32E-10
A1a: Flexible foam - automotive – foaming large site	1.00E-07	4.11E-08	4.20E-08
A1b: Flexible foam - automotive – foaming	1.25E-08	2.53E-09	3.36E-09
A2: Foam cutting	1.70E-08	1.40E-08	1.48E-08
B1: Flexible foam - furniture – foaming	9.96E-08	2.18E-08	2.27E-08
B2: Foam cutting	2.09E-08	9.09E-09	9.93E-09
C1: CONFIDENTIAL	1.67E-06	9.14E-09	9.97E-09
C2: CONFIDENTIAL	1.00E-08	2.74E-10	1.11E-09
D1: CONFIDENTIAL	4.31E-07	9.44E-08	9.53E-08
F1: CONFIDENTIAL	1.62E-04	1.33E-06	1.33E-06
F2: CONFIDENTIAL	6.63E-08	2.00E-09	2.83E-09
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	4.17E-08	1.51E-08	1.59E-08
H1: Loose Crumb	4.14E-08	6.47E-09	7.30E-09

3.1.7 Secondary poisoning

The concentrations of contaminant in food (fish or worms) of fish- or worm-eating predators ($PEC_{oral,\ predator,\ fish}$ and $PEC_{oral,\ predator,\ earthworm}$) are calculated in accordance with the TGD.

Table 3.14 sets out the values of $PEC_{oral,\ predator}$ for fish and earthworm predators for each life cycle stage. The regional background contribution to the value is already accounted for and is not evaluated separately. The regional background level does not in itself constitute a risk, and for most life cycle stages its contribution to local PEC is not significant.

Table 3.14 PEC values for secondary poisoning

	$PEC_{oral,\ predator,\ fish}$	$PEC_{oral,\ predator,\ earthworm}$
Producer 1	2.87E-04	1.60E-04
A1a: Flexible foam - automotive - foaming large site	4.58E-04	2.46E-04
A1b: Flexible foam - automotive – foaming	4.03E-03	4.95E-03
A2: Foam cutting	3.38E-04	1.44E-04
B1: Flexible foam - furniture – foaming	0.0326	0.0386
B2: Foam cutting	3.16E-04	1.47E-04
C1: CONFIDENTIAL	7.21E-04	0.0213
C2: CONFIDENTIAL	6.82E-04	3.99E-03
D1: CONFIDENTIAL	4.88E-03	5.62E-03
F1: CONFIDENTIAL	1.46E-03	0.0379
F2: CONFIDENTIAL	0.0357	0.307
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	2.76E-04	1.24E-04
H1: Loose Crumb	2.76E-04	1.23E-04

3.1.8 Calculation of $PEC_{regional}$ and $PEC_{continental}$

$PEC_{regional(water)}$ = 5.43E-06 mg/l from the EUSES v2.03 model.

$PEC_{regional(freshwater\ sediment)}$ = 3.72E-05 mg/kg wwt from the EUSES v2.03 model.

$PEC_{regional(soil)}$ = 6.36E-05 mg/kg wwt from the EUSES v2.03 model.

$PEC_{continental(water)}$ = 8.75E-07 mg/l from the EUSES v2.03 model.

$PEC_{continental(freshwater\ sediment)}$ = 5.99E-06 mg/kg wwt from the EUSES v2.03 model.

$PEC_{continental(soil)}$ = 3.49E-06 mg/kg wwt from the EUSES v2.03 model.

3.2 MARINE EXPOSURE ASSESSMENT

3.2.1 General discussion

The marine PECs for V6 are calculated using the methods given in the Technical Guidance Document.

V6 does not contain any ionisable functional groups, therefore the partition coefficients derived for the freshwater assessment can be used without adjustment.

3.2.2 Degradation

V6 is not significantly biodegradable on the basis of freshwater tests. It is considered to be persistent in the marine environment.

3.2.3 Calculation of Predicted Environmental Concentrations (PEC)

For the local assessment it is assumed that industrial effluents are not treated in a municipal biological STP and a dilution factor of 100 can be assumed for discharges to coastal regions.

Values of $PEC_{regional(seawater)}$, $C_{local(seawater)}$, $PEC_{local(seawater)}$ and $PEC_{local(marine\ sediment)}$ are evaluated in accordance with the revised TGD.

3.2.3.1 Calculation of PEC_{local} for production

PEC_{local} for production is based on site specific details of effluent concentration and wastewater treatment plant size and function. Calculated PECs are summarised in **Table 3.15**.

Table 3.15 Marine PEC for industrial and professional use

	$PEC_{sea\ water}$ [mg/l]	$PEC_{marine\ sediment}$ [mg/kg wwt]
Production	1.15E-06	7.03E-06

3.2.3.2 Calculation of PEClocal for formulation

Formulation is not a relevant life cycle stage for V6.

3.2.3.3 Calculation of PEClocal for industrial/professional use

PEC_{local} values for industrial and professional use are calculated for all life cycle stages. Calculated PECs are summarised in **Table 3.16**.

Table 3.16 Marine PEC for industrial and professional use

	$PEC_{sea\ water}$ [mg/l]	$PEC_{marine\ sediment}$ [mg/kg wwt]
A1a: Flexible foam - automotive – foaming large site	2.35E-06	1.44E-05
A1b: Flexible foam - automotive – foaming	7.57E-05	4.62E-04
A2: Foam cutting	8.60E-07	5.26E-06
B1: Flexible foam - furniture – foaming	5.99E-04	3.66E-03
B2: Foam cutting	9.30E-07	5.68E-06
C1: CONFIDENTIAL	3.30E-04	2.02E-03
C2: CONFIDENTIAL	6.07E-05	3.71E-04
D1: CONFIDENTIAL	8.58E-05	5.24E-04
F1: CONFIDENTIAL	5.84E-04	3.57E-03
F2: CONFIDENTIAL	4.77E-03	0.0291
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	5.54E-07	3.39E-06
H1: Loose Crumb	5.54E-07	3.39E-06

3.2.3.4 Calculation of PEClocal for private use

This scenario is not applicable. In-service loss and waste remaining in the environment are characterised on a regional scale.

3.2.3.5 Calculation of PEC_{local} for disposal

This scenario is not included in the assessment. Emissions from landfills are covered by discharge consents.

3.2.4 Secondary poisoning

The concentrations of contaminant in the marine food chain are calculated in accordance with the TGD.

Table 3.17 sets out the values of $PEC_{oral,\ predator}$ for marine predators for each life cycle stage. The regional background contribution to the value is already accounted for and is not evaluated separately. The regional background level does not in itself constitute a risk, and for most life cycle stages its contribution to local PEC is not significant.

Table 3.17 PEC values for secondary poisoning

	$PEC_{oral, predator, fish (marine)}$ [mg/kg wwt]	$PEC_{oral\ marine\ top\ predator}$ [mg/kg wwt]
Producer 1	3.98E-05	3.05E-05
A1a: Flexible foam - automotive - foaming large site	4.69E-05	3.19E-05
A1b: Flexible foam - automotive – foaming	4.15E-04	1.06E-04
A2: Foam cutting	3.46E-05	2.94E-05
B1: Flexible foam - furniture – foaming	3.36E-03	6.95E-04
B2: Foam cutting	3.23E-05	2.90E-05
C1: CONFIDENTIAL	7.41E-05	3.73E-05
C2: CONFIDENTIAL	7.00E-05	3.65E-05
D1: CONFIDENTIAL	5.03E-04	1.23E-04
F1: CONFIDENTIAL	1.50E-04	5.25E-05
F2: CONFIDENTIAL	3.68E-03	7.59E-04
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	2.82E-05	2.82E-05
H1: Loose Crumb	2.82E-05	2.82E-05

3.2.5 Calculation of $PEC_{regional}$ and $PEC_{continental}$

$PEC_{regional(sea\ water)}$ = 5.54E-07 mg/l from the EUSES v2.03 model

$PEC_{regional\ (marine\ sediment)}$ = 3.51E-06 mg/kg wwt from the EUSES v2.03 model.

$PEC_{continental(sea\ water)}$ = 2.66E-08 mg/l from the EUSES v2.03 model.

$PEC_{continental\ (marine\ sediment)}$ = 1.68E-07 mg/kg wwt from the EUSES v2.03 model.

3.3 EFFECTS ASSESSMENT: HAZARD IDENTIFICATION AND DOSE (CONCENTRATION) - RESPONSE (EFFECT ASSESSMENT)

The following Sections review the available toxicity data for V6 with aquatic and terrestrial organisms. A reliability assessment is given for each study (this appears in the summary Tables within each Section). The assessment is based on the Klimisch system, which includes the following categories:

1 **Reliable without restriction**. "studies or data…generated according to generally valid and/or internationally accepted testing guidelines (preferably according to GLP) or in which the test parameters documented are based on a specific (national) testing guideline….or in which all parameters described are closely related/comparable to a guideline method."

2 **Reliable with restrictions**. "studies or data….(mostly not performed according to GLP), in which the test parameters documented do not totally comply with the specific testing guidelines, but are sufficient to accept the data or in which investigations are described which cannot be subsumed under a testing guideline, but which are nevertheless well documented and scientifically acceptable."

3 **Not reliable**. "studies or data….in which there were interferences between the measuring system and the test substance or in which organisms/test systems were used which are not relevant in relation to the exposure (e.g., unphysiologic pathways of application) or which were carried out or generated according to a method which is not acceptable, the documentation of which is not sufficient for assessment and which is not convincing for an expert judgement."

4 **Not assignable.** "studies or data….which do not give sufficient experimental details and which are only listed in short abstracts or secondary literature (books, reviews, etc.)."

In terms of the risk assessment, toxicity data assigned a reliability assessment of 1 or 2 will be considered in preference to the other toxicity data when deriving the PNEC.

The extent to which V6 impurities could influence the toxicity of test media has been assessed. TCEP is considered to be the only impurity that could have influenced the results of any of the tests that have been reported below. The scope of TCEP influence is restricted to the results of the algal tests as discussed in section 3.3.1.1.3.

3.3.1 Aquatic compartment (including sediment)

Study reports have been submitted for consideration in respect of acute tests with fish, algae and micro-organisms and acute and chronic tests with invertebrates. QSAR estimates of aquatic toxicity have also been obtained using the Syracuse Research Corporation ECOSAR Program (version 0.99g). The ECOSAR data are used to support or help explain the conclusions drawn from the data in the study reports.

All ecotoxicity testing of V6 was conducted on samples which represented the commercially supplied substance. TCEP is an impurity of V6 that is present in the substance as supplied at

concentrations ranging between 4.5 and 7.5%. The implications of the presence of TCEP as an impurity for the V6 test results are discussed below in Section 3.3.1.1.

3.3.1.1 Toxicity test results

The contents of the test reports are summarised below and in **Table 3.18**.

The measured toxicity of TCEP to fish and invertebrates is lower than that of V6 by a factor of 2 and 8 times respectively. Even supposing TCEP to be non-toxic to these organisms the net effect of it being present in the substance as tested would only be to reduce the apparent toxicity of V6 by about 8%. The consequences of this change would be insignificant for the interpretation of the test results. However, because TCEP has some toxicity and would be expected to act additively with V6, the net reduction in toxicity would be expected to be less than 8%.

Table 3.18 Summary of aquatic toxicity test results for V6

Test species	Test protocol	Year test completed	Endpoint and exposure period	Result (mg/l)[1]	Reliability assessment	Comments	Reference
Toxicity to fish							
Rainbow trout (*Oncorhynchus mykiss*)	OECD 203	2002	96-h NOEC 24-h LC_{50} 48-h LC_{50} 72-h LC_{50} 96-h LC_{50}	38 >92 40-70 53 52	(1) valid without restriction	Fulfils all the reliability criteria. Semi-static test. The test was carried out at exposure concentrations of 4.9, 10, 17, 38 and 71 mg/l (expressed as geometric means of measured concentrations at 0, 24, 48, 72 and 96 hours). Measured concentrations were generally stable within +/-20% of the corresponding initial concentrations. The test was subject to GLP.	L'Haridon 2002a
Rainbow trout (*Oncorhynchus mykiss*)	OECD 203	1993	96-h NOEC 24-h LC_{50} 48-h LC_{50} 72-h LC_{50} 96-h LC_{50}	≥10 (N) >10 (N) >10 (N) >10 (N) >10 (N)	(2) valid with restrictions	Static limit test. The test was not supported by analysis of exposure concentrations or GLP.	Sewell 1993a
Fish - acute QSAR (Esters)	ECOSAR (version 0.99g)		96-h LC_{50}	32		The estimated values are of the same order as the measured values. The estimates were obtained using measured physicochemical data as inputs to the model.	
Fish – acute QSAR (Phosphate esters)	ECOSAR (version 0.99g)		96-h LC_{50}	17			
Fish – chronic QSAR (Esters)	ECOSAR (version 0.99g)		NOEC	7.0			
Toxicity to aquatic invertebrates							

Test species	Test protocol	Year test completed	Endpoint and exposure period	Result (mg/l)[1]	Reliability assessment	Comments	Reference
Cladoceran (*Daphnia magna*)	OECD 202	2002	48-h NOEC 24-h EC_{50} 48-h EC_{50}	21 84 42	(1) valid without restriction	Fulfils all the reliability criteria. The test was carried out under static conditions at exposure concentrations of 4.7, 9.8, 21, 42, 69 and 150 mg/l (expressed as geometric means of measured concentrations at 0, 24 and 48 hours). Measured concentrations were stable within +/-20% of the corresponding initial concentrations. The test was subject to GLP.	L'Haridon 2002b
Cladoceran (*Daphnia magna*)	OECD 202	1993	48-h NOEC 24-h EC_{50} 48-h EC_{50}	$\geq$10 (N) >10 (N) >10 (N)	(2) valid with restrictions	Static limit test. The test was not supported by analysis of exposure concentrations or GLP.	Sewell 1993b
Invertebrate - acute QSAR (Esters)	ECOSAR (version 0.99g)		48-h LC_{50}	81		The estimated value is of the same order as the measured values. The estimates were obtained using measured physicochemical data as inputs to the model.	
Cladoceran (*Daphnia magna*)	OECD 211	2002	23 day EC_{50} (parent mortality) 23-day NOEC reproduction	7.31 $\geq$3.68	(1) valid without restriction	Fulfils all the reliability criteria. Test duration extended to 23 days in order to achieve validity criteria for control reproduction. Some measured concentrations were not within +/-20% of nominal values therefore results analysed and expressed relative to geometric mean concentrations over 23 days (0.953, 1.77, 3.68, 8.01 and 17.5 mg/l). The study was subject to GLP.	L'Haridon 2003
Invertebrate – longer term repro QSAR (Neutral organics)	ECOSAR (version 0.99h)		16-d EC_{50} (reproduction)	6.0		A recommended valid QSAR method is not readily available for the endpoint of chronic invertebrate. The method used, while the most appropriate from ECOSAR for this substance, is not recommended by ECOSAR for this type of compound and the QSAR is not well validated. However the estimated value compares well with the measured value. The estimate was obtained using measured physicochemical data as inputs to the model.	
Toxicity to algae							
Freshwater alga	OECD 201	2002	72-h NOEC	10	(1) valid	Fulfils all the reliability criteria. The test was carried out at	L'Haridon

Test species	Test protocol	Year test completed	Endpoint and exposure period	Result (mg/l)[1]	Reliability assessment	Comments	Reference
(*Pseudokirchneriella subcapitata*)			72-h E_rC_{50} (growth rate) 72-h E_bC_{50} (biomass)	35 21	without restriction	exposure concentrations of 5.3, 10, 20, 39 and 84 mg/l (expressed as geometric means of measured concentrations at 0, 24, 48 and 72 hours). Measured concentrations were generally stable within +/-20% of the corresponding initial concentrations. The test was subject to GLP. pH value deviations in the control and lowest concentration test media cultures after 72 hours exposure exceeded the OECD guideline value of 1 unit maximum. This is likely to have been a consequence of the high rates of algal growth achieved in these cultures and is not considered justification for rejecting the test result.	2002c
Freshwater alga (*Scenedesmus subspicatus*)	OECD 201 (Limit test)	1994	72-h NOEC 72-h E_rC_{50} (growth rate) 72-h E_bC_{50} (biomass)	$\geq$10 (N) >10 (N) >10 (N)	(2) valid with restrictions	Limit test. The test was not supported by analysis of exposure concentrations or GLP.	Sewell 1993c
Algae QSAR (Esters)	ECOSAR (version 0.99g)		96-h EC_{50} 96-h NOEC	2.6 2.1		The estimated values are lower than the measured values. The estimates were obtained using measured physicochemical data as inputs to the model.	
Toxicity to micro-organisms							
Activated Sludge	OECD 209	1993	EC_{50}	> 1000	(2) valid with restrictions	The test was not subject to GLP.	Handley, Horton and Sewell 1993

Note:

[1] 'N' denotes result expressed as nominal concentration

3.3.1.1.1 Fish

Acute toxicity

Study data

Reports have been submitted for two acute tests that have been carried out with the fish species *Oncorhynchus mykiss* (Rainbow trout).

One of the tests (L'Haridon 2002a) was conducted over a range of test concentrations, was supported by analysis of exposure concentrations and was subject to GLP. The test gave a 96-hour LC_{50} value of 52 mg/l. This result provides a suitable basis for deriving a $PNEC_{water}$.

The other test (Sewell 1993a) was a limit test conducted at a nominal concentration of 10 mg/l. There were no effects on mortality in the test. The test was not supported by analysis of exposure concentrations and was not subject to GLP. The result does not provide a suitable basis for determining a definitive $PNEC_{water}$.

QSAR estimated acute toxicity

Estimated values of 32 and 17 mg/l have been derived for acute (96-hour LC_{50}) fish toxicity using ECOSAR QSARs applicable to esters and phosphate esters respectively. The values are consistent with those obtained in the reported studies.

Long-term toxicity

Study data

No test data are available for review.

QSAR estimated chronic toxicity

An estimated value of 7.0 mg/l has been derived for chronic fish toxicity using an ECOSAR QSAR applicable to esters.

3.3.1.1.2 Aquatic invertebrates

Acute toxicity

Study data

Reports have been submitted for two acute tests that have been carried out with the invertebrate species *Daphnia magna*.

One of the tests (L'Haridon, 2002b) was conducted over a range of test concentrations, was supported by analysis of exposure concentrations and was subject to GLP. The test gave a 48-hour EC_{50} value of 42 mg/l. This result provides a suitable basis for deriving a $PNEC_{water}$.

The other test (Sewell 1993b) was a limit test conducted at a nominal concentration of 10 mg/l. There were no effects on immobilisation in the test. The test was not supported by analysis of exposure concentrations and was not subject to GLP. The result does not provide a suitable basis for determining a definitive $PNEC_{water}$.

QSAR estimated acute toxicity

An estimated value of 81 mg/l has been derived for acute (48-hour LC_{50}) toxicity to invertebrates using an ECOSAR QSAR applicable to esters. The value is consistent with those obtained in the reported studies.

Long-term toxicity

A report has been submitted for one chronic invertebrate test with *Daphnia magna* (L'Haridon, 2003). The test fulfilled all the acceptability criteria for determining a PNEC. There were no significant effects on reproduction at a concentration that was lower than that that significantly affected adult mortality. A 23-day NOEC for reproduction of ≥3.68 mg/l was therefore determined.

QSAR estimated chronic toxicity

An estimated value of 6.0 mg/l has been derived for long term reproductive effects in invertebrates using an ECOSAR QSAR applicable to neutral organics. This value may not be of high reliability because the QSAR is not recommended by ECOSAR for this type of compound, and it has not been well validated).

3.3.1.1.3 Algae

Study data

Reports have been submitted for growth inhibition tests carried out with two species of unicellular freshwater algae, *Scenedesmus subspicatus* and *Pseudokirchnierella subcapitata.*

The test with *P. subcapitata* (L'Haridon 2002c) was conducted over a range of test concentrations, was supported by analysis of exposure concentrations and was subject to GLP. The test gave a 72-hour E_rC_{50} value of 35 mg/l and a 72-hour NOEC of 10 mg/l. These results provide a suitable basis for deriving a $PNEC_{water}$.

The *S. subspicatus* test (Sewell 1993c) was a limit test conducted at a nominal concentration of 10 mg/l. There were no effects on growth of the alga during the test. The test was not supported by analysis of exposure concentrations and was not subject to GLP. The result does not provide a suitable basis for determining a definitive $PNEC_{water}$.

TCEP is an impurity of V6 that is present at concentrations ranging between 4.5 and 7.5%. Toxicity data for TCEP to algae reported in an ongoing risk assessment show it to be toxic at a concentration of 1.1 mg/l and have a NOEC of 0.2 mg/l. It is therefore possible that TCEP could have contributed significantly to the toxicity of the test medium prepared for the algal tests with V6.

QSAR estimated toxicity

Estimated 96-hour EC_{50} and NOEC values of 2.6 and 2.1 mg/l have been derived for algae using an ECOSAR QSAR applicable to esters. The estimated values are lower than those obtained in the reported studies.

3.3.1.1.4 Micro-organisms

A summary report has been submitted for one microbial inhibition test (Handley *et al*, 1993). The test was not conducted to GLP but is otherwise well-conducted and is acceptable for determining the PNEC for wastewater treatment. The EC_{50} was determined to be >1000 mg/l.

3.3.1.1.5 Amphibians

No amphibian effects data were available for review.

3.3.1.1.6 Sediment-dwelling organisms

No data are available and therefore PNEC for sediment is derived by the equilibrium partitioning method and compared with the PEC values for sediment.

3.3.1.2 Calculation of Predicted No Effect Concentration (PNEC)

Test data

The lowest values available are as follows:

Acute toxicity to fish	LC_{50}	= 52 mg/l
Acute toxicity to invertebrates	EC_{50}	= 42 mg/l
Acute toxicity to algae	E_rC_{50}	= 35 mg/l
Chronic toxicity to invertebrate's	21-day NOEC	$\geq$ 3.68 mg/l
Chronic toxicity to algae	NOEC	= 10 mg/l
Toxicity to WWTP micro-organisms	EC_{50}	>1000 mg/l

QSAR estimates

Acute toxicity to fish	96-hr LC_{50}	= 17 - 32 mg/l
Chronic toxicity to fish	NOEC	= 7.0 mg/l
Acute toxicity to invertebrates	48-hr LC_{50}	= 81 mg/l
Chronic toxicity to invertebrates	16-d EC_{50}	= 6.0 mg/l
Acute toxicity to algae	96-hr EC_{50}	= 2.6 mg/l
Chronic toxicity to algae	96-hr NOEC	= 2.1 mg/l

Fish, invertebrates and algae were similarly susceptible to V6 in the acute tests. An assessment factor of 1000 is applicable to determining a $PNEC_{water}$ from a data set comprising acute LC/EC_{50} values obtained with fish invertebrates and algae. Applying this assessment factor to the algal E_rC_{50} value results in a $PNEC_{water}$ for V6 of 35/1000 = 0.035 mg/l.

There are no measured chronic data for fish but a NOEC of 7.0 mg/l was estimated by QSAR. This value is in good agreement with a corresponding value of 5.2 mg/l obtained by dividing the measured acute toxicity value of 52 mg/l by a typical acute: chronic ratio of 10. The NOEC from an algal growth study is 10 mg/l. The long-term NOEC of ≥3.68 mg/l from a 21-day *Daphnia* study suggests that the PNEC should be based on these results.

It cannot be stated with certainty that the fish NOEC would be lower, so the appropriate assessment factor is 50. The PNECaquatic based on 21-day NOEC obtained in the long-term study with *D. magna* is therefore 3.68 / 50 = 0.0736 mg/l. This value has been used for purposes of risk characterisation. In comparison, this value is lower, and hence more conservative, than a $PNEC_{aquatic}$ of 0.70 mg/l derived by applying an assessment factor of 10 (applicable to data for three trophic levels) to the fish NOEC of 7.0 mg/l estimated by QSAR. Therefore: $PNEC_{aquatic}$ = 0.074 mg/l, although if justified, and taking animal welfare into consideration, it could be refined by performance of a chronic toxicity test with fish.

The basic guidance in the TGD is not entirely clear as to whether the EC_{10} or NOEC from the algal study should be used as the main result, in the context of PNEC derivation. In this case, no EC_{10} value was available in the published report. While EC_{10} could be calculated if necessary, the *Daphnia* result is more sensitive than the algal NOEC, so this is not considered to be a significant priority for V6.

Micro-organisms

Based on the available data, the PNEC for microbial inhibition can only be a limit value. The PNEC is therefore > 10 mg/l, based on an EC_{50} > 1000 mg/l and an assessment factor of 100.

Sediment-dwelling organisms

No toxicity data are currently available for sediment-dwelling organisms, therefore it is not possible to determine a $PNEC_{sed}$ based on measured data. According to the Technical Guidance Document, $PNEC_{sed}$ can be calculated by the equilibrium partitioning method using the following equation:

$$PNEC_{sed} = \frac{K_{susp\text{-}water}}{RHO_{susp}} * PNEC_{water} * 1000$$

For V6 this is:

$$PNEC_{sed} = \frac{7.03}{1150} * 0.0736 * 1000$$

$$= 0.45 \text{ mg/kg wwt}$$

Hence $PNEC_{sed}$ =0.45 mg/kg wwt will be used for risk characterisation.

In earlier drafts of this risk assessment, an additional factor of 10 was applied to risk characterisation based on equilibrium partitioning. This was considered necessary because of the perceived high adsorption of V6 as indicated by the HPLC K_{oc} result. This has now been superseded in a new understanding of adsorption behaviour based on a new and reliable study on a structurally-related substance (TDCP). V6 has a log K_{ow} value of 2.83 and a K_{oc} value of 245, therefore there is no need to apply an additional factor of 10.

The toxicity of the related substance TDCP has been studied in detail, and it was found that the PNEC derived from these studies was similar to that derived by equilibrium partitioning. It is reasonable to conclude that the same would apply to V6, and that the PNEC derived by equilibrium partitioning is sufficiently protective.

3.3.2 Terrestrial compartment

3.3.2.1 Toxicity test results

The terrestrial test results are summarised below and in **Table 3.19**.

A short-term test has been conducted with the earthworm, *Eisenia foetida.* The result of a soil micro-organism nitrogen transformation test with TDCP and a higher plant test with TCPP are presented for comparison.

Table 3.19 Summary of terrestrial toxicity test results for V6

Test species	Test protocol	Year test completed	Endpoint and exposure period	Result (mg/kg)[1]	Reliability assessment	Comments	Reference
Toxicity to earthworm							
Earthworms (*Eisenia foetida*)	OECD 207 (Limit test)	1996	14-day NOEC (mg/kg dry weight) 7-day LC_{50} (mg/kg dry weight) 14-day LC_{50} (mg/kg dry weight)	>1000 (N) >1000 (N) >1000 (N)	(2) valid with restrictions	The test was not subject to GLP. The test is of an overall acceptable standard although there are inadequacies in some elements. Values require correction for organic matter content (10%) prior to use for risk assessment.	Wetton 1996
Toxicity to higher plants							
Wheat (*Triticum aestivum*), Mustard (*Sinapsis alba*), Lettuce (*Lactuca sativa*) (TCPP)	OECD Guideline 208	2003	NOEC (emergence): Wheat Mustard Lettuce NOEC (dry weight): Wheat Mustard Lettuce	≥98 (N) 30 (N) 17 (N) 22 (N) 29 (N) 18 (N)	(1) valid without restriction	**Study conducted using a similar test substance (TCPP)** Fulfils all reliability criteria. A fully valid GLP study. Organic matter content in the test soil was 1.4%.	Servajean, 2003
Toxicity to soil micro-organisms							
Nitrifying micro-organisms in sandy loam soil (TDCP)	OECD Guideline 216	2005	NOEC (micro-organism activity based on nitrate concentration); 28 days (mg/kg wet weight)	≥128	(1) valid without restriction	**Study conducted using a similar test substance (TDCP)** Fulfils all the reliability criteria. The study was subject to GLP. Organic matter content in the test soil was 1%.	van Ginkel (2005)

Note:

[1] 'N' denotes result expressed as nominal concentration

3.3.2.1.1 Earthworm

Acute toxicity

A report has been provided for one acute test with the earthworm *Eisenia foetida* (Wetton 1996). The test was a limit test conducted at a nominal concentration of 1000 mg/kg dry weight. There were no effects on mortality in the test. The 14-day NOEC was therefore ≥1000 mg/kg dry weight and the 14-day LC_{50} was >1000 mg/kg dry weight.

The organic matter content was approximately 10% (sphagnum moss peat 10% w/w dry weight of test soil). Therefore the results need to be corrected to obtain a result relevant for natural soils, containing a TGD default of 3.4% organic matter. A correction factor of 0.34 is therefore applied, giving standardised results of:

14-day $NOEC_{standardised} \geq 340$ mg/kg dry weight
14-day $LC_{50standardised} > 340$ mg/kg dry weight.

It should be noted that both TCPP and TDCP show acute effects on the earthworm (14-day LC_{50} values of 97and 130 mg/kg dry weight respectively).

Long-term toxicity

No data are available for review. Based on the absence of effects in the short-term test it is assumed that the earthworm, *Eisenia foetida*, would not be the most sensitive species following longer-term exposure. Both TCPP and TDCP show effects in long-term studies.

3.3.2.1.2 Higher plants

Long-term toxicity

No data are available for V6. Long-term effects on higher plants were measured for TCPP in 2003 (Servajean 2003). The study reported the results of emergence and growth tests with the plant species *Triticum aestivum* (Wheat), *Sinapis alba* (Mustard), *Lactuca sativa* (Lettuce). The tests fulfilled the criteria for acceptability for determining a PNEC. The lowest NOEC determined in the tests was 17 mg/kg dry weight for emergence of *L. sativa* seedlings. The lowest NOECs determined for *S. alba* and *L. sativa* were 28 and 18 mg/kg respectively based on 21-day post emergence plant wet weight.

In this case, correction for organic matter content in the test (1.4%) would give a more favourable result and therefore this correction has not been made.

NOEC = 17 mg/kg dry weight

Discussion of read-across

Read-across of the long-term effects data on higher plants from TCPP to V6 could be considered on the following grounds:

- TCEP, TCPP and TDCP share similar soil adsorption properties to V6 (see section 3.1.3.2.1) indicating that the bioavailability of the substances to soil organisms should be comparable. In particular, the closeness in value of log K_{ow} and K_{oc} values between

V6 (Log K_{ow} 2.83, K_{oc} 245) and TCPP (Log K_{ow} 2.68, K_{oc} 174) suggests that these two substances would be expected to partition in the terrestrial environment in a very similar way.

- Test results for these substances suggest a consistent pattern of toxicity across this taxonomic group (see **Table 3.20**). This is indicative of a consistent mode of action in higher plants, and the similarities in chemical structure between the substances would support this.
- Structural differences between V6 and the other three substances are not considered to suggest a different mode of action in environmental organisms. Whilst V6 has two phosphate groups, its side-chains are very similar to those of the other substances.
- Reliable chronic toxicity data for aquatic plants (freshwater algae) indicate that the NOEC for V6 lies within a factor of only 4 of the E_rC_{10} values for TCPP and TDCP (see **Table 3.21**).

Table 3.20 Higher plant effects data for chloroalkyl phosphates

Substance	Species	Result (mg/kg dw)	Reliability
TCEP	*Avena sativa*	EC_{50} = 64 NOEC = 10	1
TCPP	*Lactuca sativa*	NOEC = 17	1
TDCP	*Sinapis alba*	NOEC = 19.3	1

Table 3.21 Freshwater algae effects data for chloroalkyl phosphates

Substance	Species	Result (mg/l)	Reliability
V6	*Pseudokirchneriella subcapitata*	NOEC = 10	1
TCPP	*Pseudokirchneriella subcapitata*	E_rC_{10} = 42	1
TDCP	*Pseudokirchneriella subcapitata*	E_rC_{10} = 2.3	1
TCEP	*Scenedesmus subspicatus*	E_rC_{10} = 0.65 [1]	Not stated

Note 1 – The TCEP result conflicts with results of other valid test results for the same substance, which have EC_{10} or NOEC at considerably higher concentrations.

3.3.2.1.3 Terrestrial micro-organisms

Inhibition of soil nitrogen transformation by soil micro-organisms has been examined in a study with TDCP conducted voluntarily by industry (van Ginkel, 2005). A 28-day NOEC of ≥128 mg/kg wet weight (no inhibition at the highest concentration tested) was determined in the test.

In this case, correction for organic matter content in the test (1 %) would give a more favourable result and therefore this correction has not been made.

Discussion of read-across

Read-across of the result to V6 is considered justified on the grounds that:

- TCEP, TCPP and TDCP share similar soil adsorption properties to V6 (see section 3.1.3.2.1). The bioavailability of the substances should therefore be comparable.
- Reliable toxicity test data suggest a consistent low order of acute toxicity for V6 and the structurally related substances TCPP, TDCP and TCEP to micro-organisms present in waste water treatment plants (see **Table 3.22** below).
- Reliable effects data are available for a range of other freshwater and terrestrial organisms for TCEP, TCPP, TDCP and V6. In no instance does V6 cause an effect at the lowest concentration across the group or at a lower concentration than TDCP specifically. Therefore it is not anticipated that read-across of this result could result in an overly favourable conclusion in respect of V6.

Table 3.22 Waste water treatment plant (WWTP) micro-organism effects data for chloroalkyl phosphates

Substance	IC_{50} WWTP micro-organisms (mg/l)	Reliability
V6	>1000	1
TDCP	>10000	2
TCPP	784	1
TCEP	3200	1

3.3.2.2 Calculation of Predicted No Effect Concentration (PNEC)

The lowest values available for V6 itself are as follows:

Toxicity to earthworms 14 d LC_{50} >1000 mg/kg dw

Acute data are only available for one species: the earthworm *Eisenia foetida*, representative of soil invertebrates. Whilst it is not possible to derive definitive NOEC or LC_{50} values from the test results it is possible to conclude that the 14-day NOEC is ≥1000 mg/kg and the 14-day LC_{50} is >1000 mg/kg. As described above, these values are corrected for organic matter content of the test soil to give standardised results of:

14-day $NOEC_{standardised}$ ≥ 340 mg/kg dry weight, equivalent to ≥ 300 mg/kg wet weight
14-day $LC_{50standardised}$ > 340 mg/kg dry weight, equivalent to >300 mg/kg wet weight.

In the absence of a data set comprising acceptable short-term test results for at least three trophic levels or longer-term test results for at least two trophic levels it is only possible to obtain a tentative $PNEC_{soil}$ from the test data. Applying an assessment factor of 1000 to the LC_{50} value from the short-term earthworm test results in a tentative $PNEC_{soil}$ of >340/1000 = >0.34 mg/kg soil dry weight, equivalent to >0.3 mg/kg soil wet weight.

Since only one short-term test result is available, it is appropriate to compare this tentative $PNEC_{soil}$ with that obtained by the equilibrium partitioning method. The equation is:

$$PNEC_{soil} = \frac{K_{soil\text{-}water}}{RHO_{soil}} * PNEC_{water} * 1000$$

For V6 this is:

$$PNEC_{soil} = \frac{7.55}{1700} * 0.0736 * 1000$$

$$= 0.327 \text{ mg/kg wwt}$$

This is equivalent to 0.37 mg/kg dwt.

Although the equilibrium partitioning approach results in a slightly higher PNEC is than that derived from measured data, both values are considered in the risk characterisation, since in this case the aquatic data set is much stronger than the terrestrial.

Read-across of data measured for the structurally-related substances TCPP and TDCP could be considered to be justified for the reasons described in Sections 3.3.2.1.2 and 3.3.2.1.3 above. Furthermore, based on the absence of effects in the short-term test in the earthworm, it could be assumed that earthworm would not be the most sensitive species following longer-term exposure, although chronic effects of V6 on the earthworm cannot be ruled out. The PNEC for TDCP is based on the chronic earthworm study, and for TCPP the NOECs for chronic earthworm and higher plant studies are similar. Therefore an alternative PNEC for purposes of comparison with the equilibrium partitioning PNEC can be derived from the above read-across data. Applying an assessment factor of 10 to the NOEC value from the long-term higher plant test results read across from TCPP gives a $PNEC_{soil}$ of 17/10 = 1.7 mg/kg soil dry weight, equivalent to 1.5 mg/kg soil wet weight. For both TCPP and TDCP, which have been more fully studied, the PNEC from studies and the PNEC from equilibrium partitioning are very close to each other. Therefore, the preferred approach for V6 is to use the PNEC derived by the equilibrium partitioning method, acknowledging that it is possibly conservative.

$PNEC_{soil}$ = 0.37 mg/kg dwt.

3.3.3 Atmosphere

No data are available on the toxicity of V6 to plants or other organisms exposed via air. Based on its structure, V6 is not expected to have ozone depleting effects and the low level of exposure makes other effects unlikely. The evidence from the open literature indicates that a similar substance (TDCP), found in needles of pine trees (*Pinus ponderosa*), and thought to have been transported by aerial deposition processes, did not exert phytotoxic effects (Aston *et al*, 1996). The possibility of V6 contributing to atmospheric effects such as global warming, ozone depletion and acid rain is likely to be very small.

3.3.4 Secondary poisoning

3.3.4.1 Effect data

The most relevant data for derivation of the PNEC for secondary poisoning for V6 are from a 28-day study in the rat. The NOAEL is 15 mg/kg bw/day, based on liver effects.

Using the conversion factors given in the Technical Guidance Document:
NOAEL = 15 mg/kg bw/d

NOEC mammal = NOAEL mammal x CONV mammal

NOEC = 15 mg/kg bw/d x 20 (animal age > 6 weeks)
= 300 mg/kg food

3.3.4.2 Calculation of $PNEC_{oral}$

According to the Technical Guidance Document an assessment factor of 300 is appropriate for the results of a study of this duration. Therefore, applying this assessment factor:
PNEC oral = NOAEL/AF

PNEC oral = 300/300
= 1.0 mg/kg food

A PNEC for secondary poisoning of 1.0 mg/kg food will be used. This value is also applicable for the assessment of secondary poisoning in the marine environment.

3.3.5 MARINE EFFECTS ASSESSMENT

Calculation of Predicted No Effect Concentration (PNEC)

PNEC*seawater*

No measured data are currently available for marine organisms therefore marine PNECs are derived from data obtained for freshwater species (NOEC = 3.68 mg/l), applying an assessment factor of 500 to give a PNEC*seawater* of 7.4×10^{-3} mg/l.

PNEC*marine sediment*

No measured data are currently available for marine sediment organisms therefore the PNEC is derived by equilibrium partitioning to give a PNEC*marine sediment* of 0.045 mg/kg.

3.4 RISK CHARACTERISATION

The producer company has confirmed that the confidential application F of V6 (life cycle stages F1 and F2) is not applicable in Europe. The information about this application obtained in the original survey probably related to customer trials. Life cycle stages F1 and F2 have therefore not been carried forward to risk characterisation.

PEC values for fresh and marine water, sediment and soil, and for predators, are given in **Tables 3.9** to **3. 17**. PEC/PNEC values are given in **Tables 3.24** to **3.29**.

For ease of reference, the PNECs used in the risk assessment are summarised in **Table 3.23** below.

Table 3.23 PNECs used in the risk assessment of V6

Compartment	Value of PNEC
Fresh water	0.074 mg/l
Freshwater sediment	0.45 mg/kg wet weight (equilibrium partitioning)
WWTP micro-organisms	> 10 mg/l
Sea water	0.0074 mg/l (extrapolation from freshwater)
Marine sediment	0.045 mg/kg wet weight (extrapolation from freshwater)
Soil	Based on equilibrium partitioning: 0.33 mg/kg wet weight (preferred value) Based on acute earthworm result only: >0.3 mg/kg wet weight Based on read-across data from TCPP and TDCP: 1.5 mg/kg wet weight
Secondary poisoning	1.0 mg/kg food

3.4.1 Aquatic compartment (incl. sediment)

3.4.1.1 Water and sediment

Table 3.24 PEC/PNEC ratios for surface water and freshwater sediments

	PEC/PNEC$_{water}$	**PEC/PNEC$_{sediment}$**
Producer	8.16E-05	8.16E-05
A1a: Flexible foam - automotive - foaming large site	3.11E-04	3.11E-04
A1b: Flexible foam - automotive – foaming	9.97E-03	9.97E-03
A2: Foam cutting	1.14E-04	1.14E-04
B1: Flexible foam - furniture - foaming	0.079	0.079
B2: Foam cutting	1.23E-04	1.23E-04
C1: CONFIDENTIAL	0.0436	0.0436
C2: CONFIDENTIAL	8.00E-03	8.00E-03
D1: CONFIDENTIAL	0.0113	0.0113
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	7.38E-05	7.38E-05
H1: Loose Crumb	7.38E-05	7.38E-05

PEC/PNEC$_{regional(water)}$ = 7.38E-05 from the EUSES v2.03 model.

PEC/PNEC $_{regional(freshwater\ sediment)}$ = 8.27E-05 from the EUSES v2.03 model.

Conclusions to the risk assessment for the aquatic compartment including sediment:

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
This conclusion applies to all life cycle stages.

3.4.1.2 Wastewater treatment processes

Table 3.25 PEC/PNEC ratios for wastewater treatment plants

	$PEC/PNEC_{WWIP}$
Producer	<5.8E-06
A1a: Flexible foam - automotive - foaming large site	<1.75E-05
A1b: Flexible foam - automotive – foaming	<7.29E-04
A2: Foam cutting	<2.97E-06
B1: Flexible foam - furniture – foaming	<5.81E-03
B2: Foam cutting	<3.64E-06
C1: CONFIDENTIAL	<3.2E-03
C2: CONFIDENTIAL	<5.84E-04
D1: CONFIDENTIAL	<8.27E-04
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	-
H1: Loose Crumb	-

Conclusions to the risk assessment for wastewater treatment plant micro-organisms:

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
This conclusion applies to all life cycle stages.

3.4.2 Terrestrial compartment

PEC/PNEC ratios based on the PNEC derived from the equilibrium partitioning approach are presented in **Table 3.26**. For comparison, results using the PNEC derived from the acute earthworm test, and using a PNEC derived from read across data for the related substances TCPP and TDCP are also included. While the acute earthworm-based results offer the worst case, being based on the lowest PNEC, these results are limit values only. The equilibrium partitioning based results are considered to be the most sound.

Table 3.26 PEC/PNEC ratios for agricultural soil

	$PEC/PNEC_{soil}$ using equilibrium partitioning	**$PEC/PNEC_{soil}$ using acute earthworm result [14]**	**$PEC/PNEC_{soil}$ using read-across measured data[15]**
Producer	3.19E-04	<3.47E-04	6.95E-05
A1a: Flexible foam - automotive – foaming large site	6.02E-04	<6.54E-04	1.31E-04
A1b: Flexible foam – automotive – foaming	0.0160	<0.0175	3.49E-03
A2: Foam cutting	2.67E-04	<2.91E-04	5.82E-05
B1: Flexible foam - furniture – foaming	0.126	<0.138	0.0275
B2: Foam cutting	2.79E-04	<3.03E-04	6.07E-05
C1: CONFIDENTIAL	0.0698	<0.0759	0.0152
C2: CONFIDENTIAL	0.0129	<0.014	2.81E-03
D1: CONFIDENTIAL	0.0182	<0.0198	3.97E-03
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	2.04E-04	<2.21E-04	4.43E-05
H1: Loose Crumb	1.98E-04	<2.15E-04	4.30E-05

$PEC/PNEC_{regional(soil)}$ = 4.24E-05 from the EUSES v2.03 model.

Conclusions to the risk assessment for the terrestrial compartment:

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
This conclusion applies to all life cycle stages.

Applying the PNEC derived using the acute earthworm test (>0.3 mg/kg wet weight) would also suggest that no risks are identified. Since no effects were seen in the earthworm test, all ratios are 'less than' values. In addition, applying the PNEC based on measured data for TCPP (1.5 mg/kg wet weight) to V6, which is based on reliable measured data and an assessment factor of 10, would also lead to no risks being identified. This supports the current approach using the PNEC derived by equilibrium partitioning.

3.4.3 Atmosphere

Neither biotic nor abiotic effects on the atmosphere are likely because of the low predicted environmental concentrations of V6 (all concentrations are below 1E-5 mg/m^3).

[14] Since no effects were seen in the acute earthworm test, all results are less-than values.
[15] Using a PNEC of 1.5 mg/kg soil wet weight based on read-across data from TCPP and TDCP, for comparative purposes

Conclusions to the risk assessment for atmosphere:

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
This conclusion applies to all life cycle stages.

3.4.4 Secondary poisoning

Table 3.27 PEC/PNEC ratios for secondary poisoning

	PEC/PNEC$_{fish\ eating}$	**PEC/PNEC$_{worm\ eating}$**
Producer	2.87E-04	1.60E-04
A1a: Flexible foam - automotive – foaming large site	4.58E-04	2.46E-04
A1b: Flexible foam - automotive – foaming	4.03E-03	4.95E-03
A2: Foam cutting	3.38E-04	1.44E-04
B1: Flexible foam - furniture - foaming	0.0326	0.0386
B2: Foam cutting	3.16E-04	1.47E-04
C1: CONFIDENTIAL	7.21E-04	0.0213
C2: CONFIDENTIAL	6.82E-04	3.99E-03
D1: CONFIDENTIAL	4.88E-03	5.62E-03
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	2.76E-04	1.24E-04
H1: Loose Crumb	2.76E-04	1.23E-04

Conclusions to the risk assessment for secondary poisoning:

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
This conclusion applies to all life cycle stages.

3.4.5 Marine environment

3.4.5.1.1 PBT assessment

Persistence

The persistence criteria currently laid down in the TGD require a half-life >60 days in marine water (or >40 days in fresh water) or >180 days in marine sediment (or >120 days in freshwater sediment). The available screening studies show that V6 is not readily biodegradable so the screening criterion for persistence is met.

Bioaccumulation

The criterion used in the TGD for bioaccumulation is a bioconcentration factor (BCF) >2,000 l/kg. In the absence of measured bioconcentration data the value of log K_{ow} (≥4.5) can be considered as a screening criterion. V6 has a log K_{ow} = 2.83 and hence does not meet the screening criteria for B.

Toxicity

The toxicity criterion used in the TGD is a chronic NOEC <0.01 mg/l or substances classified as Carcinogenic (category 1 & 2), Mutagenic (category 1 & 2), or Toxic to Reproduction (category 1,2, & 3) or with other evidence of chronic toxicity. The lowest aquatic NOEC for V6 is ≥3.68 mg/l from a 21-day *Daphnia* study. V6 is not currently classified for human health effects, however a 2-generation fertility study and a developmental toxicity screening test are currently being conducted so this endpoint should be re-visited once results are available. Based on the aquatic toxicity data, the T criterion is not met.

Summary of PBT assessment

For the PBT assessment, V6 can be considered to be potentially persistent (P) or potentially very persistent (vP) based on its ultimate mineralisation. The available information on log K_{ow} suggests that V6 does not meet the B or vB criterion. The T criterion is not met for aquatic toxicity.

3.4.5.2 Marine risk characterisation

Table 3.28 PEC/PNEC ratios for seawater and marine sediments

	PEC/PNEC$_{sea\ water}$	**PEC/PNEC$_{marine\ sediment}$**
Producer	1.56E-04	1.56E-04
A1a: Flexible foam - automotive – foaming large site	3.20E-04	3.20E-04
A1b: Flexible foam - automotive – foaming	0.0103	0.0103
A2: Foam cutting	1.17E-04	1.17E-04
B1: Flexible foam - furniture - foaming	0.0814	0.0814
B2: Foam cutting	1.26E-04	1.26E-04
C1: CONFIDENTIAL	0.0449	0.0449
C2: CONFIDENTIAL	8.25E-03	8.25E-03
D1: CONFIDENTIAL	0.0117	0.0117
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	7.53E-05	7.53E-05
H1: Loose Crumb	7.53E-05	7.53E-05

PEC/PNEC $_{regional(sea\ water)}$ = 7.53E-05 from the EUSES v2.03 model

PEC/PNEC $_{regional\ (marine\ sediment)}$ = 7.81E-05 from the EUSES v2.03 model.

Conclusions to the risk assessment for the marine environment:

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
This conclusion applies to all life cycle stages.

Secondary poisoning in the marine environment

Table 3.29 PEC/PNEC ratios for secondary poisoning in the marine environment

	$PEC/PNEC_{marine\ predator}$	$PEC/PNEC_{marine\ top\ predator}$
Producer	3.98E-05	3.05E-05
A1a: Flexible foam - automotive – foaming large site	4.69E-05	3.19E-05
A1b: Flexible foam - automotive – foaming	4.15E-04	1.06E-04
A2: Foam cutting	3.46E-05	2.94E-05
B1: Flexible foam - furniture - foaming	3.36E-03	6.95E-04
B2: Foam cutting	3.23E-05	2.90E-05
C1: CONFIDENTIAL	7.41E-05	3.73E-05
C2: CONFIDENTIAL	7.00E-05	3.65E-05
D1: CONFIDENTIAL	5.03E-04	1.23E-04
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	2.82E-05	2.82E-05
H1: Loose Crumb	2.82E-05	2.82E-05

Conclusions to the risk assessment for secondary poisoning in the marine environment:

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
This conclusion applies to all life cycle stages.

3.4.6 Areas of uncertainty in the environmental risk assessment

The main area of uncertainty is the assumption regarding limited availability of V6 for release from foams. This is discussed in Section 3.1 and will affect all life cycle stages associated with foam production, processing and use (local life cycle stages A1a, A1b, A2, B1, B2, G1 and H1, and the regional background). The sensitivity of the risk assessment to this uncertainty has been considered, as follows. While the exact level of availability is uncertain, it would be very unlikely to be as high as 40%, which is the level that applies for the related substance TCPP (and is well supported by experimental evidence). Taking this as the worst case, PEC/PNEC ratios could potentially be (in most cases) four times higher for V6 foam-related life cycle stages. It is clear that even in this worst case, no additional risks would be identified.

Disposal to landfill is likely to be the most significant route of disposal of flexible foam and other articles containing V6. Based on the tonnage supplied and the properties of the substance, it is considered that emissions from landfills will make a negligible contribution to PECregional values, although no monitoring data for landfill leachate are available to support this view.

An additional area of uncertainty is the value of the PNEC for the terrestrial compartment. The present conclusions are based on a PNEC derived using equilibrium partitioning. If an alternative limit PNEC is used, based on an acute earthworm study with V6 showing no

effects, the PEC/PNEC ratios are ‘less than’ values slightly higher than the current values. However, all PEC/PNEC ratios are still below 1.

The Rapporteur has no reason to anticipate significant tonnage increases in the near future, based on industry information and general research.

4 HUMAN HEALTH

4.1 HUMAN HEALTH (TOXICITY)

4.1.1 Exposure assessment

4.1.1.1 Occupational exposure

General introduction

In the following sections, unless otherwise stated, the term exposure is used to denote personal exposure as measured or otherwise assessed without taking into account the attenuating effects of any personal protective equipment (PPE) which might have been worn as not enough information was available to take the actual protection of any PPE worn into account.

Occupational exposure information has been made available through the manufacturer and users of V6.

Overview of exposure

V6 is a liquid at room temperature. The calculated vapour pressure is 2.75×10^{-6} Pa at 25^0C (From environmental assessment). The calculated saturated vapour pressure concentration (SVC) is 0.65 $\mu g/m^3$ at 25^0C.

Occupational exposure to V6 may occur during its manufacture and during the manufacture and cutting of polyurethane foam. Inhalation of vapours and skin contact are the predominant routes of exposure. Oral exposure is not considered to be a significant route of exposure under normal working practices.

Descriptions of the processes and sources of occupational exposure are discussed below along with a discussion of exposure levels. Most of the data used in this assessment has been supplied by industry, either directly or through trade organisations. Data supplied by industry for the risk assessment report for TCPP (HSA/EA, 2008a) and TDCP (HSA/EA, 2008b) has also been used where appropriate. The data has been used in more than one scenario where it was felt appropriate by the Rapporteur.

The occupational exposure scenarios are:

1. Manufacture of V6
2. Manufacture of flexible PUR foam
    a. slabstock foams
    b. moulded foams
3. *Cutting of flexible foam
4. Production of foam granules and rebonded PUR foam
5. Manufacture of automotive parts

*Scenario 3 also covers the cutting of foam by furniture manufacturers where this occurs.

Following manufacture, most (over 95%) of the V6 produced is used as a flame retardant in the production of flexible polyurethane (PUR) foam, mainly for use in the automotive industry. V6 is not used in rigid foams owing to cost considerations. Flexible foams are produced by pouring the blend of two raw materials (polyol and isocyanate) onto a rolling conveyer belt (slabstock foam) or into a mould (moulded foam). Moulded foam is mainly used in the automotive industry (seat cushions headrests), with some use for office furniture. The main application of slabstock foam is for furniture.

The remaining uses (<5%) of V6 are described in the Confidential use pattern and exposure Annex. These are mainly single uses and there is no information on the number of people potentially exposed or the exposures. These small single uses will not be considered further in this risk assessment.

The total number of workers potentially exposed to V6 during the production of flexible PUR foam in the EU is difficult to estimate. Industry has informed the rapporteur that for flexible foam, EUROPUR members (representing about 85% of the market) have about 68 plants in the EU. Some plants use V6 more frequently than others. A fair assumption may be that approximately 5 operators per plant can be around the foaming tunnel during production, bearing in mind the frequency of use of V6 will vary quite a bit from plant to plant.

Occupational exposure limits

There are no occupational exposure limits set for V6.

4.1.1.1.1 Scenario 1: Occupational exposure during the manufacture of V6

There is only one producer of V6 in Europe. Total EU production in 2000 was less than 5,000 tonnes, with production taking place at one site in the UK. Some of the V6 produced in the EU is exported. Between 1999 and 2003, production has fluctuated slightly but the total EU sales tonnage has remained reasonably stable within approximately 10%. There are no imports into the EU.

V6 is produced in a closed system by adding a polyhydric alcohol to excess phosphorous trichloride in a carrier solvent in the presence of a catalyst. The crude product is washed to remove acidic impurities, dehydrated and filtered. The product is stabilised before it is packed into drums or transferred to road tanker. The processes are computer-controlled. The computers monitor and control reactors, reaction conditions such as temperature and pressure, chemical additions and process alarms. This limits the possibilities of operator contact with V6 during the production steps. There are two operators assigned to the production plant per shift. The operators spend most of their time in the control room monitoring the production process. The tasks performed where contact may take place during production are while taking samples for quality control purposes, cleaning filters and during transfers of the product to road tankers or drums for distribution. Samples are taken from a dedicated valve into a 250 g bottle. The operator wears coveralls, PVC gloves, safety spectacles and a hard hat. There is no LEV at the sampling point. It is estimated that it takes about 1 minute to take a sample. About 4 samples are taken per day. The samples are taken to the laboratory for analysis, except for one where the operator checks the pH.

Filters are cleaned using a water jet and by scraping. During this activity the operator wears coveralls, safety spectacles and Vygen Plus gloves.

Filling stations for drumming are semi-automatic and are equipped with local exhaust ventilation to remove vapours from the operator area. The plunger is also equipped to avoid drops falling down when the lance is transferred from one drum to another. The lance is moved by means of a boom, which supports it, so that the operator does not need to touch the filling head when transferring it from one drum to another. Once a pallet of drums is filled, the operator moves the boom out of the way and fits seals and caps to the drums. These are then moved with a forklift truck to the storage area. During drumming, the operator wears coveralls and safety spectacles.

V6 is produced in a batch-wise process, with 3 batches being worked on at any one time. The total number of people potentially exposed to V6 during its manufacture is approximately 30.

Measured exposure data

In a study conducted by industry (2002), inhalation and hand exposure of 4 operators in the V6 manufacturing plant was evaluated under actual working conditions. Personal air-sampling pumps and a sampling tube were used for the assessment of inhalation exposure. The air sampler was attached to the collar of the operator, thus positioning it in his breathing zone. The pump was calibrated to a nominal sample flow rate of approx. 1 L/min ± 10% L/min. The sample tube was extracted with toluene containing trioctyl phosphate. The final extract was chromatographed with flame photometric detection.

For dermal exposure monitoring, 100% cotton absorbent gloves were used as dosimeters. If protective gloves were used, the absorbent gloves were worn beneath them. The protective gloves used were Vygen plus PVC gloves, cotton lined. The absorbent gloves were peeled off and replaced at times when the worker normally washed his hands and were placed in a plastic bag. They were extracted with toluene before chromatography.

The methods for both inhalation (Akzo Nobel Method CG/6.089.3) and dermal monitoring have been developed and validated for V6. The limit of detection was evaluated to be 0.3 μg for V6 on sampling tubes and 10 μg on cotton gloves. **Table 4.1** below gives a summary of these monitoring results.

Table 4.1 Results of personal inhalation and dermal monitoring carried out on operators involved in production of V6 and blend drumming

Operator's Task	Length of time monitored (mins)	Inhalation exposure V6 (μg/m^3) 8hr TWA	Dermal exposure V6 (mg/kg bw)	Dermal exposure V6 (mg/day)
Production (1)	493	0.3	0.14	9.8
Production (2)	488	0.12	0.13	9.1
V6 Drumming (3)	252	30.4	1.2	84
V6 Blend Drumming (4)	177	0.78	2.3	161
Laboratory Technician	45		0.35	24.5

Production operator (1) was involved in V6 production. He was located in the control room during most of the monitoring period. His main tasks included the taking of a sample, plant checking and other activities related to the beginning of V6 synthesis. He wore protective gloves (Vygen plus PVC gloves, cotton lined) when carrying out activities in the V6 plant. The second production operator was also involved in V6 production and was also located in the control room for most of the monitoring period. During his shift he made up the 'carb

wash' took a sample of V6 dehydrated, V6 filtered and V6 finished. The 'carb' wash is a dilute aqueous solution of sodium carbonate. It is used to remove acidity and chlorine from the crude product. He also cleaned the V6 filter plates. He wore protective gloves when carrying out activities in the V6 plant and a tyvek disposable coverall and gloves when making up the 'carb wash'. The V6 drumming operator (operator 3) was located in the drumming area during the monitoring period. He drummed V6 for 4 h 10 mins and filled 42 x 300kg drums during this time. His inhalation exposure (30.4 $\mu g/m^3$) was much higher than the other operators monitored, but there is no indication of why. The 4th operator was located in the blend drumming area of the fluid plant. He drummed for a period of 3 hours and filled 23 drums each with 300 kg of a V6 blend. He did not wear protective equipment while carrying out this task. Both of the drumming operators were monitored for the length of time it took them to complete their tasks. Industry has indicated that theoretically, an operator could be working a full 8-hour shift, depending on requirements. Finally, a laboratory technician was monitored for dermal exposure only. During the monitoring period, he carried out V6 analysis for 45 mins. He did not wear protective equipment when carrying out his tasks. No further information on his activities was made available.

In parallel to the personal monitoring, a static measurement, with the same equipment as for personal monitoring, was performed. In the V6 plant, the static monitoring was carried out near the sampling valve and the cleaning of filter plates area. One sample of V6 was taken during the monitoring period and filter plate cleaning took place once. The monitoring period was for 349 minutes (5.82 hours). This static measurement gave a concentration of V6 of 0.41 $\mu g/m^3$. Industry has indicated that in this plant, the maximum for carrying out any particular function on the V6 plant is twice per shift (and the usual is once per shift), so an operator would not normally be in the monitored area more than twice during his shift.

The highest dermal exposures were for the operators carrying out drumming. The operator who was drumming a V6 blend had the highest exposure (2.3 mg/kg bodyweight). He did not wear any protective gloves while carrying out the drumming. There is little opportunity for dermal exposure during the production process, but the operators were observed always to wear protective gloves when working on the plant.

For the measured data, there are few data points for the study carried out in the production plant. However, the tasks carried out during the monitoring periods are typical of the normal work patterns and the results obtained appear to be representative of the V6 production industry.

Modelled exposure data

Dermal exposure modelling was carried out using EASE to supplement the real exposure monitoring carried out. For production activities the EASE parameters used were a liquid in a closed system (breached for sampling and maintenance) with no direct handling. The estimated dermal exposure is very low.

The estimated range of exposure for quality control sampling of V6 was 0 to 0.1 $mg/cm^2/day$, using the parameters non-dispersive use, direct handling with incidental contact. The exposure area was estimated to be 210 cm^2. The exposure area of 210 cm^2 was selected as there is little opportunity for large-scale dermal exposure during normal operations as most of the production takes place in closed systems with breaches for sampling and drumming.

The parameters used to estimate dermal exposure during drumming were non-dispersive use, direct handling and intermittent contact. This gives an exposure range of 0.1 to 1 $mg/cm^2/day$

with an estimated area of exposure of 210 cm^2. Assuming a bodyweight of 70 kg, the highest actual exposure value of 2.3 mg/kg/bw equates to 0.77 mg/cm^2/day, which is close to the upper estimate modelled using EASE.

Values taken forward to risk characterisation

The reasonable worst-case inhalation exposure value taken forward for risk characterisation is 30 $\mu g/m^3$, 8-hour time-weighted average. This is the highest value obtained during sampling and is much higher than any of the other results obtained. However, as there were only four data points it is difficult to assume that the one high result is an outlier. It is therefore taken forward as a precautionary figure. It is likely that in reality exposure will generally be lower. A typical exposure value for inhalation is 1 $\mu g/m^3$. Although much lower than the reasonable worst-case value it is considered to be representative of typical exposure given the other actual exposure values obtained (all less than 1 $\mu g/m^3$).

For dermal exposure the reasonable worst case value taken forward for risk characterisation is 0.8 mg/cm^2/day or 168 mg/day. This is equivalent to the highest value obtained during sampling (2.3 mg/kg bw) assuming a bodyweight of 70 kg and an exposure area of 210 cm^2. For typical exposure the value taken forward for risk characterisation is 0.2 mg/cm^2/day, or 42 mg/day, with an exposure area of 210 cm^2. This figure is similar to three of the five actual dermal exposure results obtained (0.13, 0.14, 0.35) and therefore thought to be representative of typical exposure.

4.1.1.1.2 Scenario 2a: Occupational exposure during the production of slabstock foam

Flexible polyurethane foams can be manufactured in continuous or batch processes. In a typical process the initial ingredients (mainly water, isocyanate, polyether polyols and any other additive such as a flame retardant) are mixed together at a mixing head and then immediately applied to the bottom lining of a continuously moving trough formed by a horizontal bottom paper or foil and two vertical side papers or foils. After a few seconds, a cream is formed, the volume expands and the foam reaches its maximum height in 1-3 minutes. The blocks of foam are cut off immediately after paper take-off, transferred through a transfer conveyer to the weigh scale and to the curing area. Some blocks can be randomly transferred to a specific area for temperature probing.

The amount of V6 used depends on the foam grade required and is controlled by a meter. Continuous foaming machines can produce polyurethane foam at rates up to 500 kg/minute. The foaming section of the process is enclosed within a tunnel fitted with extraction for removal of di-isocyanate vapours and blowing agent emissions (HMIP, 1995).

The main areas of potential occupational inhalation exposure during slabstock foam manufacture are at the mixing head where all ingredients are added and mixed together and when operators have to enter the tunnel to carry out duties such as removing the paper and supervising the block at cut-off areas. The practice of entering the tunnel occurs where older foaming machines are in use (the modern machines do not require it). At the beginning of the production process, in order to form a barrier for the liquid and to ensure block shape from the very beginning, two operators enter the tunnel to hold up a board. They remain in the tunnel until the foam is solid enough to be self-supporting. This typically takes 4 minutes. Due to the presence of isocyanate vapours, the operators wear PPE, including RPE, during this work. Another operator is present in the tunnel at start up of the foam manufacturing process. He

removes the bucket (or bag) which is under the mixing head with the first liquid output. He remains only for a very short time (approximately 5 seconds). The same happens at the very end of production. In both cases, PPE is worn. As mentioned above, the practice of having to enter the tunnel occurs where older foaming machines are in use. Since machine type distribution is not known among the EU foamers, it is difficult to estimate the occurrence of this procedure. In any case, the tunnel is always enclosed and extracted, due to the use of di-isocyanates in the production process. The potential for dermal exposure can occur in the mixing head area where raw materials are mixed and contact with chemicals can occur. It can also occur during temperature supervision and foam conversion.

Measured exposure data

An industry consortium carried out inhalation and dermal exposure monitoring for V6 at three EU sites where polyurethane production and cutting takes place.

At Plant X, sixteen inhalation and dermal exposure samples were taken over two days in February and March 2005. Then, in May 2005, six personal inhalation and dermal exposure samples were collected. At Plant Y, twelve inhalation and dermal exposure samples were collected on one day in February 2005.

The inhalation exposure samples were collected by drawing air at 1 litre per minute through XAD-2 OVS tubes, which were clipped to the operators' collar in order to sample from within the breathing zone. The samples were subsequently analysed using analytical method Akzo Nobel CG/6.089.2 (extraction with toluene containing tri-octyl phosphate and subject to gas chromatograph with flame photometric detection).

The samples were collected by the operators wearing cotton gloves throughout their shift which were collected for analysis. The analysis technique used was the same as for analysis of the tubes, except the volume of desorbent used was greater. The LOD for the method used was 0.3μg for the sampling tubes and 10μg for the gloves.

The activities covered during the sampling exercise included operators working at the mixing head area, the paper take-off area, the cut-off area, the production area supervisors, the laboratory technician, and the operators in the foam conversion (loop slitting) area. The results for foam cutting are considered in Scenario 3. The result for the rebond operator is considered in Scenario 4.

The operators wore the samplers for the majority of their shift. Although the foam production operators in Plants X and Y were only working with V6 for half their shift, this is considered representative of their normal work patterns. They also do not work with V6 every day; it was reported by industry that they work with V6 during approximately two half-shifts per week. The 8-hr TWA is therefore considered to be representative of exposure during normal activities.

During the shifts monitored, V6-containing foam was manufactured for the following periods:

- Plant X foam production: half a shift on each day;
- Plant X foam cutting: whole shift
- Plant Y: half a shift;

The foam manufactured contained the following quantities of V6:

- Plant X foam production: 5-10%

- Plant X foam cutting: 15%
- Plant Y: 5-10%

In addition, personal sampling data from the manufacture of foam containing TDCP and TCPP are also presented here, as the processes are identical and the flame retardants are used in the same way.

Inhalation exposure

Table 4.2 below gives a summary of the inhalation monitoring results for Plants X and Y. In addition, personal sampling data from manufacture of foam using TDCP and TCPP have also been used to determine RWC and typical exposure for inhalation exposure. These data are presented in **Tables 4.3, 4.4** and **4.5**.

Table 4.2 Inhalation exposure results for V6 measured at Plants X and Y

Plant identification	Operator	n	Inhalation Exposure 8-hr TWA (µg /m³)
Plant X	Mixing Head	2	<0.62, <0.62
Plant X	Asst. Mixing Head	4	<0.60, <0.53, <0.61, <0.63
Plant X	Side Paper Take Off	4	<0.62, 5.29, <0.63, <0.53
Plant X	Bottom Paper	4	<0.59, <0.56, <0.59, <0.57
Plant X	Block Cutter	2	<0.64,<0.59
Plant Y	Raw Material/Tank Farm	1	<0.61
Plant Y	Mixing Head	3	0.77, <0.58, <0.58
Plant Y	Supervisor	1	<0.62
Plant Y	Side Paper Take Off	1	<0.63
Plant Y	Cut Off Block	1	<0.59
Plant Y	Cut Off Start/End	1	<0.58
Plant Y	Bottom Paper	1	<0.59
Plant Y	Lab Tech	1	<0.60

Table 4.3 Personal inhalation exposures to TDCP measured at Plant A

Job title or work area	n	Inhalation TWA 8 h (µg/m³)
Supervisor/ Ass. supervisor	4	0.5, 0.8, 0.9, 2.2
Mixing head area	6	<0.2, 0.2, 0.9, 0.9, 1.5, 1.9
Paper take-off area	4	1.1, 1.1, 2.7, 3.5
Cut-off area	2	<0.2, 1.7
Lab technician	3	<0.2, <0.2, 1.3

Table 4.4 Personal inhalation exposures to TDCP measured at Plant B

Job title or work area	Inhalation TWA 8 h (µg/m3)
Raw material/ Tank Form	<0.20
Mixing head op. I	<0.20
Mixing head op. II	1.25
Mixing head op. III	<0.20
Supervisor	0.23
Side Paper take-off operator	<0.20
Cut-off block operator	<0.20
Cut-off Start/End operator	<0.20
Bottom Paper operator	0.39
Lab technician	<0.20

Table 4.5 Personal sampling data summarising exposure to TCPP during the manufacture of flexible foam

Operator	Operator activity or location	PPE worn	Length of time monitored (mins)	Measured TCPP (µg/m^3)	Calculated 8-hr TWA (µg/m^3)[j]
Production op. 1 (plant 1)	Mixing head area	Protective gloves	429	10	8.9
Production op. 2 (plant 1)	Paper take-off area	Respirator with replaceable filter and protective gloves (when entering the tunnel)	404	32	26.9
Production op. 3 (plant 1)	Temperature supervision and probing	None	426	15	13.3
Production op. 4 (plant 1)	Cut-off area	Protective gloves	445	33	30.5
Production op. 5 (plant 2)	Mixing head area	Disposable gloves	239	7.3	3.6
Production op. 6 (plant 2)	Different areas of the line	Respirator with replaceable filter and protective gloves when removing polyethylene film and cleaning tunnel	242	9.7	4.8
Production op. 7 (plant 2)	End of the tunnel	Respirator with replaceable filter and protective gloves when marking block and putting polyethylene film on	236	9.4	4.6
Sampling op. (plant 2) *	Sampling and baler production	Protective gloves	403	17	14.2

The inhalation results for V6 ranged from <0.53 to 5.29 µg/m^3, the vast majority below the limit of detection. Only two results were above the limit of detection; one at the side paper take off at Plant X (5.29 µg/m^3) and one at the mixing head at Plant Y (0.77µg/m^3). In addition, personal inhalation sampling data from flexible foam manufacturing plants using TCPP and TDCP have been used here, as the processes are identical and the flame retardants

are used in the same way. The range of exposures taking all of the personal sampling results into account is <0.2 to 30.5 μg/m^3.

Dermal exposure

A summary of the dermal monitoring results for Plants X and Y are presented in **Table 4.6** below. In addition, personal sampling data from manufacture of foam using TDCP and TCPP have also been used to determine RWC and typical exposure for dermal exposure. These data are presented in **Tables 4.7, 4.8** and **4.9**, below.

Table 4.6 Dermal exposure results for V6 measured at Plants X and Y

Plant Identification	Operator	n	mg V6 / pair of gloves (mg/day)
Plant X	Mixing Head	2	0.06, 1.39
Plant X	Asst. Mixing Head	4	0.20, 0.31, 0.79, 1.47
Plant X	Side Paper Take Off	4	0.08, 0.12, 0.21, 0.48
Plant X	Bottom Paper	4	0.28, 0.39, 1.18, 7.99,
Plant X	Block Cutter	2	0.14, 0.28
Plant Y	Raw Mat'l/Tank Farm	1	5.2
Plant Y	Mixing Head	3	0.49, 0.54, 0.75
Plant Y	Supervisor	1	0.89
Plant Y	Side Paper Take Off	1	0.39
Plant Y	Cut Off Block	1	0.34
Plant Y	Cut Off Start/End	1	0.23
Plant Y	Bottom Paper	1	0.24
Plant Y	Lab Tech	1	0.49

Table 4.7 Dermal exposure results for TCPP measured at production plants 1 and 2

Operator	Length of time monitored (mins)	Measured TCPP (mg/kg bw)	Dermal exposure (mg/day)
Production op. 1 (plant 1)	430	1.5	105
Production op. 2 (plant 1)	443	0.45	31.5
Production op. 3 (plant 1)	429	0.68	47.6
Production op. 4 (plant 1)	445	0.09	6.3
Production op. 5 (plant 2)	239	0.32	22.4
Production op. 6 (plant 2)	242	0.39	27.3
Production op. 7 (plant 2)	236	0.01	0.7
Sampling op. (plant 2)	313	0.003	0.21
Laboratory op. (plant 2)	417	0.003	0.21

Table 4.8 Dermal exposure results for TDCP measured at Plant A

Job title or work area	n	mg TDCP / pair of gloves (mg/day)
Supervisor/Ass. supervisor	4	1.0, 1.9, 2.0, 3.7
Mixing head area	6	3.4, 3.9, 11.5, 36.9, 41.6, 49.5
Paper take-off area	4	2.0, 3.0, 8.0, 12.6
Cut-off area	1	27.0
Lab technician	3	0.01, 0.02, 1.1
Truck unloading	1	0.71

Table 4.9 Dermal exposure results for TDCP measured at Plant B

Job title or work area	mg TDCP/ pair of gloves (mg/day)
Raw material/ Tank Form	0.22
Mixing head op. I	0.032
Mixing head op. II	0.052
Mixing head op. III	0.17
Supervisor	0.047
Side Paper take-off operator	0.029
Cut-off block operator	0.173
Cut-off Start/End operator	0.124
Bottom Paper operator	0.141
Lab technician	0.048

The dermal exposure results for V6 ranged from 0.06 to 7.99 mg/day, the highest being at the bottom paper take-off point. In addition, personal dermal sampling data from flexible foam manufacturing plants using TDCP and TCPP have been used here, as the processes are identical and the flame retardants are used in the same way. The range of exposures taking all of the personal sampling results into account is 0.01 to 105 mg/day or 0.002 to 0.07 mg/cm^2/day assuming an exposure area of 420cm^2.

Values taken forward to risk characterisation

For inhalation exposure, the reasonable worst case taken forward to risk characterisation is 5.1 μg/m^3. This was the 90th percentile of all the measured values obtained in the exposure monitoring carried out. The typical exposure value to be taken forward to risk characterisation is 0.62 μg/m^3, which is the median value for all the data presented.

For dermal exposure, the RWC taken forward to risk characterisation is 29.8 mg/day or 0.07 mg/cm^2/day, assuming an exposure area of 420cm^2.For typical exposure, a value of 0.7 mg/day or 0.002mg/cm^2/day will be taken forward. This is the median number from all the measured exposure values available.

4.1.1.1.3 Scenario 2b: Occupational exposure during production of moulded foam

Moulded foams can be produced from TDI and also from a mixture of TDI and MDI. Predetermined quantities of mixed reactants are automatically or manually dispensed discontinuously into moulds, which may be stationary or continuously circulating on a track (HMIP, 1995 and BASF, undated). The moulds are normally temperature conditioned prior to filling (HMIP, 1995) to around 40^0C. After the reactants have been dispensed, the lid of the mould is closed and foaming takes place. Alternatively, the mixture is automatically injected into a closed mould with defined vents. With hot cure moulding, the moulds are heated to temperatures typically in the range 150^0C to 230^0C (HMIP, 1995). On completion of the curing cycle, the moulds are opened and the moulded shapes are removed for trimming and finishing. Some moulded items are subject to a crushing stage or vacuum treatment in order to break open the closed cells in the moulding. After removal of the moulded article the mould is cleaned by removal of residual foam material from the lid and from vents, etc. The mould is then treated with a mould release agent such as a wax, which may be an organic solvent or an aqueous dispersion (HMIP, 1995).

Measured exposure data

There are no exposure data for the production of moulded foam products. However, it is thought that the dispensing of the liquid foam into moulds would be similar to the dispensing of the foam mixture from the mixing head during PUR foam block manufacture. Although not directly comparable, it is also felt that the results for work at the cutting of foam blocks would give an indication of the likely range of exposures during cutting and trimming of moulded parts.

Inhalation exposure data

Table 4.10 below contains the inhalation exposures for V6 measured at Plants X and Y. In addition, similar data is presented in **Tables 4.11**, **4.12** and **4.13** for inhalation exposure to TDCP and TCPP.

Table 4.10 Inhalation exposure to V6 measured at Plants X and Y

Plant identification	Operator	n	Inhalation Exposure 8-hr TWA (µg /m³)
Plant X	Mixing Head	2	<0.62, <0.62
Plant X	Asst. Mixing Head	4	<0.60, <0.53, <0.61, <0.63
Plant X	Side Paper Take Off	4	<0.62, 5.29, <0.63, <0.53
Plant X	Bottom Paper	4	<0.59, <0.56, <0.59, <0.57
Plant X	Block Cutter	2	<0.64,<0.59
Plant X	Laminator	4	1.7, 2.7, 6.0, 7.0
Plant X	Cutter	2	2.0, 2.6
Plant Y	Mixing Head	3	0.77, <0.58, <0.58
Plant Y	Side Paper Take Off	1	<0.63
Plant Y	Cut Off Block	1	<0.59
Plant Y	Cut Off Start/End	1	<0.58
Plant Y	Bottom Paper	1	<0.59
Plant Y	Loop slitter	1	<0.59

Table 4.11 Inhalation exposure results for TDCP measured at Plant A

Job title or work area	n	Inhalation Exposure 8-hr TWA (µg /m³)
Mixing head area	6	<0.2, 0.2, 0.9, 0.9, 1.5, 1.9
Paper take-off area	4	1.1, 1.1, 2.7, 3.5
Cut-off area	2	<0.2, 1.7
Block preparation	2	3.0, 0.8
Machine operator	7	1.7, 1.9, 3.8, 3.8, 4.1, 4.4, 4.8,

Table 4.12 Inhalation exposure results for TDCP measured at Plant B

Job title or work area	Inhalation Exposure 8-hr TWA (µg /m³)
Mixing head op. I	<0.20
Mixing head op. II	1.25
Mixing head op. III	<0.20
Side Paper take-off operator	<0.20
Cut-off block operator	<0.20
Cut-off Start/End operator	<0.20
Bottom Paper operator	0.39
Loop slitter operator	<0.20

Table 4.13 Inhalation exposure to TCPP at flexible foam manufacturing plants

Operator	Operator Activity or Location	PPE Worn	Length of time monitored (mins)	Measured TCPP (μg/m³)	Calculated 8-hr TWA (μg/m³))
Production op. 1 (plant 1)	Mixing head area	Protective gloves	429	10	8.9
Production op. 2 (plant 1)	Paper take-off area	Respirator with replaceable filter and protective gloves (when entering the tunnel)	404	32	26.9
Production op. 3 (plant 1)	Temperature supervision and probing	None	426	15	13.3
Production op. 5 (plant 2)	Mixing head area	Disposable gloves	239	7.3	3.6
Production op. 6 (plant 2)	Different areas of the line	Respirator with replaceable filter and protective gloves when removing polyethylene film and cleaning tunnel	242	9.7	4.8
Production op. 7 (plant 2)	End of the tunnel	Respirator with replaceable filter and protective gloves when marking block and putting polyethylene film on	236	9.4	4.6
Sampling op. (plant 2) *	Sampling and baler production	Protective gloves	403	17	14.2

The range of results for inhalation exposure deemed to be relevant to this scenario is <0.2 to 26.9 μg/m^3.

Dermal exposure data

Table 4.14 below contains the dermal exposures for V6 measured at Plants X and Y. In addition, similar data is presented in tables 4.15 and 4.16 for dermal exposure to TDCP. **Table 4.17** contains the dermal exposures for TCPP measured at flexible foam manufacturing plants.

Table 4.14 Dermal exposure to V6 measured at Plants X and Y

Plant Identification	Operator	n	mg V6 /pair of gloves (mg/day)
Plant X	Mixing Head	2	0.06, 1.39
Plant X	Asst. Mixing Head	4	0.20, 0.31, 0.79, 1.47
Plant X	Side Paper Take Off	4	0.08, 0.12, 0.21, 0.48
Plant X	Bottom Paper	4	0.28, 0.39, 1.18, 7.99,
Plant X	Block Cutter	2	0.14, 0.28
Plant X	Cutter	2	2.79, 6.33
Plant X	Laminator	4	3.86, 4.0, 5.36, 6.16
Plant Y	Mixing Head	3	0.49, 0.54, 0.75
Plant Y	Supervisor	1	0.89
Plant Y	Side Paper Take Off	1	0.39
Plant Y	Cut Off Block	1	0.34
Plant Y	Cut Off Start/End	1	0.23
Plant Y	Bottom Paper	1	0.24
Plant Y	Loop slitter	1	0.38

Table 4.15 Dermal exposure results for TDCP measured at Plant A

Job title or work area	n	mg TDCP /pair of gloves (mg/day)
Mixing head area	6	3.4, 3.9, 11.5, 36.9, 41.6, 49.5
Paper take-off area	4	2.0, 3.0, 8.0, 12.6
Cut-off area	1	27.0
Block preparation	2	0.4, 1.8
Machine operator	7	0.06, 0.1, 0.2, 0.3, 0.6, 2.5, 3.0

Table 4.16 Dermal exposure results for TDCP measured at Plant B

Job title or work area	mg TDCP/pair of gloves (mg/day)
Mixing head op. I	0.032
Mixing head op. II	0.052
Mixing head op. III	0.17
Side Paper take-off operator	0.029
Cut-off block operator	0.173
Cut-off Start/End operator	0.124
Bottom Paper operator	0.141
Loop slitter operator	0.41

Table 4.17 Dermal exposure results for TCPP at flexible foam manufacturing plants

Operator	Length of time monitored (mins)	Measured TCPP (mg/kg bw)
Production op. 1 (plant 1)	430	1.5
Production op. 2 (plant 1)	443	0.45
Production op. 3 (plant 1)	429	0.68
Production op. 4 (plant 1)	445	0.09
Production op. 5 (plant 2)	239	0.32
Production op. 6 (plant 2)	242	0.39
Production op. 7 (plant 2)	236	0.01
Sampling op. (plant 2)	313	0.003

The range of results for dermal exposure deemed to be relevant to this scenario is 0.029 to 105 mg/day.

Values taken forward to risk characterisation

The RWC inhalation exposure value taken forward for risk characterisation is 4.8 μg/m^3. This is the 90th percentile of the data set used for this scenario. The typical exposure taken forward for risk characterisation is 0.63 μg /m^3, which is the median value of the data set used for this scenario, in line with guidance in the TGD.

The RWC dermal exposure value taken forward for risk characterisation is 0.075 mg/cm^2/day or 31.5 mg/day. This is the 90th percentile of the data set used for this scenario, and assumes a bodyweight of 70 kg and an exposure area of 420 cm^2. The typical dermal exposure value taken forward for risk characterisation is 1.5 x 10^{-3} mg/cm^2/day or 0.63 mg/day. This is the median value of the data set used for this scenario and is taken forward in line with TGD guidance, and assumes the same bodyweight and exposure area as above.

4.1.1.1.4 Scenario 3: Occupational exposure during cutting of flexible PUR foam

Blocks of polyurethane foam generally have to be cut into the required size/shape of the final product. This operation usually occurs after the blocks have cured and cooled. Blocks are sold to cutters who cut them into the required size and shape. Foam producers operate their own cutting facilities, but also sell to a large number of cutters, most of which are small, privately owned companies. Trimmed blocks of foam are cut into the required shapes/pieces by band-knives. In the UK alone, there are hundreds of foam cutters. Therefore, the potential number of workers exposed is extensive.

This scenario also covers the instance where furniture manufacturers may cut their own foam to shape, although it has been stated by industry that this rarely happens.

Measured exposure data

A small number of inhalation and dermal exposure measurements have been taken in the foam cutting departments of three polyurethane foam manufacturing plants by industry. These

samples were collected in 2005. The samples were collected and analysed as described in Scenario 2, manufacture of flexible polyurethane foam.

In addition to data from Plants X and Y, data are also included from a TDCP monitoring exercise in Plants A and B, and at a plant using TCPP. The activities are the same and there is the possibility of exposure to dust from cutting foam containing flame retardant. It is therefore considered valid to utilise these data to supplement the V6 data.

Inhalation exposure data

Table 4.18 below summarises the inhalation exposures measured at Plants X and Y. **Table 4.19** details the personal dermal exposure data for TDCP measured at Plants A and B. **Table 4.20** details personal and static measurements for TCPP during cutting at a convoluter.

Table 4.18 Inhalation exposure to V6 measured at Plants X and Y

Plant identification	Operator	n	Inhalation Exposure 8-hr TWA (µg /m^3)
Plant X	Block Cutter	2	<0.64,<0.59
Plant X	Cutter	2	2.0, 2.6
Plant Y	Cut Off Block	1	<0.59
Plant Y	Loop slitter	1	<0.59

Table 4.19 Personal inhalation exposure to TDCP measured at Plants A and B

Plant identification	Job title or work area	n	Inhalation Exposure 8-hr TWA (µg /m^3)
Plant A	Block preparation	2	3.0, 0.8
Plant A	Machine operator	7	1.7, 1.9, 3.8, 3.8, 4.1, 4.4, 4.8,
Plant B	Loop slitter operator	1	<0.20

Table 4.20 Personal inhalation exposure to TCPP

Operator	Operator activity or location	PPE worn	Length of time monitored (mins)	Measured TCPP (µg /m^3)	Calculated 8-hr TWA (µg /m^3)
Operator at convoluter	Convoluter	None	135	5.4	1.5

The 17 personal inhalation exposures ranged between <0.2 µg/m^3 to 4.8 µg/m^3.

Dermal exposure data

Table 4.21 below summarises the dermal exposures measured at Plants X and Y. The personal dermal exposures to TDCP at Plants A and B are presented in **Table 4.22**. **Table 4.23** details the dermal exposure to TCPP during cutting at a convoluter.

Table 4.21 Dermal exposure to V6 measured at Plants X and Y

Plant Identification	Operator	n	mg V6 / pair of gloves (mg/day)
Plant X	Block Cutter	2	0.14, 0.28
Plant X	Cutter	2	2.79, 6.33
Plant Y	Cut Off Block	1	0.34
Plant Y	Loop slitter	1	0.38

Table 4.22 Personal dermal exposure to TDCP measured at Plants A and B

Plant identification	Job title or work area	n	mg TDCP / pair of gloves (mg/day)
Plant A	Block preparation	2	0.4, 1.8
Plant A	Machine operator	7	0.06, 0.1, 0.2, 0.3, 0.6, 2.5, 3.0
Plant B	Loop slitter operator	1	0.41

Table 4.23 Dermal exposure to TCPP during cutting at a convoluter

Operator	Length of time monitored (mins)	Measured TCPP (mg/kg bw)	mg/day
Operator 1 at convoluter	135	0.28	19.6
Operator 2 at convoluter	130	0.017	1.19

The 18 personal dermal exposures, both V6, TDCP and TCPP data, ranged from 0.06 mg/day to 19.6 mg/day. The highest result was obtained from one of the convoluter machine operators who were handling foam containing TCPP.

Values taken forward to risk characterisation

The value taken forward for risk characterisation for inhalation exposure is 4.1 $\mu g/m^3$, which is the 90^{th} percentile of the results presented by industry. The typical exposure taken forward is 1.9 $\mu g/m^3$, which is the median value of the results presented by industry.

The value taken forward for risk characterisation for dermal exposure is 3 mg/day or 7.1×10^{-3} $mg/cm^2/day$, assuming an exposure area of 420 cm^2. This is the 90^{th} percentile of the results presented by industry. The typical dermal exposure value taken forward for risk characterisation is 9.8×10^{-4} $mg/cm^2/day$ (or 0.41 mg/day), which is the median value of the results presented by industry.

4.1.1.1.5 Scenario 4: Occupational exposure during production of foam granules and rebonded PUR foam

V6 is present in off-cuts of slabstock foam, which undergo rebonding. Scrap foam can be shredded and granulated for use as a loose crumb for low grade furnishing such as garden furniture. The shredding and granulating processes do not introduce new V6. The scrap foam is supplied in bales. In larger factories the bale would be fed directly into a breaker using a forklift truck. In other factories the foam would be fed onto a conveyor by hand and then into the breaker. The breaker breaks the scrap foam into smaller pieces for the granulator machine which has extraction. The operators would have no exposure during these processes as they

are closed. Once the foam is granulated it is bagged for use in furniture manufacture. Scrap foam can also be shredded, granulated and rebonded into foam blocks.

As described in section 2.2.2.1.4, overall, between 45,000 and 60,000 tonnes of scrap foam is rebonded in Europe each year. Some of this scrap foam will contain V6. In Europe, the major use of rebond is reported to be in garden furniture (pers. comm., not attributable).

Measured inhalation exposure data

There is only one data point for inhalation exposure during the production of rebonded foam. This was from Plant Y. This result was <0.6 μg/m^3, which is lower than the limit of detection for the method. However, there are other data that are considered to be relevant to this scenario; the results for operators handling newly-formed foam as it leaves the tunnel and is cut into blocks, in Plants X and Y. and these are presented in **Table 4.24**, below

In addition to data from Plants X and Y, data are also included from a TDCP monitoring exercise in Plants A and B. Two data points from exposure measurements made at a foam manufacturing plant using TCPP are also included. The activities are the same for the three substances and it is therefore considered valid to utilise these data to supplement the V6 data. **Tables 4.25** and **4.26** summarise the inhalation data for TDCP and TCPP, respectively.

Table 4.24 Inhalation exposure to V6 measured at Plants X and Y

Plant identification	Operator	n	Inhalation Exposure 8-hr TWA (μg /m^3)
Plant X	Block Cutter	2	<0.64,<0.59
Plant Y	Rebond	1	<0.60
Plant Y	Cut Off Block	1	<0.59
Plant Y	Cut Off Start/End	1	<0.58

Table 4.25 Inhalation exposure for TDCP measured at Plants A and B

Plant Identification	Job title or work area	n	Inhalation Exposure 8-hr TWA (μg /m^3)
Plant A	Cut-off area	2	<0.2, 1.7
Plant B	Rebond operator	1	<0.20
Plant B	Cut-off block operator	1	<0.20

Table 4.26 Inhalation exposure from a foam manufacturing plant using TCPP

Operator	Operator activity or location	PPE worn	Length of time monitored (mins)	Measured TCPP (μg/m^3)	Calculated 8-hr TWA (μg/m^3)
Production op. 7 (plant 2)	End of the tunnel	Respirator with replaceable filter and protective gloves when marking block and putting polyethylene film on	236	9.4	4.6
Sampling op. (plant 2) *	Sampling and baler production	Protective gloves	403	17	14.2

The range of results for V6 is <0.58 to <0.64 μg/m^3. All five of the results available were below the limit of detection. The range of all results is <0.2 to 14.2 μg/m^3. Of the eleven results available, eight were below the limit of detection.

Measured dermal exposure data

There was only one data point for dermal exposure during the production of rebonded foam. This was from Plant Y. The result was 0.03 mg/day which is very low. However, there are other data that are considered to be of relevance to this scenario; the results for operators handling newly-formed foam as it leaves the tunnel and is cut into blocks, in Plants X and Y. These data are presented in **Table 4.27**, below.

In addition to data from Plants X and Y, data are also included from a TDCP monitoring exercise in Plants A and B. Two data points from exposure measurements made at a foam manufacturing plant using TCPP are also included. The activities are the same for the three substances and it is therefore considered valid to utilise these data to supplement the V6 data. **Tables 4.28** and **4.29** summarise the dermal data for TDCP and TCPP, respectively.

Table 4.27 Dermal exposure to V6 measured at Plants X and Y

Plant Identification	Operator	n	mg V6 /pair of gloves (mg/day)
Plant X	Block Cutter	2	0.14, 0.28
Plant Y	Rebond	1	0.03
Plant Y	Cut Off Block	1	0.34
Plant Y	Cut Off Start/End	1	0.23

Table 4.28 Dermal exposure for TDCP measured at Plants A and B

Plant Identification	Job title or work area	n	mg TDCP/ pair of gloves (mg/day)
Plant A	Cut-off area	1	27
Plant B	Rebond operator	1	0.01
Plant B	Cut-off block operator	1	0.173

Table 4.29 Dermal exposure for TCPP measured at a foam manufacturing plant

Operator	Length of time monitored (mins)	Measured TCPP (mg/kg bw)
Production op. 7 (plant 2)	236	0.01
Sampling op. (plant 2)	313	0.003

The range of results is 0.003 to 27 mg/day, the lowest of these results being for the rebond operator sampled.

Values taken forward to risk characterisation

The RWC exposure value for inhalation taken forward for risk characterisation is 4.6 μg/m^3. This is the 90th percentile of the data presented. The typical inhalation value taken forward for risk characterisation is 0.59 μg/m^3, which is the median value.

The RWC taken forward for dermal exposure is 0.7 mg/day or 1.7 x 10^{-3} mg/cm^2/day, with an exposure area of 420cm^2. This value is the second highest of the dataset gathered from relevant operations from manufacture of foam containing TCPP, TDCP or V6. The highest value was two orders of magnitude higher than the next, so is considered to be an outlier.

The typical exposure taken forward for risk characterisation for dermal exposure is 0.23 mg/day or 5.5 x 10^{-4} mg/cm^2/day, which is the median value for the dataset gathered from relevant operations from manufacture of foam containing TCPP, TDCP and V6.

4.1.1.1.6 Scenario 5: Occupational exposure during the manufacture of automotive parts

ISOPA data (undated) indicates that 100 foamers/moulders are involved in the production of automotive products from PUR foam in Europe, consuming 365,000 tonnes of polyurethane each year. However, only 3 or 4 EU producers of moulded foam use flame retardants (pers. comm., not attributable). (Data have been provided by the V6 producer and by companies using V6 in the production of foams for automotive applications and the number using V6 is known). Many parts of motor cars are made from PUR foam, including interior trim, seats, headrests and dashboards, soundproofing, filters, etc (Europur, 2002).

The manufacture of moulded foam is covered in Scenario 2b. This scenario covers the use of flexible foam in the manufacture of automotive products. Data provided by a foam producer indicates that V6 is used in the production of foams for use with textiles in the manufacture of car seat, door panels, soundproofing, head-liners and cushions. The bulk of the seats are made using foam that doesn't contain flame retardant. It is only the outer covering of foam associated with the covering fabric that contains V6. The assembly processes will vary depending on the product being made, but will usually involve the use of adhesives to laminate foam and the material being used for the interior of the car, cutting, trimming and stitching of components. Different operatives would carry out different tasks, so that, for example, one operator would laminate the foam and fabric, another would stitch and trim the seat covering and another would assemble the seat. Some of these activities may be carried out by employees in different companies.

Measured exposure data

There is no exposure data available for the manufacture of automotive products so exposure data from the handling and cutting of flexible PUR foam provided by industry has been used. The potential for exposure arises during the handling of the foam, and during the cutting and trimming of the foam-backed material.

The activities are not strictly directly comparable, as the flexible foam manufacturers will be handling much larger quantities of foam and the cutting takes place using machinery, whereas the automotive product manufacturers will be handling smaller quantities of foam, but will be trimming and cutting by hand. However, it is felt that the real exposure data will give a better approximation of exposure than using EASE in this instance. EASE is a general purpose predictive model for workplace exposure assessments.

In addition to data from Plants X and Y, data are also included from a TDCP monitoring exercise in Plants A and B. The activities are the same and it is therefore considered valid to utilise these data to supplement the V6 data. There are also some data points for cutting from a TCPP foam manufacturing plant that are also relevant.

Inhalation exposure data

Table 4.30 below summarises the inhalation exposures measured at Plants X and Y. **Table 4.31** details the personal inhalation exposure data for TDCP measured at Plants A and B. The inhalation exposure data from the foam manufacturing plant using TCPP are presented in **Table 4.32**.

Table 4.30 Inhalation exposure to V6 measured at Plants X and Y

Plant identification	Operator	n	Inhalation Exposure 8-hr TWA (µg /m^3)
Plant X	Block Cutter	2	<0.64,<0.59
Plant X	Cutter	2	2.0, 2.6
Plant Y	Cut Off Block	1	<0.59
Plant Y	Cut Off Start/End	1	<0.58
Plant Y	Loop slitter	1	<0.59

Table 4.31 Inhalation data for TDCP measured at Plants A and B

Plant identification	Job title or work area	n	Inhalation Exposure 8-hr TWA (µg /m^3)
Plant A	Block preparation	2	0.8, 3.0
Plant A	Machine operator	7	1.7, 1.9, 3.8, 3.8, 4.1, 4.4, 4.8,
Plant B	Loop slitter operator	1	<0.20

Table 4.32 Inhalation exposure in foam manufacturing plant using TCPP

Operator	Operator activity or location	PPE worn	Length of time monitored (mins)	Measured TCPP (µg/m^3)	Calculated 8-hr TWA (µg/m^3)
Operator at convoluter	Convoluter	None	135	5.4	1.5

Dermal exposure data

Table 4.33 summarise the dermal exposures to V6 measured at Plants X and Y. The dermal exposures to TDCP measured at Plants A and B and the dermal exposure to TCPP are summarised in **Tables 4.34** and **4.35**, respectively.

Table 4.33 Dermal exposure to V6 measured at Plants X and Y

Plant Identification	Operator	n	mg V6 /pair of gloves (mg/day)
Plant X	Block Cutter	2	0.14, 0.28
Plant X	Cutter	2	2.79, 6.33
Plant Y	Cut Off Block	1	0.34
Plant Y	Cut Off Start/End	1	0.23
Plant Y	Loop slitter	1	0.38

Table 4.34 Dermal exposure data for TDCP measured at Plants A and B

Plant identification	Job title or work area	n	mg TDCP/pair of gloves (mg/day)
Plant A	Block preparation	2	0.4, 1.8
Plant A	Machine operator	7	0.06, 0.1, 0.2, 0.3, 0.6, 2.5, 3.0
Plant B	Loop slitter operator	1	0.41

Table 4.35 Dermal exposure data at foam manufacturing plant using TCPP

Operator	Length of time monitored (mins)	Measured TCPP (mg/kg bw)	mg/day
Operator 1 at convoluter	135	0.28	19.6
Operator 2 at convoluter	130	0.017	1.19

Values taken forward for risk characterisation

The value taken forward for risk characterisation for inhalation exposure is 4.1 μg/m^3, which is the 90th percentile of the results presented by industry. The typical exposure taken forward is 1.9 μg/m^3, which is the median value of the results presented by industry.

The value taken forward for risk characterisation for dermal exposure is 7.1 x 10^{-3} mg/cm^2/day or 3.0 mg/day. This is the 90th percentile of the results presented by industry, and assumes a bodyweight of 70 kg and an exposure area of 420 cm^2. The typical dermal exposure value taken forward for risk characterisation is 9.8 x 10^{-4} mg/cm^2/day or 0.41 mg/day which is the median value of the results presented by industry, assuming the same bodyweight and exposure area as above.

4.1.1.1.7 Summary of occupational exposure

A summary of the inhalation and dermal exposures values taken forward to risk characterisation for each scenario are presented in **Table 4.36**, below.

Table 4.36 Summary of RWC and typical exposure values for inhalation and dermal exposure for all scenarios taken forward for risk characterisation

Scenario	Inhalation exposure (μg/m^3)		Dermal exposure (mg/cm^2/day)		Dermal exposure area (cm^2)
	RWC	Typical	RWC	Typical	
1: Production of V6	30	1	0.8	0.2	210
2a: Manufacture of flexible PUR foam	5.1	0.62	7.0 x 10^{-2}	2 x 10^{-3}	420
2b: Manufacture of moulded foam	4.8	0.63	7.5 x 10^{-2}	1.5 x 10^{-3}	420
3: Cutting flexible foam	4.1	1.9	7.1 x 10^{-3}	9.8 x 10^{-4}	420
4: Production of rebonded foam	4.6	0.59	1.7 x 10^{-3}	5.5 x 10^{-4}	420
5.Manufacture of automotive products	4.1	1.9	7.1 x 10^{-3}	9.8 x 10^{-4}	420

4.1.1.2 Consumer exposure

4.1.1.2.1 Potential exposure from flexible PUR foam

The current use pattern provided by industry indicates that most of the V6 produced in the EU in 2000 was used in the production of flexible PUR foam. Most of the V6 used in flexible foam is for the automotive industry, with some used in furniture. Consumers do not come in direct contact with these foams. The foam is only used in ways in which it is enclosed and therefore it is concluded that exposure to consumers is negligible.

There is no information relating to exposure of consumers to V6. There is however information relating to the release of TCPP from foam which is reported here. There is also information about long-term trials to determine flame retardant retention in foam. These trials were for foam containing TCPP and TDCP and report on the retention of phosphate and chlorine in the foam sample. This is also reported here.

Measured consumer exposure data

Chamber tests of TCPP-containing flexible PUR foams for release of TCPP

In order to evaluate possible indoor air concentrations of TCPP from flexible foam used in mattresses, EUROPUR (European Association of Flexible Polyurethane Foam Block Manufacturers) ordered chamber tests at the Institute Miljo-Kemi in Denmark. In the study, a 'worst-case' scenario was applied. The foams were uncovered, the quantity of foam in the mattress was a maximum (i.e. full depth foam with no springs) and the chamber volume was small. In everyday use, the mattress foam is always covered with a fabric material and bedding sheets, blankets, etc.

Three types of flexible PUR foam used in mattresses were tested. The samples were 2000 x 1000 x 120 mm of full depth foam (i.e. no springs), were uncovered and were reported to contain TCPP at the high end of the typical level for this application (reported to be 2.5 – 14%, 7 – 8% on average, based on industry data collected for the risk assessment of TCPP).

The mattresses were placed in a 3.2 m3 test chamber at 23°C and relative humidity of 50%, with an air exchange rate of 0.5 per hour. Volatile emissions were collected on Tenax TA absorbent and analysed by GC-MS. The limit of detection was reported as 2 µg/m^3. **Table 4.37** below gives the results of this study.

Table 4.37 Results of chamber tests with mattresses made of TCPP-containing flexible PUR foam

Mattress Type	Air Concentration (µg/m^3)				
	24h	48h	72h	120h	160h
HR[1]	6.0	22	25	19	10
CME 33[2]	9.1	16	16	19	17
CMHR[3]	1.8	1.7	2	<1	<1

[1]HR = High resilience foam, 36 kg/m^3, 1.5% TCPP

[2]CME = Combustion modified ether, 33 kg/m^3.

[3] CMHR = Combustion modified high resilience foam, 35 kg/m^3

The detection limit was 2 μg/m^3. It can be seen from the results that after 160 hrs, the concentration of TCPP in the chamber is declining in the case of HR foam, whereas for CM foam, it remains relatively constant. No TCPP was detected from the CMHR foam from 120 hours onwards.

An estimation of TCPP indoor air concentration can be made from this study. As a worst-case approach, a room with a high PU foam load should be assumed. The concentration of TCPP in the chamber remained relatively constant for the CM foam, so a value of 19 μg/m^3 will be used. This is the highest value seen with the CM foam, and was also measured at the 120hr time point with the HR foam.

The assumptions are as follows:

TCPP concentration in chamber air:	19 μg/m^3
Mattresses in the room: 2	Factor 2
Volume of room: 30 m^3	Factor 1/10
Air exchange: 0.5 h^{-1}	Factor 1

From this study, the concentration of TCPP in indoor air in rooms with a high load of flame retarded flexible PUR foam can be estimated to be 3.8 μg/m^3.

4.1.1.2.2 Determination of flame retardant retention in a foam sample

Polyurethane foam storage trials have been performed in two UK foam companies. The British Rubber Manufacturer's Association (BRMA) has provided the rapporteur with the results of the biannual analyses for these trials. Initial tests determined the distribution of flame retardant across the foam sample. Foam pieces were taken from a foam block and analysed for phosphorous and chlorine content using an internal validated method. The results obtained in this initial study showed good flame retardant distribution across the foam. Through the rest of the study, phosphorous and chlorine measurements were made on the foam on a six monthly basis. **Table 4.38** below gives a summary of the results obtained for this study.

Table 4.38 Results of BRMA long-term aging trial on flexible PUR foam

Time (months)	Company A (TDCP)		Company B (TCPP)	
	% P	% Cl	% P	% Cl
0	0.75	2.6	0.40	1.3
80°C for 100 h	0.74	2.5	-	-
6	-	-	0.39	1.7
12	0.74	2.5	0.41	1.4
18	0.75	2.7	0.40	1.2
24	0.70	2.7	0.39	1.3
30	0.72	2.7	0.37	1.3
36	0.71	2.6	0.39	1.3
42	0.73	2.6	0.40	1.2
48	0.72	2.6	0.40	1.2
54	0.74	2.5	0.41	1.2
60	0.73	2.4	0.42	1.2
78*			0.44	1.42
84*			0.45	1.42
90			0.44	1.48

Change of analytical laboratory

From this ageing study, it can be seen that flame retardants are retained within PUR foam, and so consumer exposure to flame retardants from these foams is expected to be very low.

Further work carried out by the University of Surrey looked at release of flame retardant from PUR foams. The results of this work suggest higher rates of release of FRs than the above two studies, but they looked at smaller pieces of foam and dust. The dust had a much higher rate of release, suggesting that the size of the foam pieces influenced the rate of release.

As the work carried out by EUROPUR and BRMA looked at mattress-sized pieces of foam, this data has been used to estimate consumer exposure via inhalation.

As some people, particularly the elderly, could spend a large proportion of their time indoors in a room with PU foam-containing furniture, as a RWC, 3.8 $\mu g/m^3$, 24 hour TWA could be taken forward for risk characterisation. Assuming that the majority of consumers would spend some time in areas without PU foam-containing furniture a typical exposure could be estimated as 2.8 $\mu g/m^3$ 24hr TWA (18 out of 24 hours spent in areas with PU foam-containing furniture or other items).

Dermal exposure

There are no data on dermal exposure. However, it is reasonable to assume that dermal exposure will not exceed inhalation exposure and therefore the data on inhalation will also be used for dermal exposure as a RWC. For dermal exposure the figure for inhalation will be put forward as a RWC for risk characterisation; that is 0.0011 mg/kg.

Oral exposure

This route of exposure is only of significance for young children, due to their hand to mouth behaviour. In this section, information has been taken from the TCEP exposure assessment (BAUA 2006). This is considered a valid means of generating information for risk characterisation as the two substances have similar vapour pressures and molecular weights.

It has been estimated that a three year old child would consume 100 mg dust per day (including soil). It has also been shown that the range of TCEP in house dust is 0 to 121 mg/kg. The 95th percentile of this range is 11.9 mg/kg.

Oral TCEP uptake was calculated by the formula

$$E_{TCEP(oral)} = \frac{C_{TCEP,\,dust} * I_{orl,\,dust}}{BW}$$

where $C_{TCEP,\,dust}$ is the dust concentration, $I_{orl,dust}$ is the uptake of dust, and BW is the body weight. According to the age categories of the AUH Report (1995), the oral exposure was estimated for a 1-3 year old child. The dust uptake and body weight data (normal distribution, weighted for 1 to 3 year of age) are taken from the AUH Report (1995). The dust uptake data are primarily based on the data published by Calabrese *et al.* (1989). According to these data, the values for this assessment were set as follows: normal dust uptake is set to 20 mg/day and the 95th percentile to 100 mg/day.

This estimation of uptake includes soil uptake and therefore leads to a slight overestimate of exposure via dust. It should be mentioned that the upper range of the uptake determined by Calabrese is in agreement with newer data obtained by Freeman and Adgate (2003) who found a daily dust uptake of 100 mg in small children.

The 95th percentile, 99th percentile and the maximum value for children, representing a vulnerable population due to their specific hand-mouth behaviour are 0.1, 0.2 and 0.7 µg/kg/day, respectively.

The 99th percentile of TCEP ingested with house dust of 0.2 µg/kg/day has been taken forward as a RWC for oral ingestion for a child, in line with the TCEP risk assessment.

Values taken forward to risk characterisation

A RWC inhalation exposure value of 3.8 µg/m^3 24-hour TWA will be taken forward for risk characterisation. A typical exposure value of 2.8 µg/m^3 will be taken forward for risk characterisation, on the basis of a consumer spending 18 out of 24 hours in rooms where there is PU foam-containing furniture.

For dermal exposure, the figure for inhalation will be put forward as a RWC for risk characterisation, which is 0.0011 mg/kg.

These figures have been put forward on the basis of the chamber test work carried out as described above. However the work ongoing to monitor the release of fire retardant from foam over years rather than hours seems to indicate that the loss of fire retardant is negligible, in which case exposure would be negligible. The values taken forward for risk characterisation may therefore be an over-estimate.

A value for a RWC oral ingestion for children has been taken from the risk assessment for TCEP of 0.2 µg/kg/day, assuming a bodyweight of 9.1 kg.

4.1.1.3 Humans exposed via the environment

Table 4.39, which is taken directly from the values obtained in Chapter 3, gives the predicted environmental exposures to V6 and the daily human doses arising from releases from production, processing, manufacture and use of V6. It also provides the predicted environmental exposures at a regional level.

It can be seen that the daily human intake via the environment based upon typical human consumption and inhalation rates at the regional level is 3.9×10^{-6} mg/kg/day and the highest local exposure (industrial use) is 0.0179 mg/kg/day.

These two figures will be taken forward to risk characterisation.

Table 4.39 Indirect exposure of humans to V6 via the environment

	Air [mg.kg-1.d-1]	Drinking water [mg.kg-1.d-1]	Fish [mg.kg-1.d-1]	Leaf crops [mg.kg-1.d-1]	Meat [mg.kg-1.d-1]	Milk [mg.kg-1.d-1]	Root crops [mg.kg-1.d-1]	Local total daily intake [mg.kg-1.d-1]
Producer	2.38E-10	6.65E-07	4.90E-07	4.05E-06	9.32E-10	8.12E-10	1.01E-06	6.22E-06
A1a: Flexible foam - automotive - foaming large site	1.20E-08	1.24E-06	1.05E-06	7.75E-06	1.45E-09	1.26E-09	1.89E-06	1.19E-05
A1b: Flexible foam - automotive - foaming	9.61E-10	3.29E-05	1.28E-05	2.01E-04	2.08E-08	1.81E-08	4.99E-05	2.96E-04
A2: Foam cutting	4.24E-09	5.59E-07	6.57E-07	3.46E-06	9.20E-10	8.02E-10	8.48E-07	5.53E-06
B1: Flexible foam - furniture - foaming	6.47E-09	2.60E-04	1.07E-04	1.58E-03	1.60E-07	1.40E-07	3.94E-04	2.34E-03
B2: Foam cutting	2.84E-09	5.82E-07	5.85E-07	3.58E-06	9.15E-10	7.98E-10	8.82E-07	5.64E-06
C1: CONFIDENTIAL	2.85E-09	1.43E-04	1.92E-06	8.72E-04	8.88E-08	7.74E-08	2.17E-04	1.23E-03
C2: CONFIDENTIAL	3.16E-10	2.64E-05	1.79E-06	1.61E-04	1.68E-08	1.47E-08	4.01E-05	2.29E-04
D1: CONFIDENTIAL	2.72E-08	3.74E-05	1.56E-05	2.28E-04	2.39E-08	2.09E-08	5.68E-05	3.38E-04
F1: CONFIDENTIAL	3.81E-07	2.55E-04	4.33E-06	1.56E-03	1.63E-07	1.42E-07	3.86E-04	2.20E-03
F2: CONFIDENTIAL	8.09E-10	2.07E-03	1.17E-04	0.0126	1.27E-06	1.11E-06	3.13E-03	0.0179
G1: Flexible foam - Furniture, seating, mattresses - re-bonding of scrap	4.55E-09	4.28E-07	4.53E-07	2.67E-06	8.43E-10	7.35E-10	6.49E-07	4.21E-06
H1: Loose Crumb	2.09E-09	4.15E-07	4.53E-07	2.56E-06	8.03E-10	7.00E-10	6.30E-07	4.06E-06
Regional	2.38E-10	4.09E-07	4.53E-07	2.50E-06	7.78E-10	6.78E-10	6.21E-07	3.9E-06

4.1.1.4 Combined exposure

The combined exposure to V6 is the sum of all the specific sources (occupational exposure, consumer exposure and indirect exposure via the environment) and by all routes of exposure (oral, dermal and inhalation). Therefore, the worse case estimate for this combined exposure would be the sum of the RWC estimates, for inhalation and dermal exposures, for the three populations, i.e. workers, consumers and man exposed via the environment.

Occupational inhalation and dermal exposures for the identified worker exposure scenarios are presented in **Table 4.36** (see section 4.1.1.1.7). The highest occupational reasonable worst case inhalation and dermal exposures occur during the manufacture of V6 (scenario 1). The occupational dermal exposure level is significantly higher than the estimated exposure to consumers or indirect exposure via the environment, and thus will dominate the combined exposure estimate. Therefore, it is not considered necessary to include occupational exposure in the combined exposure calculation.

Consumers may be exposed to V6 indirectly from flexible foam used in upholstery and bedding. Exposure is also possible indirectly via environmental sources.

The RWC exposures used in calculating the combined exposure are presented in **Table 4.40** below.

Table 4.40 Exposures taken into account for combined V6 exposure estimate (excluding occupational exposure)

Source of exposure	Exposure
Consumer	
Release of TCPP from flexible polyurethane foam	
Inhalation	0.0038 mg/m^3
Dermal	0.0011 mg/kg
Man via the environment	
Local exposure	17.9 x 10^{-3} mg/kg/day*
Regional exposure	3.9 x 10^{-6} mg/kg/day

*Highest exposure scenario for local exposure (Confidential use: F2)

4.1.2 Effects assessment: Hazard identification and dose (concentration)-response (effect) assessment

4.1.2.1 Toxicokinetics, metabolism and distribution

4.1.2.1.1 Studies in animals

In vivo studies

Inhalation

No studies are available. In line with the draft TGD (2005), 100% absorption is taken forward to risk characterisation.

Dermal

No studies are available.

Oral and intravenous

The distribution and kinetics of [^{14}C]-V6 in male and female rats was investigated in accordance with OECD Guideline No. 417 and to GLP (TNO Quality of Life, 2008). Four Wistar rats (Crl:(WI)WU BR)/sex/dose group received either a single dose of 15 or 600 mg/kg (oral) or 15 mg/kg (IV) [^{14}C]-V6 (specific activity of 24.3 mCi/mmol), corresponding to a radioactive dose of 200 µCi/kg bw. The oral dose was prepared in 0.5% hydroxypropyl methylcellulose, and the IV dose prepared in a mixture of Cremophor ELP/ethanol and saline. Blood samples were taken at 30 min, 1, 2, 3, 4, 6, 8, 24, 48 and 96 hr post oral dosing, and 15, 30, 45 min and 1, 2, 4, 6, 8, 24, 48 and 96 hr post iv dosing. Urine and faeces were collected at 24 hour intervals for 168 hours and expired air (CO_2 and volatiles) were sampled at 24 hour intervals for 48 hours. At sacrifice, tissues, organs and residual carcass were collected. Cage wash was collected at the end of the collection period in each cage. The radioactivity in each sample was determined by liquid scintillation counting. Pharmacokinetic parameters were calculated for IV and oral dosing. Metabolites in excreta were profiled using HPLC and identified using LC-MS analysis.

Following oral administration of [^{14}C]-V6, highest concentrations of radioactivity in the blood were found at 8 hours post dosing in both sexes and both concentrations. The Cmax values for males and females of the low dose were comparable (1.73 and 1.5 µg/g, respectively), but were higher for females in the high dose (18.9 and 29.5 µg/g, for males and females respectively). The study director comments in the study report that the higher Cmax values observed in high dose females can be attributed to slow absorption of the test substance and a faster transit time in GI tract of male rats compared with female rats.

The elimination half life was 99-113 hours, irrespective of the dose, route or sex.

In the oral low dose and IV dose groups, the $AUC_{0\text{-}168hr}$ and $AUC_{0\text{-}infinity}$ values were comparable for males and females. However, in the oral high dose group, the AUC values were higher in females than males. The higher AUC values following the oral dose when compared with the IV dose are probably due to differences in metabolism, since the elimination half-lives for the two routes are comparable. The bioavailability after low dose,

derived from the area under the curve ratios, was calculated to be approximately 142% for both sexes. The study report does not provide any information on saturation of metabolism following IV dosing. However, as the elimination half lives for the oral and IV routes are comparable, the difference in AUC, and therefore the greater than 100% bioavailability for the oral low dose is most likely due to differences in metabolism. The bioavailability in the high dose group was 47% and 55% in male and female rats respectively. It should be noted that in calculating the bioavailability in the high dose, the reference IV AUC was taken from a lower dose IV administration. Also, after oral high dose administration only very little radioactivity attributable to the intact parent compound was found in the faeces (<1%) indicating practically complete absorption from the gastro-intestinal tract.

The total recovered radioactivity was around 80%, regardless of the dose, route of administration or sex. Following oral dosing, the total retention of radioactivity was around 2.5% after the low dose and 0.8% after the high dose, with most of the radioactivity excreted within 3 days. Excretion occurred mainly by the biliary route (approx. 60%), with excretion in urine approximately 20% and a small amount of radioactivity exhaled as $^{14}CO_2$. Volatile radioactivity could not be detected; however the study report states that it is possible that part of the radioactivity was exhaled as ethylchloride or more likely 2-chloroethanol, as all major metabolites were missing an ethylchloride group. These compounds are very volatile and could not be trapped in the conditions of the experimental design. The study director also comments in the study report that this could explain the low recovery of total radioactivity (of 80%) since one ethylchloride group attributes 25% of the radioactivity of the molecule.

At 168 hours post dose, the highest concentrations of radioactivity were found in the liver, kidney, adrenals and abdominal skin in both sexes, and in uterus of both low and high dose females. The lowest radioactivity was found in brain, plasma and fat, the latter indicating no bioaccumulation of V6. Therefore, [^{14}C]-V6, or its metabolites, was distributed all over the body, but no specific target organs, other than the organs of elimination, were identified.

Metabolic profiling in pooled urine identified at least 12 metabolites, with only one major metabolite, present at up to 5% of the administered dose. The early retention time of this metabolite in the HPLC column points to a small polar compound such as: 2-chloroethanol, ethylene glycol, acetic acid or 2-hydroxy acetic acid. The parent V6 was not observed in urine. In female urine, one of the minor metabolites (present at approximately 2-5%) was also the major metabolite identified in faeces (referred to metabolite 1, below).

In faeces at least 14 metabolites were identified and four of these were major metabolites (referred to as metabolites 1-4 below) which were present at greater than 5% of the administered dose. A small amount (<1%) of intact ^{14}C-V6 was found in faeces, but only up to 48 hours post dosing. Metabolite 1 was present at up to 30%, irrespective of sex, the dose administered or the route of administration. Metabolite 2 was present at up to 20% of the administered dose, but at a lower level (approximately 8%) in the low dose animals. Metabolites 3 and 4 were present at up to approximately 9 % in the low oral and IV dose groups, but at lower level in high oral dose group (approximately 2%).

Deconjugation experiments with pooled urine and faeces showed that conjugated metabolites were either not present, or present only in very small amounts.

The major metabolite identified in urine could not be found by LC-MS, indicating that this metabolite is probably a compound of low molecular weight. The elemental composition of metabolites 1-4 observed in faeces were determined by LC-MS and are presented in **Table 4.41**.

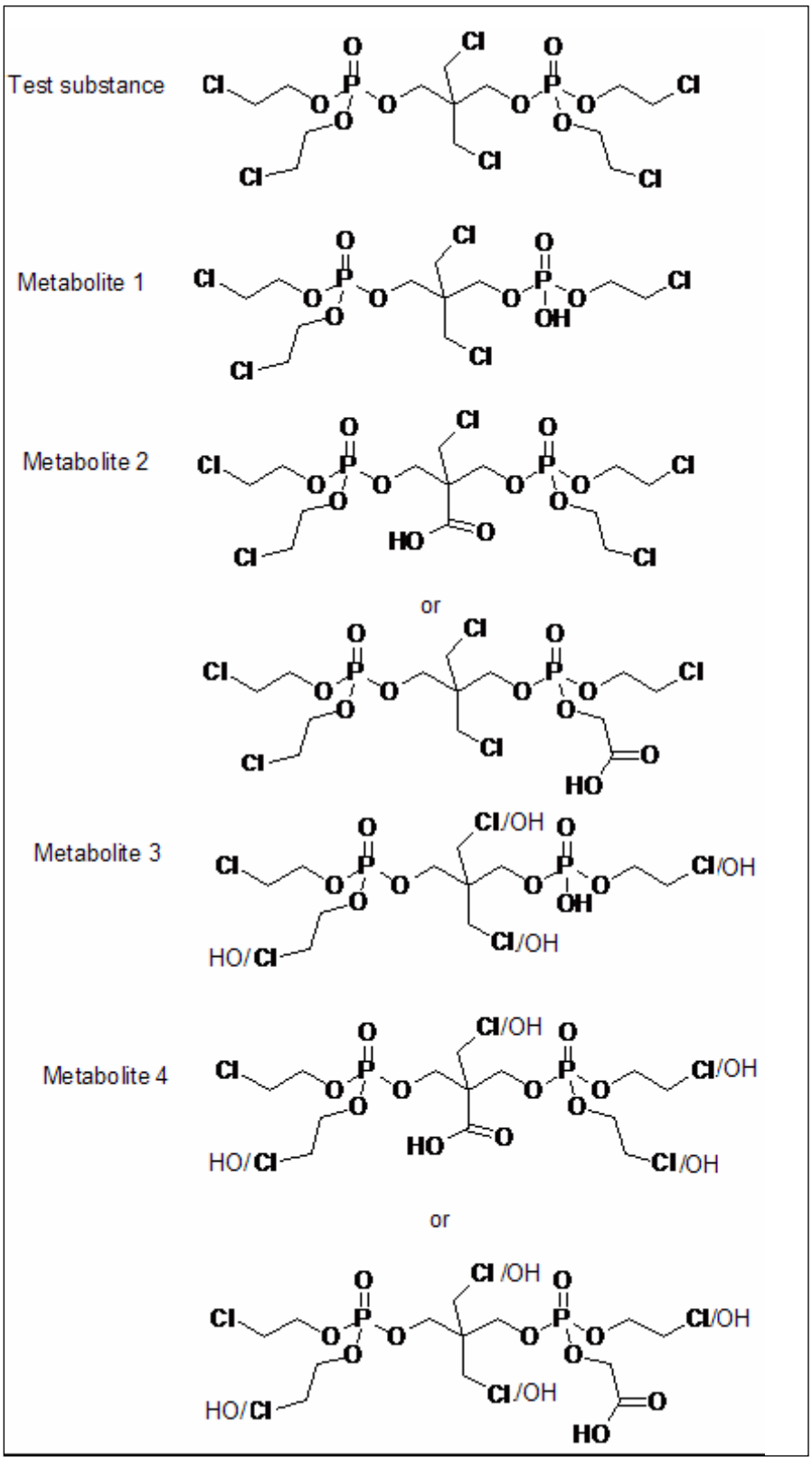
Table 4.41 Elemental composition of metabolites 1-4 determined by LC-MS

	Elemental composition	**Difference from Parent**
Test substance – V6	$C_{13}H_{25}O_8Cl_6P_2$	-
Metabolite 1	$C_{11}H_{22}O_8Cl_5P_2$	$-C_2H_3Cl$
Metabolite 2	$C_{13}H_{24}O_{10}Cl_5P_2$	-HCl + 2O
Metabolite 3	$C_{11}H_{23}O_9Cl_4P_2$	$-C_2H_3Cl$ –Cl + OH
Metabolite 4	$C_{13}H_{25}O_{11}Cl_4P_2$	-HCl +2O –Cl +OH

Metabolites 1-4 are either missing a chloroethyl moiety or the chlorine was replaced by an OH group, and further oxidised to a carboxyl group. The likely major metabolic pathways are the cleavage of one phosphate ester bond (metabolite 1) and the oxidation (substitution) of one chloroethyl sidechain to the corresponding hydroxyl and further oxidation to the carboxy group (metabolites 4 and 2, respectively). It is the opinion of the study director that metabolite 3 is likely to be a secondary metabolite of metabolite 1, undergoing a further hydroxylation on a second chloroethyl group.

The proposed structures of metabolites 1-4 are presented in **Figure 4.1**, below. The exact structure of metabolites 2, 3 and 4 were not elucidated. Metabolite 2 has two possible structures. For metabolites 3 and 4, the possible place of the substitution of Cl by OH group is shown.

Figure 4.1 Proposed structures of the major metabolites of V6 identified in faeces



In vitro studies

Dermal

An *in vitro* percutaneous absorption study (Charles River Laboratories, 2006) conducted to GLP guidelines and to OECD Guideline 428, was carried out to determine the rate and extent of absorption following topical application of commercial grade [^{14}C]-V6, either "neat" (14 mg/cm^2, the maximal obtainable dose) or in an ethanol vehicle, to human skin. An ethanol vehicle was used so that V6 could be applied at a lower occupationally relevant exposure of *ca* 200 µg/cm^2, corresponding to a typical exposure of *ca* 0.6 mg/kg/day. The vehicle was expected to rapidly volatilise from the skin surface without affecting the barrier properties of the stratum corneum.

Split thickness human skin membranes, 8 membranes per dose level, were mounted into flow-though diffusion cells. Receptor fluid was pumped underneath the skin at a rate of *ca* 1.5 ml/h. The receptor fluid was changed to ethanol: water (1:1 v/v) for the test item permeability assessment.

"Neat" or diluted V6 was applied at an application volume of 10µl/cm^2. Absorption was assessed by collecting receptor fluid in hourly fractions from 0-8 hours post dose and then in 2-hourly fractions from 8-24 hours post dose. At 8 hours post dose, exposure was terminated by washing the skin surface and then drying with tissue swabs. At 24 hours post dose, the underside of the skin was rinsed with receptor fluid. 25 successive tape strips were then taken, and the remaining skin was solubilised. The tissue swabs were analysed by combustion / liquid scintillation counting, all other samples were analysed by liquid scintillation counting.

For each dose tested, the absorbed dose, defined as the mass of the test item reaching the receptor fluid or systemic circulation within a specified period of time, and the dermal delivery, defined as the sum of the applied dose found in the treated skin and the absorbed dose at the end of the experiment, was calculated.

Table 4.42 below gives a summary of the amount of V6 found in each sample.

Table 4.42 Summary of percutaneous penetration of V6 through human skin *in vitro*

Test Preparation	"Neat" V6	V6 in Ethanol
Target V6 Concentration (g/L)	Neat	20
V6 Concentration by Radioactivity (g/L)	1403	20.96
N	7	8
Application Rate (mg equiv./cm^2)	14.03	0.210
Dislodgeable Dose 8 h (% Applied Dose)	99.53	68.82
Total Dislodgeable Dose (% Applied Dose)	102.63	78.10
Unabsorbed Dose (% Applied Dose)	104.52	92.47
Mean Total Absorbed Dose (% Applied Dose) [SD]	0.19 [0.18]	2.19 [1.77]
Mean Dermal Delivery (% Applied Dose) [SD]	0.51 [0.50]	6.10 [4.2]
Mass Balance (% Applied Dose)	105.03	98.57
Total Dislodgeable Dose (µg equiv./cm^2)	14393.91	163.69
Unabsorbed Dose (µg equiv./cm^2)	14657.75	193.81
Absorbed Dose (µg equiv./cm^2)	26.95	4.60
Dermal Delivery (µg equiv./cm^2)	72.04	12.78
Mass Balance (µg equiv./cm^2)	14729.79	206.58

For [^{14}C]-V6 applied "neat", the dermal delivery ranged from 0.05 % to 1.48 %, with a mean value of 0.51 %. 99.53% of the applied dose was removed by washing at 8 hours post dose. The stratum corneum retained 1.83% of the applied dose; most of this (1.36%) was removed with the first 5 tape strips. Steady state flux was achieved from 14 to 24 hours (1.10 µg equiv./cm^2/h).

For [^{14}C]-V6 applied in ethanol, the dermal delivery ranged from 0.82% to 12.14%, with a mean value of 6.10%. 68.82% of the applied dose was removed by washing at 8 hours post dose. The stratum corneum retained 9.71% of the applied dose and *ca*. 60% of this (5.79%) was removed with the first 5 tape strips. Steady state flux was achieved from 2 to 5 hours (0.24 µg equiv./cm^2/h).

In *in vitro* dermal absorption studies, the amount of penetrated substances found in the receptor fluid are considered to be systemically available. The epidermis (except for the stratum corneum) and the dermis are considered as a sink, and therefore amounts found in these tissues should also be considered absorbed (SCCNFP/0750/03 Final, October 2003). The amount of test material retained by the stratum corneum after 24 hours is not considered to be percutaneously absorbed and thus will not contribute to the systemic dose and so is not included in the calculation of the dermal delivery value. Therefore, the worst case dermal delivery value of 6% has been taken forward to risk characterisation for exposure scenarios where there is exposure to "neat" V6. This value is considered to be a reasonable worst case value since 12 of the total 15 individual membrane measurements taken were found to be 6 % or lower.

Two *in vitro* studies were conducted on the structurally similar substance, TCPP: one to determine the rate and extent of absorption following topical application of "neat" TCPP to the skin and the second to determine the percentage of TCPP absorbed across the skin as a result of handling flexible PUR foam (HSA/EA, 2008a). The results showed that the

percentage absorption from handling foam treated with TCPP is approximately twice that obtained following contact of the skin with "neat" TCPP (40% compared with 23%). Therefore, as a reasonable worst case approach for V6, 12 % dermal absorption will be taken forward to risk characterisation for exposure scenarios 3, 4 and 5, where there is exposure due to handling of foam containing V6. It should be noted that V6 is a very bulky molecule and so it is anticipated that V6 would migrate slowly from treated foam. Therefore, the value of 12% is likely to represent a worst case absorption value.

4.1.2.1.2 Studies in humans

No data are available.

4.1.2.1.3 Summary of toxicokinetics, metabolism and distribution

The ADME characteristics of V6 were investigated by the oral and IV routes in the rat. The bioavailability after the oral low and high doses were > 100% and approximately 50%, respectively. However, the bioavailability for the high dose was calculated using a lower IV dose. In addition, less than 1% of the parent compound was found in the faeces after the oral high dose, indicating practically complete absorption from the gastrointestinal tract. Therefore, 100% absorption by the oral route is assumed and is taken forward to risk characterisation. No sex difference was observed in blood kinetics at the low dose, however, in the high dose group, Cmax and AUC were higher in females than males. The elimination half life was 99-113 hours, irrespective of the dose, route or sex. The retention of radioactivity was low, with the majority (60%) of the radioactivity excreted by biliary route within 3 days of dosing. Approximately 20% was excreted in urine and a small amount of radioactivity exhaled as $^{14}CO_2$. [^{14}C]-V6 or its metabolites were distributed all over the body, but no target organs, other than organs of elimination were identified. The major metabolites which could be identified were found in the faeces.

An *in vitro* percutaneous absorption study using human skin membranes in flow-through diffusion cells was conducted to determine the rate and extent of absorption following topical application of commercial grade [^{14}C]-V6, either "neat" or in an ethanol vehicle, to human skin. The skin membranes were exposed to V6 for 8 hours, mimicking a normal working day. The dermal delivery for V6 and V6 in ethanol (0.2 mg/cm^2) was 0.51 % and 6 %, respectively. A value of 6 % dermal absorption is taken forward to risk characterisation for exposure scenarios where there is potential exposure to "neat" V6 and 12 % dermal absorption is assumed for scenarios 3, 4 and 5, where there is exposure due to handling of foam containing V6.

No inhalation studies, either in animals or humans, are available. Using the default values in the TGD, 100% absorption by the inhalation route is assumed.

4.1.2.2 Acute toxicity

4.1.2.2.1 Studies in animals

In vivo studies

Inhalation

A group of 10 Sprague Dawley rats (5 males and 5 females) was exposed to a dose of 1.65 mg/l V6 by the "snout only" method for a period of 4 hours in an acute inhalation study conducted to OECD Guideline No. 403 (1981) (Inveresk Research International, 1990a). This was the highest concentration attainable due to the viscous nature of the test material. Observations for clinical signs were carried out at least once daily for 14 days post-treatment. Animals were then sacrificed and subjected to a gross post mortem examination. The estimation of the particle size distribution revealed that the percentage of particles <3.5 μm was 70.2% by weight. The mass mean diameter of the aerosol particles generated was determined to be 2.5 μm. There were no mortalities. No clinical observations were recorded during the exposure period. All animals appeared slightly unkempt and had red staining around the snout and eyes immediately after dosing. No abnormalities were observed during the subsequent 14-day observation period. No adverse effect on body weight gain was observed following exposure to V6. The LC_{50} of V6 was deemed to be > 1.65 mg/l (highest concentration attainable). No gross pathological abnormalities were observed at necropsy. As V6 was tested by the "snout only" method, the potential role of dermal absorption of vapours and aerosols could not be assessed.

Dermal

A single dose of 2000 mg/kg V6 was applied evenly onto a gauze dressing onto the shaved back of 5/sex Sprague Dawley rats in an acute dermal toxicity test conducted to OECD Guideline No. 402 (1987) (Inveresk Research International, 1989a). Up to at least 10% of the body surface was in contact with the test material. At 24 hours post-administration, the skin was wiped with a water-dampened tissue to remove excess test material. Observations were made for 14 days. There were no deaths and no clinical signs noted in any of the treated animals. No abnormalities were noted at necropsy. Body weight gains were recorded and were acceptable. The dermal LD_{50} of V6 was estimated to be > 2000 mg/kg bw

V6 was administered topically to 3 female New Zealand White rabbits at 2000 mg/kg bw (Mobil Environmental and Health Science Laboratory, 1985d). Serum and whole blood cholinesterase activities of these rabbits were measured at 0, 7, and 24 hours post-administration and brain cholinesterase activities at 24 hours. No statistically significant changes in these enzyme activities were observed.

Oral

Groups of 5 male and 5 female Sprague Dawley rats were dosed once by oral gavage with V6 at 2000 or 5000 mg/kg bw (Mobil Environmental and Health Science Laboratory, 1984). The animals were observed frequently on the day of treatment and daily thereafter for 14 days. Eight of the 10 animals dosed at 5000 mg/kg bw, and 1 of the 10 dosed at 2000 mg/kg bw were found dead within 48 hours post-dosing. Clinical signs observed included decreased activity, respiratory distress, lacrimation, oral discharge, soft stool, decreased faeces, and

perianal discharge. By day 3, all surviving animals dosed with 2000 mg/kg bw were observed to be normal and remained so throughout the study. There was no information provided on the 2 surviving animals at 5000 mg/kg bw. Macroscopic post mortem observations in the animals that died included injected blood vessels and mucoid material in the small intestine, darkened and congested kidneys, reddened lungs, darkened lymph nodes, darkened and mottled thymus, pale liver and injected blood vessels, air and a red/yellow material in the stomach. The oral LD_{50} of the substance was estimated to be between 2000 and 5000 mg/kg bw.

In a limit test conducted to OECD Guideline No. 401 (1987) (Safepharm Laboratories Ltd., 1994a), a group of 5/sex Sprague Dawley rats was given a single oral dose of 2000 mg/kg bw of V6 as a solution in arachis oil B.P. The animals were observed for 14 days post-dosing. Two animals (1 male and 1 female) were found dead on day 1 post-dosing. No clinical signs of toxicity were noted in any other animal during the study period. Surviving animals showed expected bodyweight gain during the study. Abnormalities noted at necropsy of animals that died during the study were haemorrhagic lungs, patchy pallor of the liver and dark kidneys. No abnormalities were noted at necropsy of animals that were sacrificed at the end of the study. The oral LD_{50} of V6 was deemed to be > 2000 mg/kg bw.

V6 was administered orally to two groups of Sprague Dawley rats (4/group; 2/sex) to evaluate the potential for V6 to inhibit cholinesterase activity (Mobil Environmental and Health Science Laboratory, 1985a). One group received 1500 mg/kg bw, and the other 500 mg/kg bw. Serum cholinesterase activities were measured at 0, 1, 2, 4, 8, and 24 hours post-administration. At 1 hour, serum cholinesterase activities of rats dosed at 1500 mg/kg bw decreased by an average of 31% for males and 83% for females compared with pretreatment levels and those dosed at 500 mg/kg bw showed similar decreases of cholinesterase activities of 35% and 73% for males and females respectively. Maximum observed decreases at the 1500 mg/kg bw dose level were 66% for males at 8 hours and 96 and 97% for females at 8 and 24 hours respectively. The largest decreases of cholinesterase activity observed at 500 mg/kg bw were 59% for males and 91% for females, both after 8 hours.

In a follow-up, briefly reported, study to the Mobil Environmental and Health Science Laboratory, 1985a one above, a second study was carried out designed to more precisely define the dose-response relationship of V6 on serum cholinesterase activity and evaluate the potential effect of V6 on brain cholinesterase activity. Six groups of four female Sprague Dawley rats were administered V6 in polyethylene glycol 200/water (1:1) orally at 0, 15, 50, 150, 1500 mg/kg (Mobil Environmental and Health Science Laboratory, 1985b). Serum cholinesterase activities were measured at 0 and 4 hours post-administration. With the exception of the lowest dose (15 mg/kg), all treatments showed statistically significant decreases in serum cholinesterase activities when compared to the control group (the magnitude of the decreases was not provided in the report). A linear dose response relationship was found between decreased serum cholinesterase activity and the administered substance over a range of 0-500 mg/kg. The brain cholinesterase activities of these same rats were measured 4 hours after dose administration. No significant decreases of brain cholinesterase activities were observed in rats treated with V6 at any of the tested doses. From the linear dose response observed over a certain range of dose levels, it was determined that a 250 mg/kg oral dose of the substance would cause a 50% decrease of serum cholinesterase activity in female Sprague Dawley rats.

In a poorly reported study (Mobil Environmental and Health Science Laboratory, 1985c), three groups of 4 female Sprague Dawley rats were administered three different samples (MCP 4569, PP-20 and MCP 7666) of V6 orally at 250 mg/kg in polyethylene glycol 200/water (1:1). Information from industry indicates that sample PP20 had a comparatively

low content of tris 2-chlorethyl phosphates. This sample produced the same effect on plasma cholinesterase as the normal blend in previous studies. Sample MCP7666 had been washed to remove/hydrolyse pyrophosphates. There was no information on the composition of sample MCP 4569. Serum cholinesterase activities were measured at 0 and 4 hours post-administration. Enzyme activity was decreased by 60-70% with V6 samples MCP4569 and PP-20 and by 30% with the V6 sample MCP7666. As the V6 sample MCP7666 produced a much lower decrease in plasma cholinesterase, and this sample had been washed to remove pyrophosphates, industry tentatively concluded from this that pyrophosphates or other low level contaminants are responsible for the anti-enzyme activity.

4.1.2.2.2 Studies in humans

No data are available.

4.1.2.2.3 Summary of acute toxicity

Studies conducted in rats show that V6 has low acute toxicity by the oral, dermal and inhalation routes. V6 significantly decreases serum cholinesterase activity in rats of both sexes following oral administration. Serum cholinesterase activity was unaffected following dermal administration of V6. Brain cholinesterase activity was unaffected by either oral or dermal administration of V6. There were no clinical signs associated with this decrease.

Overall, the observed decrease in serum cholinesterase activity is not considered to be toxicologically relevant. In accordance with the TGD, the WHO/FAO Joint Meeting of Experts on Pesticides Residues recommendations on "Interpretation of Cholinesterase Inhibition" can be extended to existing chemicals. Those recommendations state that *"the inhibition of brain cholinesterase activity and clinical signs are considered to be the primary end-points of concern in toxicological studies on compounds that inhibit acetylcholinesterase……plasma acetylcholinesterase inhibition is considered not relevant"* (FAO: Pesticide Residues in Food. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group (1998) and FAO: Plant production and Protection Paper, No. 148, 17-19 (1999)).

Based on this, it is concluded that the decrease in plasma cholinesterase activity is not toxicologically significant and that V6 is not acutely toxic.

4.1.2.3 Irritation

4.1.2.3.1 Skin

Studies in animals

A single 4-hour, semi-occluded application of 0.5 ml of V6 was made to the intact skin of 3 female New Zealand White rabbits in an acute dermal irritation study carried out to OECD Guideline No. 404 (1981) (Safepharm Laboratories Limited, 1994b). Observation of the treated skin sites was carried out for evidence of primary irritation at 1, 24, 48 and 72 hours post-treatment and maintained for 7 days subsequently. Very slight erythema was noted at two treated sites and well-defined erythema was noted in one at 1 hour post-treatment. Very

slight erythema persisted at all treated sites at the 24 and 48-hour observations and at one up to 72 hours. Very slight oedema was noted at all treated skin sites at 1 and 24 hours after patch removal. Desquamation was noted at two treated skin sites 7 days post-treatment. The other treated skin site appeared normal at this stage.

In a second study conducted to OECD Guideline No. 404 (1981), 0.5 g of V6 was applied to the intact skin of each of 3 New Zealand White rabbits (1 male/2 female) in a single 4-hour, semi-occluded application (Inveresk Research International, 1989b). Observation of the treated skin sites was carried out for evidence of primary irritation at 1, 24, 48 and 72 hours post-treatment. Well defined erythema was recorded at one treated site, with very slight erythema at the 2 other treated sites 1 hour after patch removal. There was no sign of oedema. All treated skin sites had returned to normal by 24 hours post-treatment.

In another study, V6 was shown to be non-irritant to rabbit skin when 0.5 ml of it was applied occlusively for 24 hours to the back of the New Zealand White rabbit (Mobil Environmental and Health Science Laboratory, 1983a). One intact and one abraded test site was prepared on each of 6 rabbits. Based on the scores of skin reactions at 26 and 72 hours (according to Draize), the primary irritation index was calculated to be 1.0/8.0.

Studies in humans

No data are available.

4.1.2.3.2 Eye

Studies in animals

A single dose of 0.1 ml of V6 was instilled into the right eye of 3 New Zealand White rabbits (1 female and 2 males) (Safepharm Laboratories Ltd., 1994c). This study was carried out to OECD Guideline No. 405 (1987). The other eye served as a control in each case. Assessment of ocular damage/irritation was made approx. 1, 24, 48 and 72 hours following treatment. No corneal or iridial effects were noted during the study. Minimal conjunctival redness was noted in all treated eyes 1 hour post-instillation only. All treated eyes appeared normal by 24 hours post-treatment.

In a second study carried out to OECD Guideline No. 405 (1987), 0.1 ml V6 was instilled into the right eye of 3 New Zealand White rabbits (1 male and 2 females) (Inveresk Research International, 1990b). The other eye served as a control in each case. Assessment of ocular damage/irritation was made approx. 1, 24, 48 and 72 hours following treatment. No corneal or iridial responses were noted. No conjunctival responses were noted at the 1-hour observation time point. Slight conjunctival redness was noted in one rabbit 24 hours post-instillation, but this was reversed by 48 hours.

A volume of 0.1 ml of V6 was instilled into one eye of 6 New Zealand White rabbits (Mobil Environmental and Health Science Laboratory, 1983b). The eyes remained unwashed and were scored for irritation at 1, 24, 48, and 72 hours post-treatment. The average irritation scores at observation time points were 5, 0, 0, and 0 respectively.

Studies in humans

No data are available.

4.1.2.3.3 Respiratory tract

No studies are available. However, in the acute inhalation study (see section 4.1.2.2.1), there was no evidence of nasal/respiratory irritation effects seen at concentrations up to 1.65 mg/l air for 4 hours. All animals appeared slightly unkempt and had red staining around the snout and eyes immediately after dosing. This was not considered to be of toxicological relevance.

4.1.2.3.4 Summary of irritation

The available data indicate that V6 is non-irritant to the rabbit eye and skin. The lack of any skin or eye irritation and the lack of irritation observed in the acute inhalation studies suggest that V6 would be unlikely to produce significant respiratory tract irritation.

4.1.2.4 Corrosivity

No human data were available. Results from animal skin and eye irritation studies suggest that V6 is not corrosive.

4.1.2.5 Sensitisation

4.1.2.5.1 Studies in animals

Skin

In a guinea pig maximisation test, carried out to OECD Guideline No. 406 (1992) (Safepharm Laboratories Ltd., 1994d), a group of 20 test animals received an intradermal injection of a 5% w/v dilution of V6 in a 1:1 mixture of acetone in arachis oil B.P. and Freund's Complete Adjuvant/distilled water (1:1). At topical induction, undiluted test material was applied and covered with an occlusive dressing, which was kept in place for 48 hours. At challenge, undiluted test material and 75 % v/v test material in acetone were applied and covered with an occlusive dressing. 10 control animals received vehicle only. After 24 hours, the challenge sites were cleaned of any residual material. Evaluation took place at approximately 24 and 48 hours after challenge dressing removal and the degree of erythema and oedema was evaluated using the Draize scale.

Very slight to well-defined erythema was noted at the test material intradermal injection sites of all test group animals at the 24 and 48 hour observations. No skin reactions were noted at the vehicle intradermal injection sites of the control group animals at the 24 and 48-hour observations.

Following topical induction, two test group animals were found dead, one on day 8 and the second on day 9. The cause of death was not determined but the absence of these animals was considered not to affect the purpose or integrity of the study. Very slight erythema with or without very slight oedema was noted at the induction sites of 16 test group animals at the 1 hour observation and persisted in 5 test group animals at the 24 hour observation. Very slight erythema was noted at the treatment sites of 7 control group animals at the 1-hour observation. Very slight oedema was also noted in one control group animal at this time. No

skin reactions were noted at the treatment sites of the control group animals at the 24-hour observation.

Very slight erythema was noted at the challenge sites of two test group animals treated with undiluted V6 at the 24-hour observation. Very slight erythema developed at the challenge site of another test group animal at the 48-hour observation. No skin reactions were noted at the challenge sites of the test group animals at the 72-hour observation. No skin reactions were noted at the challenge sites of the control group animals at the 24, 48 and 72-hour observations.

No skin reactions were noted at the challenge sites of the test animals treated with 75% v/v V6 in acetone or in any control group animals at the 24, 48 and 72-hour observations.

Bodyweight gains of guinea pigs in the test group were comparable to those observed in the control group animals over the same period.

Overall, it can be concluded that V6 lacks significant skin sensitisation potential.

Respiratory tract

No studies are available.

4.1.2.5.2 Studies in humans

No data are available.

4.1.2.5.3 Summary of sensitisation

Evidence from a study in guinea pigs indicates that V6 does not possess significant skin sensitisation potential.

4.1.2.6 Repeated dose toxicity

4.1.2.6.1 Studies in animals

In vivo studies

Inhalation

No studies are available.

Dermal

No studies are available.

Oral

A 7-day range-finding study was carried out prior to a 28-day study. Three groups of three male and three female rats received V6 by oral gavage at the dose levels 150, 450 or 1000 mg/kg/day bw for 7 days. An additional group of 3 males and 3 females received the control

vehicle, olive oil. One female dosed at 1000 mg/kg/day died on day 7. Prior to death signs of poor clinical condition were noted from day 4. Clinical signs included piloerection in males from 150 mg/kg/day and ptyalism in all animals from 450 mg/kg/day. A higher liver weight correlated to liver enlargement was noted in all animals from 450 mg/kg/day. Lower spleen and thymus weights correlated to small spleens and thymus were observed in animals dosed at 1000 mg/kg/day and lower mean body weights and food consumption were also noted at the highest dose.

In a 28-day study conducted to OECD guidelines nos. 407 (1995) and 424 (neurotoxicological investigation) (CIT, 2001a), 5/sex Sprague Dawley rats were dosed daily by gavage with 0, 15, 150 and 600 mg/kg/day V6 (Antiblaze V6) in olive oil. Animals were checked daily for morbidity, mortalities and general clinical signs. A detailed clinical examination was made weekly. Body weight and food consumption were measured weekly. Blood samples were taken, following a 14-hour fast, for haematological examination and clinical chemistry assessment. All animals were assessed using a standard functional observation battery (FOB) at the end of treatment. Macroscopic examination was carried out at necropsy and organs weighed and sampled for histopathological examination.

There were no mortalities and no clinical signs of toxicity observed. No treatment-related alterations in autonomic or physiological functions were observed and there were no changes in neurotoxicological parameters. A slight to moderate dose-dependent increase in motor activity was seen in treated male animals. The increases were 4%, 11% and 19% greater than controls in treated males at 15, 150 and 600 mg/kg/day, respectively. In females, total motor activity was also increased, although not in a dose-dependent manner. The increases were 34%, 23% and 28% in treated females at 15, 150 and 600 mg/kg/day, respectively. In the absence of other changes in the functional observation battery, the toxicological significance of the increases in motor activity is questionable. A slight decrease in weight gain was seen in males (–16% in high-dose group) and a slightly increased weight gain in females (+9% in high-dose group). The changes were not statistically significant and not consistent between sexes and so were unlikely to be treatment related. Food consumption was unaffected.

A statistically significant higher mean prothrombin time (21.5s Vs 15s; 42%, $p<0.01$) was seen in high dose males. However, all values remained within the historical background data of the test laboratory. In addition, the effect was not observed in treated female animals. Consequently, the changes were not considered to be of toxicological significance. There were no other treatment-related effects on haematological parameters. A significantly higher mean cholesterol level was detected in the high dose males (+43%) and females (+63%). These increases were greater than the historical control values. Lower mean alkaline phosphatase values at 600 mg/kg/day in rats were significant (-44% in males and –32% in females) but within the historical control range and not considered to be toxicologically relevant.

Significantly greater absolute (35% and 78%) and relative (30% and 73%) liver weight was noted in females at 150 mg/kg/day and 600 mg/kg/day respectively and in males at 600 mg/kg/day (absolute: 52% and relative: 68%). These findings were correlated with evidence of hepatocellular hypertrophy among females at 150 mg/kg/day and findings of slight to marked centrilobular hypertrophy at 600 mg/kg/day in all males and females. There was no evidence of nuclear or cytoplasmic degenerative/necrotic changes. A biologically significant increase in absolute and relative thyroid weight was also noted in rats dosed with 600 mg/kg/day. The absolute weights were increased by 36 and 58% and the relative weights were increased by 48 and 54% in males and females, respectively, when compared to controls. These were correlated to evidence of thyroid hyperactivity at microscopic examination such

as follicular cell hypertrophy, decreased diameter of the follicular lumen and decreased eosinophilic colloidal contents.

Based on liver weight changes and liver histopathology at 150 and 600 mg/kg/day, the NOAEL from this study is taken as 15 mg/kg/day.

In an oral two-generation reproductive toxicity study in rats (TNO Quality of Life, 2007) 28 rats/sex /group received V6 in the diet corresponding approximately to 0, 28.9, 85.8 and 261.9 mg/kg bw/day for males and 0, 33.2, 97.1 and 302.3 mg/kg bw/day for females, over two successive generations. The animals were fed diets containing the test substance from the start of the study, during the premating period of at least 10 weeks, during mating, gestation and lactation, until sacrifice. Dams were allowed to raise one litter per generation. On PN 21, the litters were weaned and 28 males and 28 females were selected at random from as many litters as possible in each group to rear the next generation. Animals were observed for clinical signs, food consumption and body weight changes. Dams were sacrificed at, or shortly, after weaning and subjected to a necropsy. Parental males were euthanized after 77, 78 or 79 (F0) and 91, 92 and 93 (F1) days of exposure for sperm analysis and necropsy.

During gestation period, a female of the mid dose group of the F0 generation showed haemorrhagic discharge from the vagina; this animal delivered 1 live and 11 dead pups on GD 22. In the F1 generation, a female in the high dose group showed stiffness of the legs from week 8 of the premating period until sacrifice at the end of the lactation period (the animal delivered 11 live pups). One female of the mid dose group (C521) was found dead 22 days after copulation with 8 dead newborn pups; at necropsy hydrothorax was observed and one dead pup was found in the uterus. In the uterus 9 implantation sites were observed. No other remarkable clinical signs were observed.

During the premating and mating period, mean body weights of F0 males in mid and high dose groups were significantly decreased in weeks 4 and 10 and in the mid dose group in weeks 8 and 9. Mean body weights of mid dose F1 females were decreased in weeks 2, 3 and 6. There was no effect on body weight in F0 females or F1 males during this period. During gestation, mean body weight was decreased in F1 females of the mid and high dose groups on GD 21. Body weights were unaffected during lactation. Mean food consumption of females of the mid and high dose groups was decreased during gestation and lactation.

In both generations, terminal body weights were unaffected. Organ weight changes in both males and females are presented in **Tables 4.43** and **4.44**, below.

Table 4.43 Summary of the significant absolute and relative organ weight changes in males in the 2-generation reproductive toxicity study

	F0-generation						F1-generation					
	Low		Mid		High		Low		Mid		High	
Organ weight	**A**	**R**	**A**	**R**	**A**	**R**	**A**	**R**	**A**	**R**	**A**	**R**
Brain	-	-	-	-	-	-	-	-	↓	-	-	-
Kidneys	-	-	-	-	-	-	↓	-	↓	-	↓	-
Liver	-	-	-	↑	↑	↑	-	-	-	↑	↑	↑
Pituitary	-	-	-	-	-	-	-	-	↓	-	↓	-
Seminal vesicles	↓	↓	-	-	-	-	-	-	-	-	-	-
Spleen	-	-	↓	-	↓	↓	↓	-	-	-	↓	↓
Thyroid	-	-	-	↑	↑	↑	-	-	↑	↑	↑	↑

A: absolute weight; R: relative weight

Table 4.44 Summary of the significant absolute and relative organ weight changes in females in the 2-generation reproductive toxicity study

	F0-generation						F1-generation					
	Low		Mid		High		Low		Mid		High	
Organ weight	**A**	**R**	**A**	**R**	**A**	**R**	**A**	**R**	**A**	**R**	**A**	**R**
Brain	-	-	-	-	-	-	-	-	↓	-	-	-
Liver	-	-	-	-	↑	↑	-	-	-	-	↑	↑
Spleen	-	-	-	-	↓	↓	-	-	-	-	↓	↓
Thyroid	-	-	-	-	↑	↑	-	-	-	-	↑	↑

A: absolute weight; R: relative weight

There were no treatment related macroscopic findings in F0 animals. Examination of the mid dose female (C521) of the F1 generation which was found dead with 8 newborn pups revealed increased transparent liquid in the thorax and one dead pup in the uterus, which are indicative of dystocia. Since this finding was only observed in one female, it was not thought to be treatment related.

In F0 animals, there were treatment related changes in the liver and thyroid. In the liver, slight to moderate hepatocellular hypertrophy was observed in males (10/10) and females (8/10) of the high dose group. This finding was not observed in control, low or mid dose animals. In the thyroid diffuse hypertrophy of the follicular epithelial cells and a reduction of colloid, indicative of an activated state, was observed in 0/10 control, 3/10 low, 6/10 mid and 10/10 high dose males and in 5/10 high dose females. This finding reached statistical significance in the mid dose group of the males.

The low dose of 29 mg/kg bw/day is considered the NOAEL for parental toxicity in males. This is based on thyroid weight changes in mid and high dose males of both generations, and histopathological changes in this organ, the latter reaching statistical significance in mid dose F0 animals. The mid dose of approximately 97 mg/kg bw/day is considered to be the NOAEL

for parental toxicity in females, based on effects in liver and thyroid observed at the high dose.

4.1.2.6.2 Studies in humans

No studies are available.

4.1.2.6.3 Summary of repeated dose toxicity

The main target organs following repeated oral exposure to V6 are the liver and thyroid. In a 28-day study, significantly greater absolute and relative liver weights were noted in females from the mid dose of 150 mg/kg/day and in males at the highest dose (600 mg/kg/day). A significantly higher mean cholesterol level was detected in the high dose animals. A significant increase in absolute and relative thyroid weight was also noted in the high dose group. The higher liver and thyroid weights were considered treatment-related and correlated with histopathological changes observed in these organs among these animals. A NOAEL for V6 of 15 mg/kg/day can be determined from this study based on the absolute and relative liver weight changes and the correlated liver histopathology. It is noted that the dose spacing in this study was large (10 fold) and therefore, the true NOAEL may actually be higher than 15 mg/kg.

In a 2-generation reproductive toxicity study, an increase in absolute and relative thyroid weight was observed in mid dose (86 mg/kg/day) males of the F0 generation, and high dose males and females (corresponding to 262 mg/kg and 302 mg/kg, respectively) in both generations. In the F0 generation, the increase in organ weight was accompanied by evidence of an activated state in the thyroid; follicular cell hypertrophy and a reduction in colloid in mid dose males and high dose animals. In both generations, there was an increase in relative liver weight in mid dose males and absolute and relative liver weight was increased in high dose males and females. In the F0 high dose animals this was accompanied by hepatocyte hypertrophy. The low dose of 29 mg/kg bw/day is considered to be the NOAEL for parental toxicity (males). This is based on effects on the thyroid at mid and high doses in males following at least 77 days exposure.

As the 28-day study included haematology and clinical chemistry analyses, FOB and a detailed histopathological examination, which are not routinely conducted as part of a 2-generation study, the NOAEL derived from this study is considered to be more robust for the endpoint of repeated dose toxicity and is taken forward to risk characterisation. It is noted that the target organs identified in the 28-day and the 2-generation reproductive toxicity studies with V6 are the same (liver and thyroid). In addition, the doses at which the effects in these organs were observed and the severity of the effects are comparable between the two studies. Therefore, the NOAEL of 15 mg/kg bw/day taken from the 28-day study, while conservative, can be considered to be relatively robust and that an increase in the duration of exposure (to sub-chronic exposure) does not increase the severity of the effect observed.

No data are available on inhalation and dermal repeated dose toxicity.

4.1.2.7 Mutagenicity

4.1.2.7.1 Studies *in vitro*

Studies in bacteria

In a plate incorporation mutagenicity test conducted to OECD Guideline No. 471 (1997), Antiblaze V6 did not produce any increase in the number of revertants (CIT, 2001b). *Salmonella typhimurium* strains TA 1535, TA1537, TA 98, TA 100 and TA 102 were tested with concentrations of 312.5, 625, 1250, 2500 and 5000 μg/plate, both with and without S9 mix. Two independent experiments were performed, each using 3 plates/dose-level for each of the 5 strains of bacteria, both with and without S9 mix. Both experiments were performed according to the direct plate incorporation method except for the second test with S9 mix, which was performed according to the pre-incubation method. The vehicle used was DMSO and recommended positive controls were used, yielding the expected responses.

Except for some thinning of the bacterial lawn observed in the second experiment in all the strains mainly at 5000 μg/plate, no toxicity was induced either with or without S9 mix. Antiblaze V6 did not induce any significant increase in the number of revertants, in any of the five strains of bacteria, either in the presence or absence of metabolic activation.

In another plate incorporation assay based on the technique described by Ames *et al* (1970, 1975), McGann *et al* (1975) and Garner *et al* (1972), V6 was not mutagenic to *Salmonella typhimurium* strains TA 98 & 100 in a GLP study (Safepharm Laboratories Ltd., 1993). Cells from a log-phase culture of each strain were used supplemented with biotin and trace histidine and liver S9 fraction isolated from adult male Sprague-Dawley rats pretreated with Aroclor 1254. Test compound was added to give a final concentration of 0, 312.5, 625, 1250, 2500 and 5000 μg/plate. These concentrations were determined in a preliminary toxicity test in strain TA-100 in which no toxicity was recorded at any dose level. Each dose was tested in triplicate. The solvent and negative control was DMSO. The plates were incubated at 37°C for 48 hours. Positive non-activation controls were N-ethyl-N'-nitro-N-nitrosoguanidine (TA 100) and 4-nitroquinoline-1-oxide (TA 98). The positive activation control was benzo(a)pyrene (TA 98 & 100). All experiments were performed in duplicate.

Studies in mammalian cells

V6 was shown to be non-mutagenic in an *in vitro* mammalian cell mutagenesis assay (Mobil Environmental and Health Science Laboratory, 1983c). Mouse lymphoma cells ($L5178Y/TK^{+/-}$) were treated with V6 at concentrations of 0.06 - 0.10 μl/ml (corresponding to 8.8 - 147.3 μg/ml) (without metabolic activation), and 0.13 - 0.2 μl/ml (corresponding to 191.5 - 294.6 μg/ml) (with metabolic activation). The use of positive controls was not recorded. No significant increase was observed in the frequency of mutations at the thymidine kinase locus of mouse lymphoma cells treated with the test substance either in the presence or absence of metabolic activation.

In a second study, V6 was not mutagenic when mouse lymphoma cells ($L5178Y/TK^{+/-}$) were treated with concentrations of the substance between 0.01 and 0.08 μl/ml (corresponding to 14.73 – 117.8 μg/ml) test substance (without metabolic activation), and of between 0.06 and 0.15 μl/ml (corresponding to 88.4 – 221 μg/ml) test substance (with metabolic activation) (Mobil Environmental and Health Science Laboratory, 1983d). The use of positive controls

was not recorded. No significant increase was observed in the frequency of mutations at the thymidine kinase locus of mouse lymphoma cells treated with the test substance either in the presence or absence of metabolic activation.

The potential for V6 to increase the frequency of cells with chromosomal aberrations was investigated in human lymphocytes in a GLP study conducted to OECD Guideline No. 473 (1981) (Safepharm Laboratories Ltd., 1994e). The concentrations of V6 tested were 0, 39, 78.1, 156.3 and 312.5 μg/ml (-S9 fraction) or 0, 78.1, 156.3, 312.5, 625 and 1250 μg/ml (+S9 fraction). The metabolic activation used was liver S9 fraction isolated from adult male Sprague-Dawley rats pre-treated with Aroclor 1254. The duration of treatment was 4 hours. DMSO was used as a solvent and negative control. Where possible, the first 100 well-spread metaphases from each culture were counted for chromosomal aberrations. Approximately 2000 cell nuclei were used to estimate the mitotic index. The positive non-activation control was ethyl methanesulfonate and the positive activation control was cyclophosphamide. All experiments were performed in duplicate and the positive and negative controls gave the expected responses.

The mitotic index was reduced by treatment with V6 reaching 50% and 58% of negative control values at 625 and 156.25 μg/ml in the presence and absence of S9 fraction, respectively. These were the maximum dose levels that yielded scorable metaphase chromosomes. In the absence of metabolic activation, the total number of gaps was slightly increased (in a dose-dependent manner), though the increases did not reach statistical significance. In the presence of metabolic activation, there was a statistically significant increase in the frequency of cells with chromosome aberrations including gaps in the 312.5 μg/ml treatment group. When gap-type aberrations were excluded from the analysis, the increase in cells with aberrations was not statistically significant, but was greater than the historical maximum seen in the test laboratory. In addition, three cells contained chromatid exchange observations, which are rare in control cultures. A further set of slides was prepared from the original cell cultures and evaluated for aberrations. A similar increase in aberration frequency or of rare aberration types was not observed. Therefore, because the original data was non-reproducible and there was an absence of a dose-response effect, the original finding was not considered to be toxicologically relevant.

4.1.2.7.2 Studies *in vivo*

V6 was not clastogenic in a mouse micronucleus test conducted in accordance with OECD Guideline No. 474 and Commission Directive 2000/32, B12 (CIT, 2002). Groups of 5 male and 5 female Swiss Ico mice were orally dosed with 500, 1000 or 2000 mg/kg/day and 437.5, 875 or 1750 mg/kg/day V6 respectively. There were two treatments, 24 hours apart and animals were sacrificed 24 hours after the last treatment. The doses selected were based on a preliminary toxicity study in which toxic effects were noted at 2000 mg/kg/day in females only. The vehicle used was olive oil (negative control) and the positive control was cyclophosphamide. After sacrifice, bone marrow smears were prepared. For each animal, the number of micronucleated polychromatic erythrocytes (MPE) was counted in 2000 polychromatic erythrocytes; the polychromatic (PE) and normochromatic (NE) erythrocyte ratio was established by scoring a total of 1000 erythrocytes (PE + NE).

For both males and females, the mean values of MPE in groups treated with V6 were equivalent to those of the vehicle group, and no statistical difference was noted. The PN/NE ratio in treated groups was equivalent to that of the vehicle control, except for the highest-

dose group of males where a significant ($p<0.01$) decrease was noted. The mean values of MPE and the PE/NE ratio for the vehicle and positive controls were consistent with historical data.

4.1.2.7.3 Summary of mutagenicity

Evidence from bacterial mutagenicity studies show that V6 is not a bacterial cell mutagen. In mammalian cells, V6 was non-mutagenic in mammalian cell mutagenesis assays. *In vitro*, in human lymphocytes, V6 caused a statistically significant increase in the frequency of cells with chromosome aberrations including gaps at the mid dose evaluated (312.5µg/ml) in the presence of metabolic activation only. When gap-type aberration were excluded from the analysis, the increase, while not statistically significant, was greater than the historical maximum seen in the test laboratory. The findings were, however, non-reproducible and in the absence of a dose-response effect, were not considered to be toxicologically relevant. *In vivo*, V6 was not clastogenic in a mouse micronucleus test.

Table 4.45 below summarises the results from the *in vitro* and *in vivo* mutagenicity tests.

Table 4.45 Summary of mutagenicity data for V6

Test	Result	Comments	Ref.
In vitro plate incorporation assay, bacteria (Ames)	Non-mutagenic	2nd test +S9 performed according to the pre-incubation method	(CIT, 2001b)
In vitro plate incorporation assay, bacteria (Ames)	Non-mutagenic		(Safepharm Labs Ltd. 1993)
Mammalian cell gene mutation (L5178Y $TK^{+/-}$ cells)	Non-mutagenic	Use of positive controls not recorded	(Mobil Environ. & Health Sci. Lab. 1983c)
Mammalian cell gene mutation (L5178Y $TK^{+/-}$ cells)	Non-mutagenic	Use of positive controls not recorded	(Mobil Environ. & Health Sci. Lab. 1983d)
Induction of chromosome aberrations (Human lymphocytes)	Non-mutagenic	A statistically significant increase in frequency of cells with chromosome aberrations (incl., gaps) at 312.5 µg/ml +S9 observed. (excl. gaps, increases not stat. sign. but greater than historical max.). Not reproducible in 2nd experiment; therefore not considered to be toxicologically relevant.	(Safepharm Labs Ltd. 1994e)
In vivo Mouse Micronucleus assay	Non-clastogenic		(CIT, 2002)

4.1.2.8 Carcinogenicity

There are no carcinogenicity data for V6. There was no evidence of mutagenicity in either *in vitro* or *in vivo* genotoxicity studies with V6 and there were no indications of a potential concern for carcinogenicity (for example pre-neoplastic and hyperplasic lesions) from repeated dose toxicity studies with V6.

In addition, no structurally related analogues were identified for V6 which would lead to a concern for carcinogenicity. This information is outlined in Appendix D.

4.1.2.9 Toxicity for reproduction

4.1.2.9.1 Effects on fertility

Studies in animals

An oral two-generation reproductive toxicity study in rats was carried out in accordance with OECD Guideline No. 416 and to GLP (TNO Quality of Life, 2007). The main study was preceded by a preliminary range finding study (one-generation reproductive toxicity study), in which 10 male and 10 female rats were administered the test substance in the diet at 0, 500, 1500 and 7500 mg/kg diet (corresponding to approximately: 0, 31, 97 and 468 mg/kg bw/day for males and for females 0, 34, 107 and 543 mg/kg bw/day during premating, 0, 33, 99 and 482 mg/kg bw/day during gestation and 0, 67, 192 and 827 mg/kg bw/day during lactation). Males and females were treated for 5 weeks prior to mating and during mating, and then during gestation and lactation to post-natal day (PN) 21. Dams were allowed to raise one litter. On PN 4, litter sizes were adjusted to 4 males and 4 females per litter, where possible. Animals were observed for clinical signs, food consumption and body weight gain. Fertility and reproductive performance were recorded. Dams were sacrificed for necropsy at PN 21. Males were euthanized after at least 42 days of exposure for sperm analysis and necropsy.

There were no treatment related clinical signs. For parental males, mean body weights were increased in the low dose group on Days 21 and 28 of premating and mean body weight change was decreased in the high dose group on Days 35-42 of premating. For females, mean body weight change was decreased in the low dose group on Days 0-7 of premating and in the high dose group on Days 1-21 of lactation. Food consumption was decreased in females of the high dose group during Days 14-21 of lactation.

All treated females were found sperm positive within 4 days, and all mated females, except one of the high dose group (D61), were pregnant. There was no difference in pre-coital time, mating index, male and female fertility index and duration of gestation between the control and V6 treated groups. The post-implantation loss was comparable in all groups.

The number of pups was comparable in all groups. Pup mortality (PN 1-4) was statistically significantly higher in the high dose group; 10 pups of one dam and 2 pups of another died or were missing (the statistical significance was essentially due to one litter). Litter and pup data are presented in section 4.1.2.9.2.

In parental males, epididymal sperm count was statistically significantly increased in the low dose group. There was no effect on motility of epididymal sperm or on sperm morphology. Parental terminal body weights were comparable between the treated groups and the control. In males, there was a statistically significant increase in absolute and relative liver weight in the high dose group. There was a significant increase in the relative weight of the adrenals in high dose males. Relative epididymides weight of the mid-dose group was statistically significantly decreased when compared with the control. In females, the absolute and relative liver weight was statistically significantly increased in the mid and high dose groups. The absolute and relative spleen, ovary and vagina weights were significantly decreased in the high dose group. The relative weight of the vagina was decreased in the mid dose and the relative weight of the kidneys was significantly increased in the high dose group females.

No treatment related gross or histopathological changes were observed in any of the treated males. In females, microscopic examination of the ovaries revealed a reduced number of

corpora lutea in 2/10 females of the high dose group. In addition, reduced follicular development was observed in 9/10 females of the high dose group.

Based on the results of the preliminary study, 28 rats (Wistar outbred Crl:WI(WU)) per sex per group received V6 in the diet over two successive generations. In each dose group, the concentration of the test substance was adjusted over the course of the study to maintain target concentrations of 0, 30, 100 and 300 mg/kg bw/day. The animals were fed diets containing the test substance from the start of the study, during the premating period of at least 10 weeks, during mating, gestation and lactation until sacrifice. Vaginal smears were made 3 weeks prior to mating to evaluate the length and normality of the oestrus cycle and daily during the mating period to determine if sperm was present. The day of observation of sperm in the vaginal smear was considered Day 0 of pregnancy. Upon evidence of copulation the females were caged individually for the birth and rearing of pups until PN 21 or shortly thereafter when they were weaned and sacrificed. Dams were allowed to raise one litter per generation. On PN 4, litters were adjusted to 4 males and 4 females per litter, where possible. On PN 21, the litters were weaned and 28 males and 28 females were selected at random from as many litters as possible in each group to rear the next generation. Animals were observed for clinical signs, food consumption and body weight changes. Fertility and reproductive performance were measured. Dams were sacrificed at or shortly after weaning and necropsied. Parental males were euthanized after 77, 78 or 79 (F0) and 91, 92 and 93 (F1) days of exposure for sperm analysis and necropsy.

The overall intake of V6 was 0, 28.9, 85.8 and 261.9 mg/kg bw/day for males and 0, 33.2, 97.1 and 302.3 mg/kg bw/day for females, for the control, low, mid and high dose groups, respectively.

During gestation period of the F0 generation, a female of the mid dose group showed haemorrhagic discharge from the vagina; this animal delivered 1 live and 11 dead pups on GD 22. In the F1 generation, a female in the high dose group showed stiffness of the legs from week 8 of the premating period until sacrifice at the end of the lactation period (the animal delivered 11 live pups). One female of the mid dose group (C521) was found dead 22 days after copulation with 8 dead newborn pups; at necropsy hydrothorax was observed and one dead pup was found in the uterus. In the uterus 9 implantation sites were observed. No other remarkable clinical signs were observed.

During the premating and mating period, mean body weights of F0 males in mid and high dose groups were significantly decreased in weeks 4 and 10 and in the mid dose group in weeks 8 and 9. Mean body weights of mid dose F1 females were decreased in weeks 2, 3 and 6. There was no effect on body weight in F0 females or F1 males during this period. During gestation, mean body weight was decreased in F1 females of the mid and high dose groups on GD 21. Body weights were unaffected during lactation. Mean food consumption of females of the mid and high dose groups was decreased during gestation and lactation.

Effects on oestrus cycle were evaluated in control and high dose females. No differences were observed in the oestrus cycle in F0 females. In F1 females, the mean length of the longest oestrus cycle was statistically significantly increased in high dose females (5 days) when compared with the control (4.2 days). As a result, the number of cycles per animal in this group was decreased. The study director comments that a mean cycle length of 5 days is common for this strain of rat and the significant difference was also due to the low mean cycle length in the F1 control females. In addition, this effect was not consistent across generations. Therefore, the effect on cycle length in F1 females is not considered to be biologically significant.

All females, except one of the low dose group in F0, were found sperm positive. In both generations, no treatment related differences were observed in pre-coital time, mating index, female fecundity index, male and female fertility index, duration of gestation and post-implantation loss. With the exception of one mid dose dam (C521) of the F1 generation, all dams delivered and there were no dams with stillborn pups. Three other F1 dams of the mid dose group lost their litter between PN 1 and 4. These effects were not considered to be toxicologically significant. The mean number of pups delivered was comparable between the groups. Litter data is presented in full in section 4.1.2.9.2.

In parental males, relative liver weight was increased in the mid dose groups of both generations, and absolute and relative liver weights were increased in the high dose groups. Absolute and relative thyroid weights were increased in mid dose F1 animals and high dose animals of both generations. Relative thyroid weight was also increased in mid dose F0 animals. The effects observed on thyroid and liver organ weights at mid and high dose are considered to be the main treatment related effects Other organ weight changes included a decrease in absolute pituitary weight in mid and high dose F1 animals, a decrease in absolute kidney weight in all dosed F1 animals, an increase in absolute spleen weight in low dose F1, mid dose F0 and high dose animals of both generations and a decrease in relative spleen weights in high dose F0 and F1 males.

In parental females, the main treatment related organ weight changes were an increase in absolute and relative liver and thyroid weights and a decrease in spleen weights in high dose animals of both generations. **Tables 4.46** and **4.47** below summarise the significant organ weight changes.

Table 4.46 Mean terminal body weights and significant organ weights for males of F0 and F1 generations

		Dose Group			
Organ	**Generation**	**0**	**Low**	**Mid**	**High**
Mean terminal body weight	F0	405.1	390.7	386.2	389.5
	F1	399.5	386.8	383.5	381.3
Mean absolute organ weight (g)					
Kidney	F0	2.338	2.244	2.231	2.288
	F1	2.278	2.112**	2.110**	2.140*
Liver	F0	14.4	13.993	14.579	15.986**
	F1	14.312	13.544	14.088	15.357*
Pituitary	F0	0.015	0.014	0.014	0.014
	F1	0.016	0.015	0.014*	0.014*
Spleen	F0	0.744	0.704	0.681**	0.646***
	F1	0.746	0.686*	0.692	0.646***
Thyroid	F0	0.023	0.022	0.025	0.029***
	F1	0.023	0.024	0.026*	0.029***
Mean organ weights relative to terminal body weight (g/kg bw)					
Kidney	F0	5.786	5.750	5.780	5.875
	F1	5.601	5.468	5.520	5.616
Liver	F0	35.458	35.783	37.740**	41.018***
	F1	35.184	35.006	36.760*	40.240***
Pituitary	F0	0.036	0.035	0.036	0.036
	F1	0.040	0.039	0.038	0.038
Spleen	F0	1.849	1.805	1.766	1.662***
	F1	1.835	1.775	1.810	1.691**
Thyroid	F0	0.056	0.058	0.065**	0.075***
	F1	0.057	0.062	0.068**	0.075***

*/**/*** statistically significantly different to the control group p< 0.05/ 0.01/ 0.001

Table 4.47 Mean terminal body weights and significant organ weights for females of F0 and F1 generations

		Dose Group			
Organ	**Generation**	**0**	**Low**	**Mid**	**High**
Mean terminal body weight	F0	266.4	264.2	264.1	265.5
	F1	262.1	259.3	254.0	259.5
Mean absolute organ weight (g)					
Liver	F0	13.318	13.348	12.798	16.002***
	F1	13.137	13.230	12.742	15.974***
Spleen	F0	0.506	0.494	0.470	0.452**
	F1	0.507	0.508	0.486	0.446**
Thyroid	F0	0.020	0.019	0.021	0.023***
	F1	0.020	0.020	0.020	0.023***
Mean organ weights relative to terminal body weight (g/kg bw)					
Liver	F0	49.938	50.501	48.488	60.131***
	F1	50.059	51.105	50.107	61.521***
Spleen	F0	1.902	1.872	1.783	1.705**
	F1	1.937	1.963	1.914	1.718***
Thyroid	F0	0.074	0.074	0.080	0.086***
	F1	0.076	0.079	0.079	0.090***

/* statistically significantly different to the control group $p < 0.01/ 0.001$

At necropsy, no effect was observed on motility, count or morphology of the epididymal sperm in parental males of either generation. Daily sperm production was comparable between control and high dose groups. Corpora lutea were not counted in females at scheduled sacrifice.

There were no treatment related macroscopic findings in F0 animals. Examination of the mid dose female (C521) of the F1 generation which was found dead with 8 newborn pups, revealed increased transparent liquid in the thorax and one dead pup in the uterus, which are indicative of dystocia. Since this finding was only observed in one female it was not thought to be treatment related.

There were no treatment related microscopic findings in the reproductive organs of either generation. In F0 animals, there was a treatment related change in the liver and thyroid. In the liver, slight to moderate hepatocellular hypertrophy was observed in males (10/10) and females (8/10) of the high dose group. This finding was not observed in control, low or mid dose animals. In the thyroid diffuse hypertrophy of the follicular epithelial cells and a reduction of colloid, indicative of an activated state, was observed in 0/10 control, 3/10 low, 6/10 mid and 10/10 high dose males and in 5/10 high dose females. This finding reached statistical significance in the mid dose group.

It is considered that there were no effects on the male or female reproductive systems in this study, up to the highest doses tested. Therefore, the NOAEL is greater than approx. 262 and 302 mg/kg bw/day for male and female animals, respectively.

The low dose of 29 mg/kg/day is considered to be the NOAEL for parental toxicity in males. This is based on thyroid weight changes in the mid and high dose males of both generations, and histopathological changes in this organ. The mid dose of approximately 97 mg/kg/day is considered the NOAEL for parental toxicity in females.

Studies in humans

No studies are available.

4.1.2.9.2 Developmental toxicity

Studies in animals

Developmental toxicity of V6 to rats was investigated as part of the two-generation reproductive toxicity study described in section 4.1.2.9.1 above (TNO Quality of Life, 2007). In the preliminary range finding study (one-generation reproductive toxicity study), 10 male and 10 female rats were administered the test substance in the diet at 0, 500, 1500 and 7500 mg/kg diet (corresponding to approximately: 0, 31, 97 and 468 mg/kg bw/day for males and for females 0, 34, 107 and 543 mg/kg bw/day during premating, 0, 33, 99 and 482 mg/kg bw/day during gestation and 0, 67, 192 and 827 mg/kg bw/day during lactation). Males and females were treated for 5 weeks prior to mating and during mating, and then during gestation and lactation to PN 21. Dams were allowed to raise one litter. On PN 4, litter sizes were adjusted to 4 males and 4 females per litter, where possible. At birth, litter size, sex and weight of pups were reported. At PN21 or shortly thereafter, pups were weaned and sacrificed.

There were no treatment related clinical signs. Maternal mean body weight change was decreased in the low dose group on Days 0-7 of premating and in the high dose group on Days 1- 21 of lactation. Food consumption was decreased in females of the high dose group during Days 14-21 of lactation.

Pup mortality (PN 1-4) was statistically significantly higher in the high dose group; 10 pups of one dam and 2 pups of another died or were missing (the statistical significance was essentially due to one litter). Mean pup weights were decreased in males of the high dose group on PN 7 and in males and females of this group on PN 14 and 21. **Table 4.48** summarises the pup and litter data.

Table 4.48 Pup and Litter data from the preliminary study

Effect	Dose (mg V6/kg diet)			
	0	**500**	**1500**	**7500**
Total no. of pups delivered	98	106	103	84
Live birth index (%)	99	100	100	100
No. of pups lost (dying, missing and/ or cannibalized) on:				
Days 1-4	0	1	1	12***
Days 5-7	0	0	0	0
Days 8-14	0	0	0	0
Days 15-21	0	1	0	0
No. pups alive Day 21	74	79	75	64
Sex ratio on PN1 (M/F)	44/54	50/56	46/57	48/36
Mean no. of live pups per litter on PN1	9.7	10.6	10.3	9.33
Post implantation loss (%)	14.87	9.10	8.33	9.64

*** Statistically significantly different to the control group ($p<0.001$)

Pup weight changes (males, females and both combined) of the high dose group were decreased from PN 7-14 and 14-21. The number of runts was significantly increased in the high dose group on PN 4, 14 and 21. There were no remarkable abnormalities observed in stillborn pups or pups that died during lactation.

Based on the results of the preliminary study, 28 rats (Wistar outbred Crl:WI(WU)) per sex per group received V6 in the diet at target concentrations of 0, 30, 100 and 300 mg/kg bw/day over two successive generations. The animals were fed diets containing the test substance from the start of the study, during the premating period of at least 10 weeks, during mating, gestation and lactation until sacrifice. Dams were allowed to raise one litter per generation. Pup body weights and clinical signs were recorded on Days 1, 4, 7, 14 and 21 of lactation. On PN 4, litters were adjusted to 4 males and 4 females per litter, where possible. On PN 21, the litters were weaned and 28 males and 28 females were selected at random from as many litters as possible in each group to rear the next generation. Of the remaining pups, 1 male and 1 female pup of each litter were subjected to a necropsy. After necropsy, the thoracic parts of the skeletons were stained and the ribs and sternum of these pups were examined for skeletal abnormalities. Markers of sexual maturation were recorded in pups of the F2 generation.

The overall intake of V6 was 0, 28.9, 85.8 and 261.9 mg/kg bw/day for males and 0, 33.2, 97.1 and 302.3 mg/kg bw/day for females, for the control, low, mid and high dose groups, respectively.

Mean maternal body weights were significantly decreased in mid dose animals of F1 generation in weeks 2, 3 and 6 of the premating period and in mid and high dose F1 animals on GD 21. Mean food consumption was decreased in mid and high dose females during gestation and lactation.

The mean number of pups delivered was comparable between the groups. In the mid dose groups of both generations, the number of liveborn pups was significantly decreased and the number of stillborn pups and pup mortality (PN 1-4) were significantly increased. The effect

seen in the mid dose group of the F0 generation was mainly due to one dam with 11 of 12 pups stillborn. These effects were not considered to be toxicologically significant. All F0 pups remained alive after PN 4. In the F1 generation, 3 control and 2 high dose pups died between PN 4 and PN 21. The sex ratio was comparable in all dose groups, apart from the high dose group of F1, which showed a statistically significant decreased in the number of male pups. It is noted however, that the control group had a high number of male pups. **Table 4.49** summarises the delivery, pup and litter data.

Table 4.49 Delivery, pup and litter data for F0 and F1 generations

		Dose Group		
Effect	**0**	**Low**	**Mid**	**High**
F0:				
Mean no. of pups delivered	10.72	9.79	9.92	10.71
No. of liveborn	265	233	236*	249
No. of stillborn	3	2	12*	8
No. of pups lost (dying, missing and/ or cannibalized) on:				
Days 1-4	28	29	60***	24
Days 5-7	0	0	0	0
Days 8-14	0	0	0	0
Days 15-21	0	0	0	0
Mean no. live pups/litter (PN1)	10.6	9.71	9.44	10.38
Sex ratio on PN1 (M/F)	132/136	104/131	125/123	134/123
No. pups alive Day 21	184	171	147	178
F1:				
Mean no. of pups delivered	10.36	10.50	9.86	9.58
No. of liveborn	258	250	251***	249
No. of stillborn	1	2	25***	0
No. of pups lost (dying, missing and/ or cannibalized) on:				
Days 1-4	7	1	23**	5
Days 5-7	2	0	0	2
Days 8-14	0	0	0	0
Days 15-21	0	0	0	0
Mean no. live pups/litter (PN1)	10.32	10.42	9.3*	9.58
Sex ratio on PN1 (M/F)	145/114	136/116	132/144	110**/139
No. pups alive Day 21	191	191	188	203

*/**/*** statistically significantly different to the control group p< 0.05/ 0.01/ 0.001. [1] Animal found dead just after delivery with 8 dead pups. One dead pup found in uterus at necropsy

A runt is defined as a pup with a body weight lower than 2 standard deviations below the mean body weight of the control pups. In the F0 generation, the number of runts was statistically significantly increased in all dose groups on PN 1, and in the mid dose group on PN 4, 7 and 14. It is noted however, that most of the runts in the low dose of the F0

generation are from the 2 dams with the lowest body weight of the group. In the F1 generation, the number of runts was increased in the low dose group on PN 14 and 21 and in the mid and high dose groups during the entire lactation period. As the increase in the number of runts in the low dose group PN 1 was not observed consistently across generations, it is considered to be biologically significant only at the mid and high dose groups. The increased numbers of runts in the treated pups in the mid and high groups in both generations on PN 1 could indicate systemic toxicity to the pups *in utero*. The number of cold pups and pups with no milk in stomach (5 pups of one litter) was statistically significantly increased in the F1 mid dose group on PN 1. **Table 4.50** summarises the number of runts in F0 and F1 generations.

Table 4.50 Clinical observations in pups of F0 and F1 generations on Days 1-21 of lactation

Dose Group	0	Low	Mid	High
F0				
Runts				
Day 1	4(2)	19***(7)	110***(16)**	31***(9)
Day 4	1	3(3)	21***(8)**	4(4)
Day 7	2(2)	1	21***(7)	4(4)
Day 14	2(2)	2(1)	16***(3)	3(3)
Day 21	2(2)	0	6(3)	2(2)
F1				
Runts				
Day 1	10(4)	18(6)	37***(8)	41***(7)
Day 4	8(3)	12(5)	23**(4)	40***(7)
Day 7	5(3)	12(5)	24***(7)	48***(9)
Day 14	0	17***(7)**	13***(7)**	14***(11)***
Day 21	4(3)	28***(11)*	41***(13)**	84***(16)***

*/**/*** statistically significantly different to the control group p< 0.05/ 0.01/ 0.001

Figures in brackets represent the number of litters with pups showing the observation

In the F0 generation, a significant decrease in the mean pup weight was observed in mid dose at PN 1 and 7 and in the high dose on PN 7 and 21. In the F1 generation, mean pup weights were decreased in all dose groups during the entire lactation period, except for the mid dose group on PN 4. As the decrease on pup weight was not observed consistently in the low dose groups, this effect is considered to be biologically significant only from the mid dose group.

The anogenital distance of females of mid and high dose groups of the F2 generation were statistically significantly decreased, however the delay is most likely related to the lower body weight in these groups. There was no effect on vaginal opening. Preputial separation was significantly delayed in the males of the high dose group when compared with the control (45.12 days versus 43 days). Mean body weights were significantly decreased in male and female F2 pups in all dose groups on PN 28 and 35, with body weights also decreased in high dose males at PN 42. Therefore, the delay in preputial separation is most is likely to be due to the decreased body weight observed in this group from PN 28-42.

At necropsy of the pups, one low dose F1 pup showed an enlarged thymus. There were no other findings in either generation. Absolute spleen weight was decreased in high dose F0

pups and in all treated F1 pups. Relative spleen weight was decreased in high dose F1 pups. Absolute brain weight was decreased in all treated F1 pups; relative weights were significantly increased. Absolute thymus weight of low and high dose F1 pups was also decreased. No skeletal abnormalities or retarded ossification were observed in the ribs of F1 pups.

In deriving a N(L)OAEL for developmental toxicity, consideration is given to the increased number of runts observed on PN1, which may indicate toxicity to the offspring *in utero,* and the decrease in pup weights, both of which were observed in mid and high dose groups in both generations. As the increase in the number of runts in the low dose group PN 1 was not observed consistently across generations, it is considered to be biologically significant only at the mid and high dose groups. Therefore, the low dose of 29 mg/kg bw/day is considered to be the NOAEL for developmental toxicity and this value will be taken to risk characterisation.

Studies in humans

No studies are available.

4.1.2.9.3 Summary of toxicity for reproduction

In a two-generation reproductive toxicity study with V6, no treatment related differences were observed in pre-coital time, mating index, female fecundity index, male and female fertility index, duration of gestation and post-implantation loss. With the exception of one mid dose dam (C521) of the F1 generation, all dams delivered and there were no dams with stillborn pups. The mean number of pups delivered was comparable between the groups. There was no effect on sperm parameters at necropsy and there were no treatment related microscopic findings in the reproductive organs of either generation.

No effects on male or female reproductive system were observed up to the highest dose, and therefore, the NOAEL is greater than approx. 262 and 302 mg/kg bw/day for male and female animals, respectively.

The low dose of 29 mg/kg/day is considered to be the NOAEL for parental toxicity in males. This is based on thyroid weight changes in the mid and high dose males of both generations, and histopathological changes in this organ. The mid dose of approximately 97 mg/kg/day is considered the NOAEL for parental toxicity in females.

From the same study, a NOAEL of 29 mg/kg bw/day is derived for developmental toxicity. This is based on an increase in the number of runts on PN1 and a decrease in mean pup weights observed in the mid and high dose groups of both generations.

4.1.3 Risk characterisation [16]

4.1.3.1 General aspects

This section provides an overview of the occupational use, exposure and toxicological profile of V6.

Occupational exposure to V6 may occur during the:

1. Manufacture of V6
2. Manufacture of flexible PUR foam
    a. slabstock foams
    b. moulded foams
3. Cutting of flexible foam
4. Production of foam granules and rebonded PUR foam
5. Manufacture of automotive parts

V6 is a liquid at room temperature. The vapour pressure has been estimated using EPIWIN Version 3.05, modified Grain method, and is reported as 2.75×10^{-6} Pa at 25^0C.

The sole use of V6 is as a flame retardant. The main downstream use of V6 is in the production of flexible polyurethane foam. The flame retardant is not chemically reacted, but physically bound within the matrix and therefore has the potential for migration.

The manufacturing process is carried out in a predominantly closed system, with transfers done using closed lines. The process is mostly computer controlled, thus minimising worker exposure during its manufacture. The closed system is breached only for sampling and maintenance. Monitoring for dermal and inhalation exposure during V6 manufacture was carried out by industry in the EU production plant.

During blending of the manufactured substance and drumming, worker exposure can potentially occur. In addition, during the manufacture and subsequent use of polyurethane foam, there is the potential for worker exposure to V6.

For the purposes of risk characterisation, two types of worker exposure are considered. 'Typical' exposure covers the circumstances in which most workers are exposed and is based on normal industry working practice. 'Reasonable worst case' (RWC) exposures are intended to cover exposure situations where adequate control is lacking. RWC exposures are not considered as extreme incidents, but rather higher end exposures which are reasonably foreseeable.

V6 inhalation exposures varied across the industry sectors. The highest inhalation exposure occurred during the manufacture of V6, with the reasonable worst case exposure of 30 $\mu g/m^3$. The highest typical exposure was 1.9 $\mu g/m^3$, which occurred during the cutting of flexible foam and manufacture of automotive parts (**Table 4.36**). The lowest inhalation exposures occurred during the production of rebonded foam, with a typical exposure of 0.59 $\mu g/m^3$.

[16] Conclusion (i) There is a need for further information and/or testing.
Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

V6 dermal exposures again varied across the industry sectors. The highest dermal exposure occurred during the production of V6, with a reasonable worst-case exposure of 168 mg/day and a typical exposure of 42 mg/day. The lowest dermal exposure was measured during the production of rebonded foam, with a typical exposure of 0.23 mg/day.

The ADME characteristics of V6 were investigated by the oral and IV routes in the rat. V6 was almost completely absorbed and therefore, 100% absorption by the oral route is assumed. There was no difference in blood kinetics in low dose animals. However, in the high dose group, Cmax and AUC were higher in females than males. The retention of radioactivity was low, with the majority of the radioactivity excreted within 3 days of dosing. [^{14}C]-V6 or its metabolites were distributed all over the body, but no target organs, other than organs of elimination were found. The major metabolites which could be identified were found in the faeces.

An *in vitro* percutaneous absorption study determined the percentage dermal penetration through human skin at two doses. At 14 mg/cm^2, the maximal obtainable dose, 0.51% dermal delivery was recorded, while at 0.2 mg/cm^2, corresponding to the typical dermal exposure during production of V6, 6% dermal delivery was found. Based on these results, 6% dermal absorption of V6 is assumed where there is exposure to "neat" V6 and 12% dermal absorption is assumed for scenarios 3, 4 and 5, where there is exposure due to handling of foam containing V6.

No inhalation studies are available and therefore 100% absorption by the inhalation route is assumed.

Assessment of available data indicates that V6 has low acute toxicity by the oral, dermal and inhalation routes.

V6 is non-irritant to skin and eyes and the lack of any skin or eye irritation and the lack of irritation observed in the acute inhalation studies suggests that it would be unlikely to produce significant respiratory tract irritation. Evidence from a sensitisation study indicates that V6 does not possess significant skin sensitisation potential.

Repeated exposure (28 days) to V6 by the oral route indicated moderate systemic toxicity. Significantly greater absolute and relative liver weights were noted in females from 150 mg/kg/day and in males at the highest dose of 600 mg/kg/day. A significant increase in absolute and relative thyroid weight was also noted in the high dose male group. The higher liver and thyroid weights were considered treatment-related and correlated with histopathological changes observed in these organs among these animals. A NOAEL of 15 mg/kg/day will be used from this study in the risk characterisation.

In the 2-generation reproductive toxicity study, an increase in liver and thyroid weights were observed, which were accompanied by histopathological changes in these organs. The low dose of 29 mg/kg/day is considered to be the NOAEL for parental toxicity. This was based on effects observed in the thyroid at the mid and high dose males.

The target organs identified in the 28-day and the 2-generation reproductive toxicity studies with V6 are the same (liver and thyroid). In addition, the doses at which the effects in these organs were observed, and the severity of the effects, are comparable between the two studies. Therefore, the NOAEL of 15 mg/kg bw/day taken from the 28-day study can be considered to be relatively robust and that an increase in the duration of exposure (to sub-chronic exposure) does not increase the severity of the effects observed.

Evidence from bacterial mutagenicity studies show that V6 is not a bacterial cell mutagen. In mammalian cells, V6 was non-mutagenic in mammalian cell mutagenesis assays. When investigated in human lymphocytes, V6 did not produce significant increases in the frequency of chromosomal aberrations. *In vivo*, V6 was not clastogenic in a mouse micronucleus test.

There are no carcinogenicity data for V6. V6 showed no evidence of mutagenicity in either *in vitro* or *in vivo* genotoxicity studies. There was no indication from repeated dose toxicity studies with V6 of a concern for carcinogenicity.

In a two-generation reproductive toxicity study, there were no treatment related effects in pre-coital time, mating index, female fecundity index, male and female fertility index, duration of gestation and post-implantation loss. There were no effects on sperm parameters and there were no histopathological findings in the reproductive organs of either generation up to the highest dose tested (approx. 262 mg/kg/day and 302 mg/kg/day for males and females, respectively).

In the same study, an increased in the number of runts was observed in the mid and high dose groups of both generations on PN 1. Mean pup weights were decreased in the mid and high dose groups during the lactation period. No treatment related macroscopic alterations were observed at necropsy of the pups. Absolute spleen weight was decreased in F0 pups of the high dose group and in all treated F1 pups. Relative spleen weight was also decreased in high dose F1 pups. Based on the increased number of runts and decreased mean body weight observed in the mid and high dose groups, a NOAEL of 29 mg/kg bw/day is derived for developmental toxicity and this value is taken forward to risk characterisation.

4.1.3.2 Workers

The total number of persons occupationally exposed to V6 in the EU through the various exposure scenarios is unknown.

For the purpose of risk characterisation, it is assumed that inhalation and skin exposure are the main routes of exposure. Oral exposure is not considered to be a significant route of exposure under normal working practice.

Exposure levels used for the manufacture and use of V6 have been derived from measured data.

To make a comparison between exposure data and data from the toxicological studies for each end-point, body burdens have been calculated (inhalation, dermal and both combined) for workers for the worst-case and typical inhalation and dermal exposures for all of the identified exposure scenarios. The body burdens have been calculated assuming 6% dermal absorption in scenarios where exposure to "neat" V6 is expected and 12% dermal absorption is assumed for scenarios 3, 4 and 5, where there is exposure due to handling of foam containing V6.

Scenario 1: Manufacture of V6

With regard to the manufacture of V6, the reasonable worst-case (RWC) inhalation exposure is 30 $\mu g/m^3$. Using default values of a 70 kg worker inhaling 10 m^3 of air per 8-hour day and assuming 100% absorption, the inhalation body burden is 4.3 x 10^{-3} mg/kg. For dermal exposure in this scenario, the RWC exposure is 0.8 mg/cm^2/day. Using default values of a 70 kg worker with 210 cm^2 of exposed skin and assuming 6% absorption, the dermal body

burden is 0.144 mg/kg. Combining the two values gives a RWC total body burden of 0.148 mg/kg for this scenario.

The typical inhalation exposure for this scenario is 1 μg/m^3. Using the default values stated above, the inhalation body burden is 1.4 x 10^{-4} mg/kg. For dermal exposure in this scenario, the typical exposure is 0.2 mg/cm^2/day, leading to a dermal body burden of 3.6 x 10^{-2} mg/kg. Combining the two values gives a typical total body burden of 3.6 x 10^{-2} mg/kg.

Scenario 2a: Manufacture of flexible PUR foam: slabstock foams

Regarding the manufacture of flexible polyurethane foam (slabstock), the RWC inhalation exposure is 5.1 μg/m^3. Using default values of a 70 kg worker inhaling 10 m^3 of air per 8-hour day and assuming 100% absorption, the inhalation body burden is 7.3 x 10^{-4} mg/kg. For dermal exposure in this scenario, the RWC exposure is 7 x 10^{-2} mg/cm^2/day. Using default values of a 70 kg worker with 420 cm^2 of exposed skin and assuming 6% absorption, the dermal body burden is 2.5 x 10^{-2} mg/kg. Combining the two values gives a RWC total body burden of 2.6 x 10^{-2} mg/kg for this scenario.

The typical inhalation exposure for this scenario is 0.62 μg/m^3. Using the default values stated above, the inhalation body burden is 8.9 x 10^{-5} mg/kg. For dermal exposure in this scenario, the typical exposure is 2 x 10^{-3} mg/cm^2/day, leading to a dermal body burden of 7.2 x 10^{-4} mg/kg. Combining the two values gives a typical total body burden of 8.1 x 10^{-4} mg/kg.

Scenario 2b: Manufacture of flexible PUR foam: moulded foams

Regarding the manufacture of flexible polyurethane foam (moulded), the RWC inhalation exposure is 4.8 μg/m^3. Using the default values stated above in scenario 2a, the inhalation body burden is 6.9 x 10^{-4} mg/kg. For dermal exposure in this scenario, the RWC exposure is 7.5 x 10^{-2} mg/cm^2/day. Using default values above, the dermal body burden is 2.7 x 10^{-2} mg/kg. Combining the two values gives a RWC total body burden of 2.8 x 10^{-2} mg/kg for this scenario.

The typical inhalation exposure for this scenario is 0.63 μg/m^3, giving an inhalation body burden of 9 x 10^{-5} mg/kg. For dermal exposure in this scenario, the typical exposure is 1.5 x 10^{-3} mg/cm^2/day, leading to a dermal body burden of 5.4 x 10^{-4} mg/kg. Combining the two values gives a typical total body burden of 6.3 x 10^{-4} mg/kg.

Scenario 3: Cutting of flexible foam

With regard to the scenario of cutting flexible PUR foam, the RWC inhalation exposure is 4.1 μg/m^3. Using default values of a 70 kg worker inhaling 10 m^3 of air per 8-hour day and assuming 100% absorption, the inhalation body burden is 5.9 x 10^{-4} mg/kg. For dermal exposure in this scenario, the RWC exposure is 7.1 x 10^{-3} mg/cm^2/day. Using default values of a 70 kg worker with 420 cm^2 of exposed skin and assuming 12% absorption, the dermal body burden is 5.1 x 10^{-3} mg/kg. Combining the two values gives a RWC total body burden of 5.7 x 10^{-3} mg/kg for this scenario.

The typical inhalation exposure for this scenario is 1.9 μg/m^3. Using the default values stated above, the inhalation body burden is 2.7 x 10^{-4} mg/kg. For dermal exposure in this scenario, the typical exposure is 9.8 x 10^{-4} mg/cm^2/day, leading to a dermal body burden of 7.1 x 10^{-4} mg/kg. Combining the two values gives a typical total body burden of 9.8 x 10^{-4} mg/kg.

Scenario 4: Production of foam granules and rebonded PUR foam

Regarding the exposure scenario of the production of rebonded foam, the RWC inhalation exposure is 4.6 μg/m^3. Using default values of a 70 kg worker inhaling 10 m^3 of air per 8-hour day and assuming 100% absorption, the inhalation body burden is 6.6 x 10^{-4} mg/kg. RWC dermal exposure for handling the blocks of foam is 1.7 x 10^{-3} mg/cm^2/day. Using default values of a 70 kg worker with 420 cm^2 of exposed skin and assuming 12% absorption, the dermal body burden is 1.2 x 10^{-3} mg/kg. The combined RWC body burden is 1.9 x 10^{-3} mg/kg.

The typical inhalation exposure for this scenario is 0.59 μg/m^3, which gives a body burden of 8.4 x 10^{-5} mg/kg and the typical dermal exposure is 5.5 x 10^{-4} mg/cm^2/day, giving a dermal body burden of 4 x 10^{-4} mg/kg. This leads to a total typical body burden of 4.8 x 10^4 mg/kg.

Scenario 5: Manufacture of automotive parts

With regard to occupational exposure during the manufacture of automotive parts, the RWC inhalation exposure is 4.1 μg/m^3. Using default values of a 70 kg worker inhaling 10 m^3 of air per 8-hour day and assuming 100% absorption, the inhalation body burden is 5.9 x 10^{-4} mg/kg. For dermal exposure in this scenario, the RWC exposure is 7.1 x 10^{-3} mg/cm^2/day. Using default values of a 70 kg worker with 420 cm^2 of exposed skin and assuming 12% absorption, the dermal body burden is 5.1 x 10^{-3} mg/kg. Combining the two values gives a RWC total body burden of 5.7 x 10^{-3} mg/kg for this scenario.

The typical inhalation exposure for this scenario is 1.9 μg/m^3. Using the default values stated above, the inhalation body burden is 2.7 x 10^{-4} mg/kg. For dermal exposure in this scenario, the typical exposure is 9.8 x 10^{-4}mg/cm^2/day, leading to a dermal body burden of 7.1 x 10^{-4} mg/kg. Combining the two values gives a typical total body burden of 9.8 x 10^{-4} mg/kg.

Table 4.51 below summarises the inhalation, dermal and combined total body burdens for all V6 exposure scenarios.

Table 4.51 Summary of dermal and inhalation body burdens for all V6 exposure scenarios

Scenario	Inhalation body burden worst-case (mg/kg)	Dermal body burden worst-case (mg/kg)	Combined worst case body burden (mg/kg)	Inhalation body burden Typical case (mg/kg)	Dermal body burden typical case (mg/kg)	Combined typical case body burden (mg/kg)
1	4.3 x 10^{-3}	0.144	0.148	1.4 x 10^{-4}	3.6 x 10^{-2}	3.6 x 10^{-2}
2 (a)	7.3 x 10^{-4}	2.5 x 10^{-2}	2.6 x 10^{-2}	8.9 x 10^{-5}	7.2 x 10^{-4}	8.1 x 10^{-4}
2 (b)	6.9 x 10^{-4}	2.7 x 10^{-2}	2.8 x 10^{-2}	9 x 10^{-5}	5.4 x 10^{-4}	6.3 x 10^{-4}
3	5.9 x 10^{-4}	5.1 x 10^{-3}	5.7 x 10^{-3}	2.7 x 10^{-4}	7.1 x 10^{-4}	9.8 x 10^{-4}
4	6.6 x 10^{-4}	1.2 x 10^{-3}	1.9 x 10^{-3}	8.4 x 10^{-5}	4 x 10^{-4}	4.8 x 10^{-4}
5	5.9 x 10^{-4}	5.1 x 10^{-3}	5.7 x 10^{-3}	2.7 x 10^{-4}	7.1 x 10^{-4}	9.8 x 10^{-4}

The exposure scenarios referred to by number in the above table are:

1. Manufacture of V6
2. Manufacture of flexible PUR foam
    a. slabstock foam
    b. moulded foam

3. Cutting of flexible foam
4. Production of foam granules and rebonded PUR foam
5. Manufacture of automotive parts

4.1.3.2.1 Acute toxicity

Assessment of available data indicates that V6 has low acute toxicity by the oral, dermal and inhalation routes. V6 significantly decreased serum cholinesterase activity in rats following a single oral dose. However, this decrease in serum cholinesterase is not considered to be toxicologically significant. Therefore, there is no concern for acute toxicity and so **conclusion (ii)** is drawn for this end-point for all exposure scenarios.

4.1.3.2.2 Irritation and corrosivity

V6 is not a skin or eye irritant and is considered unlikely to be a respiratory irritant and therefore **conclusion (ii)** is drawn for this end-point, for all exposure scenarios.

4.1.3.2.3 Sensitisation

Based on available data, V6 is not considered to be a skin sensitiser. **Conclusion (ii)** is drawn for this end-point, for all exposure scenarios.

No data are available on the respiratory sensitisation potential of V6. There is currently no validated test method available to identify respiratory sensitisers. As V6 is produced in a closed system, and has a low vapour pressure, it is expected that exposure of the respiratory tract will be low. V6 is not suspected to be a respiratory sensitiser in humans as no specific cases of suspected respiratory sensitisation in the workplace have been reported. **Conclusion (ii)** is drawn for this end-point, for all exposure scenarios.

4.1.3.2.4 Repeated dose toxicity

In relation to repeated dose toxicity, a NOAEL of 15 mg/kg/day was derived from a 28-day study in rats. This NOAEL was based on increased liver weights with correlating histopathological changes. Assuming 100% absorption by the oral route, this leads to an internal body burden of 15 mg/kg/day.

In line with the draft TGD (2005), the minimal MOS for repeated dose toxicity is 100. This is established by taking into account an interspecies factor of 10 (4 for metabolic size differences * 2.5 for sensitivity differences) and intraspecies factor of 5. A factor of 2 has been employed to take account of sub-acute / sub-chronic to chronic exposure. The NOAEL is derived from a 28-day study. The target organs identified in the two-generation reproductive toxicity study were the same as those identified in the 28-day study. In addition, the doses at which the effects were observed and the severity of the effects were comparable between the two studies. Therefore, the NOAEL of 15 mg/kg bw/day can be considered to be relatively robust and an increase in duration of exposure (from sub-acute to sub-chronic) does not increase the severity of the effects seen.

For scenario 1, V6 manufacture, with respect to inhalation exposure, the body burden for reasonable worst case is 4.3×10^{-3} mg/kg. When this is compared with the internal body

burden of 15 mg/kg/day, the MOS value is 3,488. Regarding dermal exposure, the body burden for reasonable worst-case is 0.144 mg/kg, leading to a MOS of 104. The combined worst case body burden is 0.148 mg/kg, leading to a MOS of 101. The typical inhalation body burden is 1.4 x 10^{-4} mg/kg leading to MOSs of 107,143. The dermal and combined body burdens for this scenario are 3.6 x 10^{-2} mg/kg, leading to a MOS of 417 for both.

When the MOSs are compared to the minimal MOS of 100, there is no concern for this scenario. The MOSs for the reasonable worst case dermal and combined exposure (104 and 101, respectively) are close to the minimal MOS of 100. As discussed above, the NOAEL derived for this endpoint is considered to be robust. It is noted there was a ten-fold difference between the low and mid doses in the 28-day study. Therefore, it is likely also that the true NOAEL for this endpoint is higher than 15 mg/kg/day and this point is supported by the higher NOAEL of 29 mg/kg (the low dose) for parental toxicity, derived from the 2-generation study. In addition, an uncertainty factor has already been employed to take account of the duration of exposure. Therefore, this conclusion is valid and **conclusion (ii)** is drawn for this scenario.

Regarding scenario 2a, the manufacture of flexible slabstock foam, the body burden for reasonable worst-case inhalation exposure is 7.3 x 10^{-4} mg/kg. When this is compared with the internal body burden of 15 mg/kg/day, the MOS value is 20,548. The body burden for reasonable worst-case dermal exposure is 2.5 x 10^{-2} mg/kg and when compared with the internal body burden gives a MOS of 600. The combined body burden for reasonable worst-case exposure is 2.6 x 10^{-2} mg/kg, leading to a MOS of 577. The typical body burden for inhalation exposure is 8.9 x 10^{-5} mg/kg, which when compared to the internal body burden leads to a MOS of 168,539. The typical body burden for dermal exposure for this scenario is 7.2 x 10^{-4} mg/kg leading to a MOS of 20,833 and the combined typical body burden for this scenario is 8.1 x 10^{-4} mg/kg, leading to a MOS of 18,519.

When the MOSs are compared to the minimal MOS of 100, there is no concern for this scenario for inhalation, dermal or combined exposure. Therefore, **conclusion (ii)** is drawn for this scenario.

For scenario 2b, the manufacture of moulded foam, the body burden for reasonable worst-case inhalation exposure is 6.9 x 10^{-4} mg/kg. When this is compared to the internal body burden of 15 mg/kg/day, it leads to a MOS of 21,739. The body burden for reasonable worst-case dermal exposure is 2.7 x 10^{-2} mg/kg, leading to a MOS of 556. The combined body burden for reasonable worst-case exposure is 2.8 x 10^{-2} mg/kg, which when compared with the internal body burden results in a MOS of 536. The typical body burden for inhalation exposure is 9 x 10^{-5} mg/kg, leading to a MOS of 166,667. The typical body burden for dermal exposure for this scenario is 5.4 x 10^{-4} mg/kg, leading to a MOS of 27,778 and combined typical exposure for this scenario is 6.3 x 10^{-4} mg/kg, leading to a MOS of 23,810.

When the MOSs are compared to the minimal MOS of 100, there is no concern for this scenario. There is no concern for dermal, inhalation and combined exposure. Therefore, **conclusion (ii)** is drawn for this scenario.

Regarding scenario 3, the machine cutting of flexible PUR foam, the body burden for reasonable worst-case inhalation exposure is 5.9 x 10^{-4} mg/kg, which compared with the internal body burden gives a MOS of 25,424. The body burden for reasonable worst-case dermal exposure is 5.1 x 10^{-3} mg/kg. This gives a MOS of 2,941. The combined body burden for reasonable worst-case exposure is 5.7 x 10^{-3} mg/kg, leading to a MOS of 2,632. The typical body burden for inhalation exposure is 2.7 x 10^{-4} mg/kg, which when compared to the

internal body burden leads to a MOS of 55,556. The typical body burden for dermal exposure for this scenario is 7.1 x 10^{-4} mg/kg, resulting in a MOS of 21,127 and the combined typical exposure is 9.8 x 10^{-4} mg/kg, leading to a MOS of 15,306.

When the MOSs are compared to the minimal MOS of 100, there is no concern for this scenario, for dermal, inhalation or combined exposure. Therefore, **conclusion (ii)** is drawn.

Regarding scenario 4, the production of rebonded foam, with respect to inhalation exposure when handling foam during rebonding, the body burden for reasonable worst-case exposure is 6.6 x 10^{-4} mg/kg. When this is compared with the internal body burden the resulting MOS value is 22,727. The dermal body burden is 1.2 x 10^{-3} mg/kg, leading to a MOS of 12,500. The combined body burden is 1.9 x 10^{-3} mg/kg, resulting in a MOS of 7,895. The typical inhalation body burden is 8.4 x 10^{-5} mg/kg, leading to a MOS of 178,571. The typical dermal body burden is 4 x 10^{-4} mg/kg, leading to a MOS of 37,500. The total combined body burden for the typical exposure is 4.8 x 10^{-4} leading to a MOSs of 31,250.

When the MOSs are compared to the minimal MOS of 100, there is no concern for this scenario. There is no concern for dermal, inhalation and combined exposure. Therefore, **conclusion (ii)** is drawn.

For scenario 5, the manufacture of automotive parts, the body burden for reasonable worst-case inhalation exposure is 5.9 x 10^{-4} mg/kg. This, when compared with the internal body burden of 15 mg/kg/day, gives a MOS value of 25,424. With respect to dermal exposure, the body burden for reasonable worst-case exposure is 5.1 x 10^{-3} mg/kg, leading to a MOS of 2,941. The total body burden for reasonable worst-case for this scenario is 5.7 x 10^{-3} mg/kg, resulting in a MOS of 2,632. For this scenario, the typical inhalation body burden is 2.7 x 10^{-4} mg/kg. This gives a MOS value of 55,556. For dermal exposure, the typical body burden is 7.1 x 10^{-4} mg/kg, leading to a MOS of 21,127. The total typical body burden is 9.8 x 10^{-4} mg/kg, which gives a MOS of 15,306.

When the MOSs are compared to the minimal MOS of 100, there is no concern for this scenario for inhalation, dermal or combined exposure. Therefore, **conclusion (ii)** is drawn for this scenario.

Tables 4.52 and **4.53** below summarise the MOS values and the conclusions for repeat dose toxicity for the realistic worst case and typical exposure scenarios, respectively.

Table 4.52 MOS values and conclusions for repeated dose toxicity of V6 – Reasonable worst case exposure

Minimal MOS :100									
Scenario	**Inhalation**			**Dermal**			**Combined**		
	Body burden (mg/kg)	**MOS**	**Concl.**	**Body burden (mg/kg)**	**MOS**	**Concl**	**Body burden (mg/kg)**	**MOS**	**Concl**
1.Manufacture of V6	4.3×10^{-3}	3,488	(ii)	0.144	104	(ii)	0.148	101	(ii)
2a.Manufacture of flexible PUR foam: Slabstock	7.3×10^{-4}	20,548	(ii)	2.5×10^{-2}	600	(ii)	2.6×10^{-2}	577	(ii)
2b.Manufacture of flexible PUR foam: Moulded	6.9×10^{-4}	21,739	(ii)	2.7×10^{-2}	556	(ii)	2.8×10^{-2}	536	(ii)
3.Cutting of flexible PUR foam	5.9×10^{-4}	25,424	(ii)	5.1×10^{-3}	2,941	(ii)	5.7×10^{-3}	2,632	(ii)
4.Production of foam granules & rebonded foam	6.6×10^{-4}	22,727	(ii)	1.2×10^{-3}	12,500	(ii)	1.9×10^{-3}	7,895	(ii)
5.Manufacture of automotive parts	5.9×10^{-4}	25,424	(ii)	5.1×10^{-3}	2,941	(ii)	5.7×10^{-3}	2,632	(ii)

Table 4.53 MOS values and conclusions for repeated dose toxicity of V6 – Typical exposure

Minimal MOS : 100									
Scenario	**Inhalation**			**Dermal**			**Combined**		
	Body burden (mg//kg)	**MOS**	**Concl.**	**Body burden (mg/kg)**	**MOS**	**Concl**	**Body burden (mg/kg)**	**MOS**	**Concl**
1.Manufacture of V6	1.4×10^{-4}	107,143	(ii)	3.6×10^{-2}	417	(ii)	3.6×10^{-2}	417	(ii)
2a.Manufacture of flexible PUR foam: Slabstock	8.9×10^{-5}	168,539	(ii)	7.2×10^{-4}	20,833	(ii)	8.1×10^{-4}	18,519	(ii)
2b.Manufacture of flexible PUR foam: Moulded	9×10^{-5}	166,667	(ii)	5.4×10^{-4}	27,778	(ii)	6.3×10^{-4}	23,810	(ii)
3.Cutting of flexible PUR foam	2.7×10^{-4}	55,556	(ii)	7.1×10^{-4}	21,127	(ii)	9.8×10^{-4}	15,306	(ii)
4. Production of foam granules & rebonded foam	8.4×10^{-5}	178,571	(ii)	4×10^{-4}	37,500	(ii)	4.8×10^{-4}	31,250	(ii)
5.Manufacture of automotive parts	2.7×10^{-4}	55,556	(ii)	7.1×10^{-4}	21,127	(ii)	9.8×10^{-4}	15,306	(ii)

4.1.3.2.5 Mutagenicity

V6 showed no evidence of mutagenicity, either *in vitro* or *in vivo*. Therefore, **conclusion (ii)** is drawn for this end-point, for all exposure scenarios.

4.1.3.2.6 Carcinogenicity

There are no carcinogenicity data for V6. No evidence of mutagenicity was observed in either *in vitro* or *in vivo* genotoxicity studies with V6 and there were no indications of concerns for carcinogenicity from repeated dose toxicity studies. Therefore, **conclusion (ii)** is drawn for this end-point, for all exposure scenarios.

4.1.3.2.7 Toxicity for reproduction

Effects on fertility

No effects were observed on the male or female reproductive systems in the two-generation reproductive toxicity study. Therefore, there is no concern for fertility and **conclusion (ii)** is drawn for this endpoint for all exposure scenarios.

Developmental toxicity

In a two-generation reproductive toxicity study in rats with V6, a NOAEL of 29 mg/kg bw/day is derived for developmental toxicity. This is based on a treatment related increase in the number of runts and a decrease in pup body weight observed in mid and high dose groups. Assuming 100% absorption by the oral route, this leads to an internal body burden of 29 mg/kg/day.

In line with the draft TGD (2005), the minimal MOS for developmental toxicity is 50. This is established by taking into account an interspecies factor of 10 (4 for metabolic size differences * 2.5 for sensitivity differences) and intraspecies factor of 5.

For scenario 1, manufacture of V6, with respect to inhalation exposure, the body burden for the reasonable worst case exposure is 4.3×10^{-3} mg/kg. When this is compared with the internal body burden of 29 mg/kg/day, the MOS value is 6,744. The body burden for the reasonable worst case dermal exposure is 0.144 mg/kg, leading to a MOS of 201. The body burden for the combined exposure is 0.148 mg/kg, resulting in a MOS of 196. For the typical exposure, the inhalation body burden is 1.4×10^{-4} mg/kg, leading to a MOS of 207,143. The body burdens for the typical dermal and combined exposures are 3.6×10^{-2} mg/kg, leading to a MOS of 806 for both.

When the MOS are compared with the minimal MOS of 50, there is no concern for this scenario. Therefore, **conclusion (ii)** is drawn for this scenario.

Regarding scenario 2a, the manufacture of flexible slabstock foam, the body burden for the reasonable worst case inhalation exposure is 7.3×10^{-4} mg/kg, which results in a MOS of 39,726. For the reasonable worst case dermal exposure, the body burden is 2.5×10^{-2} mg/kg and when this is compared with the internal body burden, results in a MOS of 1,160. The body burden for the combined exposure is 2.6×10^{-2} mg/kg, leading to a MOS of 1,115. For the typical exposures for this scenario, the inhalation body burden is 8.9×10^{-5} mg/kg, resulting in a MOS of 325,843. The typical dermal body burden is 7.2×10^{-4} mg/kg, leading to

a MOS of 40,278. The body burden for the typical combined exposure is 8.1 x 10^{-4} mg/kg, resulting in a MOS of 35,802.

When the MOS are compared with the minimal MOS of 50, there is no concern for this scenario. Therefore, **conclusion (ii)** is drawn for this scenario.

For scenario 2b, the manufacture of moulded foam, the body burden for the reasonable worst case inhalation exposure is 6.9 x 10^{-4} mg/kg. When this is compared with the internal body burden of 29 mg/kg, the MOS is 42,029. The body burden for the reasonable worst case dermal exposure is 2.7 x 10^{-2} mg/kg, leading to a MOS of 1,074. The body burden for the combined reasonable worse case exposure is 2.8 x 10^{-2} mg/kg, resulting in a MOS of 1,036. For the typical exposure, the inhalation body burden is 9 x 10^{-5} mg/kg, which when compared with the internal body burden results in a MOS of 322,222. The body burden for the dermal exposure is 5.4 x 10^{-4} mg/kg, giving an MOS of 53,704. For the typical combined exposure, the body burden is 6.3 x 10^{-4} mg/kg, which results in a MOS of 46,032.

When the MOS are compared with the minimal MOS of 50, there is no concern for this scenario. Therefore, **conclusion (ii)** is drawn.

For scenario 3, the machine cutting of flexible PUR foam, with respect to the reasonable worst case exposure, the inhalation body burden is 5.9 x 10^{-4} mg/kg. When this is compared with the internal body burden, the resulting MOS is 49,153. The dermal body burden is 5.1 x 10^{-3} mg/kg. This gives a MOS of 5,686. The body burden for the combined reasonable worst case exposure is 5.7 x 10^{-3} mg/kg, leading to a MOS of 5,088. For the typical exposures, the inhalation body burden is 2.7 x 10^{-4} mg/kg, resulting in a MOS of 107,407. The dermal body burden is 7.1 x 10^{-4} mg/kg, giving a MOS of 40,845. The typical combined body burden is 9.8 x 10^{-4} mg/kg, leading to a MOS of 29,592.

When the MOS are compared with the minimal MOS of 50, there is no concern. Therefore, **conclusion (ii)** is drawn for this scenario.

For scenario 4, the production of rebonded foam, the body burden for the reasonable worst case inhalation exposure is 6.6 x 10^{-4} mg/kg, which when compared with the internal body burden of 29 mg/kg results in a MOS of 43,939. The reasonable worst case dermal body burden is 1.2 x 10^{-3} mg/kg, leading to a MOS of 24,167. The combined body burden is 1.9 x 10^{-3} mg/kg, resulting in MOS of 15,263. With respect to the typical exposure, the inhalation body burden is 8.4 x 10^{-5}mg/kg. This gives a MOS of 345,238.The body burden for the typical dermal exposure is 4 x 10^{-4} mg/kg, leading to a MOS of 72,500. The typical combined body burden is 4.8 x 10^{-4} mg/kg, which results in a MOS of 60,417.

When the MOS are compared with the minimal MOS of 50, there is no concern for this scenario and therefore **conclusion (ii)** is drawn.

For scenario 5, the manufacture of automotive parts, the reasonable worst case body burden for the inhalation exposure is 5.9 x 10^{-4} mg/kg, resulting in a MOS of 49,153. The reasonable worst case dermal body burden is 5.1 x 10^{-3} mg/kg, which when compared with the internal body burden results in a MOS of 5,686. The body burden for the combined reasonable worst case exposure is 5.7 x 10^{-3} mg/kg, leading to a MOS of 5,088. For the typical exposure, the inhalation body burden is 2.7 x 10^{-4} mg/kg, resulting in a MOS of 107,407. The dermal body burden is 7.1 x 10^{-4} mg/kg. This gives a MOS of 40,845. The typical combined exposure body burden is 9.8 x 10^{-4} mg/kg, resulting in a MOS of 29,592.

Tables 4.54 and **4.55** below summarise the MOS values and the conclusions for developmental toxicity for the realistic worst case and typical exposure scenarios, respectively.

Table 4.54 MOS values and conclusions for developmental toxicity for V6 – Reasonable worst case exposure

Minimal MOS :50									
Scenario	**Inhalation**			**Dermal**			**Combined**		
	Body burden (mg/kg)	**MOS**	**Concl.**	**Body burden (mg/kg)**	**MOS**	**Concl**	**Body burden (mg/kg)**	**MOS**	**Concl**
1.Manufacture of V6	4.3×10^{-3}	6,744	(ii)	0.144	201	(ii)	0.148	196	(ii)
2a.Manufacture of flexible PUR foam: Slabstock	7.3×10^{-4}	39,726	(ii)	2.5×10^{-2}	1,160	(ii)	2.6×10^{-2}	1,115	(ii)
2b.Manufacture of flexible PUR foam: Moulded	6.9×10^{-4}	42,029	(ii)	2.7×10^{-2}	1,074	(ii)	2.8×10^{-2}	1,036	(ii)
3.Cutting of flexible PUR foam	5.9×10^{-4}	49,153	(ii)	5.1×10^{-3}	5,686	(ii)	5.7×10^{-3}	5,088	(ii)
4.Production of foam granules & rebonded foam	6.6×10^{-4}	43,939	(ii)	1.2×10^{-3}	24,167	(ii)	1.9×10^{-3}	15,263	(ii)
5.Manufacture of automotive parts	5.9×10^{-4}	49,153	(ii)	5.1×10^{-3}	5,686	(ii)	5.7×10^{-3}	5,088	(ii)

Table 4.55 MOS values and conclusions for developmental toxicity for V6 – Typical exposure

Minimal MOS : 50									
Scenario	**Inhalation**			**Dermal**			**Combined**		
	Body burden (mg/kg)	**MOS**	**Concl.**	**Body burden (mg/kg)**	**MOS**	**Concl**	**Body burden (mg/kg)**	**MOS**	**Concl**
1.Manufacture of V6	1.4×10^{-4}	207,143	(ii)	3.6×10^{-2}	806	(ii)	3.6×10^{-2}	806	(ii)
2a.Manufacture of flexible PUR foam: Slabstock	8.9×10^{-5}	325,843	(ii)	7.2×10^{-4}	40,278	(ii)	8.1×10^{-4}	35,802	(ii)
2b.Manufacture of flexible PUR foam: Moulded	9×10^{-5}	322,222	(ii)	5.4×10^{-4}	53,704	(ii)	6.3×10^{-4}	46,032	(ii)
3.Cutting of flexible PUR foam	2.7×10^{-4}	107,407	(ii)	7.1×10^{-4}	40,845	(ii)	9.8×10^{-4}	29,592	(ii)
4. Production of foam granules & rebonded foam	8.4×10^{-5}	345,238	(ii)	4×10^{-4}	72,500	(ii)	4.8×10^{-4}	60,417	(ii)
5.Manufacture of automotive parts	2.7×10^{-4}	107,407	(ii)	7.1×10^{-4}	40,845	(ii)	9.8×10^{-4}	29,592	(ii)

4.1.3.2.8 Summary of risk characterisation for workers

Conclusion (ii) is drawn for all worker exposure scenarios in relation to all toxicological endpoints.

4.1.3.3 Consumers

The current use pattern provided by industry indicates that most of the V6 produced in the EU is used in the production of flexible PUR foam. Most of the V6 used in flexible foam is for the automotive industry, with some used in furniture. Consumers do not come in direct contact with these foams. The foam is only used in ways in which it is enclosed and therefore it is concluded that exposure to consumers is negligible.

For exposure to V6 due to its release from flexible PUR foam, the end-points of concern are repeated dose toxicity, mutagenicity, carcinogenicity and reproductive toxicity.

Ageing studies that have been carried out have indicated that flame retardants are retained within PUR foam. Therefore, consumer exposure to flame retardants from these foams is expected to be very low. From the chamber tests that were performed on two other flame retardants, TCPP and TDCP, a RWC inhalation exposure value of 3.8 μg/m^3 24 hour TWA is used for risk characterisation. This is to allow for people, particularly elderly people, who spend a large proportion of their time indoors in a room with PU foam-containing furniture. A typical exposure value of 2.8 μg/m^3 is used for risk characterisation, on the basis of a consumer spending 18 out of 24 hours in rooms where there is PU foam-containing furniture. A RWC dermal body burden is taken as 0.0011 mg/kg. A value for RWC oral ingestion for children of 0.2 μg/kg/day, assuming a bodyweight of 9.1 kg is taken forward (taken from BAUA, 2006).

It is worth noting that the work ongoing to monitor the release of fire retardant from foam over years rather than hours, seems to indicate that the loss of fire retardant is negligible, in which case exposure would be negligible. The values taken forward for risk characterisation may therefore be an over-estimate.

The reasonable worst-case inhalation exposure is 3.8 μg/m^3. Using default values of a 70 kg person inhaling 20 m^3 of air per 24-hour day and assuming 100% absorption, the inhalation body burden is 1 μg/kg. The typical exposure of 2.8 μg/m^3 leads to an inhalation body burden of 0.6 μg/kg, assuming a 70 kg person inhales 0.75 x 20 m^3 in 18 hours.

4.1.3.3.1 Acute toxicity

As with the worker section above, **conclusion (ii)** is drawn for consumers in relation to acute toxicity.

4.1.3.3.2 Irritation and corrosivity

V6 is not a skin or eye irritant and is considered unlikely to be a respiratory irritant and therefore **conclusion (ii)** is drawn for this endpoint.

4.1.3.3.3 Repeated dose toxicity

In relation to repeated dose toxicity, a NOAEL of 15 mg/kg/day is derived from a 28-day study in rats. This NOAEL is based on increased liver weights with correlating histopathological changes. Assuming 100% absorption by the oral route, this leads to an internal body burden of 15 mg/kg/day.

In line with the draft TGD (2005), the minimal MOS for repeated dose toxicity for consumers is 200. This is established by taking into account an interspecies factor of 10 (4 for metabolic size differences * 2.5 for sensitivity differences), an intraspecies factor of 10. As discussed in section 4.1.3.2.4, a factor of 2 is employed to take account of duration of exposure.

Regarding potential inhalation exposure to V6 due to its release from flexible PUR foam, the body burden for reasonable worst-case exposure is 1 μg/kg. This gives a MOS value of 15,000. It is concluded that this MOS is sufficient and there are no concerns for repeated dose toxicity to consumers for this scenario and so **conclusion (ii)** is drawn

Regarding potential dermal exposure due to the release of V6 from flexible PUR foam, the reasonable worst-case body burden is taken as 0.0011 mg/kg, leading to a MOS of 13,636. Given this MOS, a **conclusion (ii)** can be drawn for dermal exposure for consumers for this scenario.

For children, the oral route is also considered. A RWC oral ingestion of 0.2 μg/kg (assuming a body weight of 9.1 kg) has been taken from the TCEP risk assessment report. When this is compared to the internal body burden of 15 mg/kg, taken from the repeated dose toxicity study, then an MOS of 75,000 results. When compared to the minimal MOS of 200, it is considered that this MOS is sufficient. There is no concern for exposure of children via the oral route i.e. **conclusion (ii).**

4.1.3.3.4 Mutagenicity

As with the workers section above, **conclusion (ii)** is drawn for mutagenicity for consumers.

4.1.3.3.5 Carcinogenicity

There are no carcinogenicity data for V6. No evidence of mutagenicity was observed in either *in vitro* or *in vivo* genotoxicity studies with V6 and there were no indications of concerns for carcinogenicity from repeated dose toxicity studies. Therefore, **conclusion (ii)** is drawn for this end-point, for all exposure scenarios.

4.1.3.3.6 Toxicity for reproduction

Effects on fertility

No effects were observed on the male or female reproductive systems in the two-generation reproductive toxicity study. Therefore, there is no concern for fertility and **conclusion (ii)** is drawn.

Developmental toxicity

A NOAEL of 29 mg/kg bw/day is derived for developmental toxicity. This is based on a treatment related increase in the number of runts and a decrease in pup body weight observed at the mid and high dose groups. Assuming 100% absorption by the oral route, this leads to an internal body burden of 29 mg/kg/day.

In line with the draft TGD (2005), the minimal MOS for developmental toxicity is 100. This is established by taking into account an interspecies factor of 10 (4 for metabolic size differences * 2.5 for sensitivity differences) and intraspecies factor of 10.

Regarding potential inhalation exposure to V6 due to its release from flexible PUR foam, the body burden for reasonable worst-case exposure is 1 μg/kg. When this is compared with the internal body burden, the MOS is 29,000. It is concluded that this MOS is sufficient and so **conclusion (ii)** is drawn.

Regarding potential dermal exposure due to the release of V6 from flexible PUR foam, the reasonable worst-case body burden is taken as 0.0011 mg/kg, which leads to a MOS of 26,364. A **conclusion (ii)** can be drawn for dermal exposure for consumers for this scenario.

For children, the oral route is also considered. A reasonable worst case oral ingestion of 0.2 μg/kg (assuming a body weight of 9.1 kg) has been taken from the TCEP risk assessment report. When this is compared to the internal body burden, the MOS is 145,000. It is considered that this MOS is sufficient and a. **conclusion (ii)** is drawn.

4.1.3.3.7 Summary of risk characterisation for consumers

Conclusion (ii) is drawn for consumers for all exposure scenarios. This conclusion applies to all endpoints.

4.1.3.4 Humans exposed via the environment

4.1.3.4.1 Regional exposure

Repeated dose toxicity

In relation to repeated dose toxicity, a NOAEL of 15 mg/kg/day is derived from a 28-day study. This NOAEL is based on increased liver weights with correlating histopathological changes. Assuming 100% absorption by the oral route, this leads to an internal body burden of 15 mg/kg/day.

In line with the draft TGD (2005), the minimal MOS for repeated dose toxicity is 200. This is established by taking into account an interspecies factor of 10 (4 for metabolic size differences * 2.5 for sensitivity differences), an intraspecies factor of 10. As discussed in section 4.1.3.2.4, a factor of 2 is employed to take account of duration of exposure.

From section 4.1.1.3, the total daily human exposure to V6 from regional sources is 3.9×10^{-6} mg/kg/day. Comparing this to an internal body burden of 15 mg/kg leads to a MOS of 3,846,154. There is a sufficient margin of safety and therefore, **conclusion (ii)** is drawn.

Mutagenicity

As with the previous sections, **conclusion (ii)** is drawn for mutagenicity for man exposed via regional exposure.

Carcinogenicity

There are no carcinogenicity data for V6. No evidence of mutagenicity was observed in either *in vitro* or *in vivo* genotoxicity studies with V6 and there were no indications of concerns for carcinogenicity from repeated dose toxicity studies. Therefore, **conclusion (ii)** is drawn for this end-point, for all exposure scenarios.

Reproductive toxicity

Effects on fertility

No effects were observed on the male or female reproductive systems in the two-generation reproductive toxicity study. Therefore, there is no concern for fertility and **conclusion (ii)** is drawn.

Developmental toxicity

In relation to developmental toxicity, a NOAEL of 29 mg/kg/day is derived from a two-generation reproductive toxicity study with V6. Assuming 100% absorption by the oral route, this leads to an internal body burden of 29 mg/kg/day.

In line with the draft TGD (2005), the minimal MOS for developmental toxicity is 100. This is established by taking into account an interspecies factor of 10 (4 for metabolic size differences * 2.5 for sensitivity differences) and intraspecies factor of 10.

The total daily human exposure to V6 from regional sources is 3.9×10^{-6} mg/kg/day. When this is compared with the internal body burden it results in a MOS of 7,435,897. There is a sufficient margin of safety and therefore, **conclusion (ii**) is drawn.

4.1.3.4.2 Local exposure

Repeated dose toxicity

In relation to repeated dose toxicity, a NOAEL of 15 mg/kg/day is derived from a 28-day study. This NOAEL is based on increased liver weights with correlating histopathological changes. Assuming 100% absorption by the oral route, this leads to an internal body burden of 15 mg/kg/day.

In line with the draft TGD (2005), the minimal MOS for repeated dose toxicity is 200. This is established by taking into account an interspecies factor of 10 (4 for metabolic size differences * 2.5 for sensitivity differences), an intraspecies factor of 10. As discussed in section 4.1.3.2.4, a factor of 2 is employed to take account of duration of exposure.

From section 4.1.1.3., the total daily human exposure to V6 from local sources is 17.9×10^{-3} mg/kg/day. Comparing this to an internal body burden of 15 mg/kg leads to a MOS of 838. There is a sufficient margin of safety and so **conclusion (ii)** is drawn.

Mutagenicity

As with the previous sections, **conclusion (ii)** is drawn for mutagenicity for man exposed via local exposure.

Carcinogenicity

There are no carcinogenicity data for V6. No evidence of mutagenicity was observed in either *in vitro* or *in vivo* genotoxicity studies with V6 and there were no indications of concerns for carcinogenicity from repeated dose toxicity studies. Therefore, **conclusion (ii)** is drawn for this end-point, for all exposure scenarios.

Reproductive toxicity

Effects on fertility

No effects were observed on the male or female reproductive systems in the two-generation reproductive toxicity study. Therefore, there is no concern for fertility and **conclusion (ii)** is drawn.

Developmental toxicity

In relation to developmental toxicity, a NOAEL of 29 mg/kg/day is derived from a two-generation reproductive toxicity study with V6. Assuming 100% absorption by the oral route, this leads to an internal body burden of 29 mg/kg/day.

In line with the draft TGD (2005), the minimal MOS for developmental toxicity is 100. This is established by taking into account an interspecies factor of 10 (4 for metabolic size differences * 2.5 for sensitivity differences) and intraspecies factor of 10.

The total daily human exposure to V6 from local sources is 17.9×10^{-3} mg/kg/day. When this is compared with the internal body burden of 29 mg/kg it results in a MOS of 1,620. It is considered that there is a sufficient margin of safety and so **conclusion (ii)** is drawn.

4.1.3.4.3 Summary of risk characterisation for exposure via the environment

Conclusion (ii) is drawn for both regional and local exposures for all endpoints.

4.1.3.5 Combined exposure

The combined exposure to V6 is the sum of all the specific sources (occupational exposure, consumer exposure and indirect exposure via the environment) and by all routes of exposure (oral, dermal and inhalation). Therefore, a worst case estimate for this combined exposure would be the sum of the reasonable worst case estimates, for inhalation and dermal exposures, for the three populations, i.e. workers, consumers and man exposed via the environment.

Consumers may be exposed to V6 indirectly from flexible foam used in upholstery and bedding. Exposure is also possible indirectly *via* environmental sources. In calculating the combined exposures, the RWC exposures have been used, and these are presented in **Table 4.56**, below.

Table 4.56 Combined regional and local exposure to TDCP (excluding occupational exposure)

Source of exposure	Exposure	Body burdens (mg/kg/day)
Consumer		
Release of TCPP from flexible polyurethane foam		
Inhalation	0.0038 mg/m^3	0.001
Dermal	0.0011 mg/kg	0.0011
Man via the environment		
Local exposure	1.79 x 10^{-2} mg/kg/day*	1.79 x 10^{-2}
Regional exposure	3.9 x 10^{-6} mg/kg/day	3.9 x 10^{-6}
Combined exposures		
Local		2 x 10^{-2}
Regional		2.1 x 10^{-3}

*Highest exposure scenario for local exposure (Confidential Use: F2)

As discussed in section 4.1.1.4, occupational exposures are not included in the combined exposure calculation. As can be seen from **Table 4.51** in section 4.1.3.2 the body burdens for the reasonable worst case and typical occupational exposures are significantly higher than those for consumers or for indirect exposure via the environment. Therefore, the occupational exposure value would dominate the combined exposure estimate, resulting in **conclusion (iii)**'s being drawn. It is therefore considered more appropriate to exclude occupational exposure from the combined exposure risk characterisation.

Repeated dose toxicity

In relation to repeated dose toxicity, a NOAEL of 15 mg/kg/day is derived from a 28-day study. This NOAEL is based on increased liver weights with correlating histopathological changes. Assuming 100% absorption by the oral route, this leads to an internal body burden of 15 mg/kg/day.

In line with the draft TGD (2005), the minimal MOS for repeated dose toxicity is 200. This is established by taking into account an interspecies factor of 10 (4 for metabolic size differences * 2.5 for sensitivity differences), an intraspecies factor of 10. As discussed in section 4.1.3.2.4, a factor of 2 is employed to take account of duration of exposure.

The body burden for the combined local exposure is 2 x 10^{-2} mg/kg. When this is compared with the internal body burden, the resulting MOS is 750. The MOS is considered to be sufficient and so **conclusion (ii)** is drawn.

For the combined regional exposure, the body burden is 2.1 x 10^{-3} mg/kg. Comparing this with the internal body burden, results in a MOS of 7,143. There is no concern for regional exposure and so **conclusion (ii)** is drawn.

Mutagenicity

As with the previous sections, **conclusion (ii)** is drawn for the combined exposures in relation to mutagenicity.

Carcinogenicity

There are no carcinogenicity data for V6. However, V6 showed no evidence of mutagenicity in either *in vitro* or *in vivo* genotoxicity studies and there are no indications of concerns for carcinogenicity from repeated dose toxicity studies. Therefore, **conclusion (ii)** is drawn for this end-point.

Reproductive toxicity

Effects on fertility

No effects were observed on the male or female reproductive systems in the two-generation reproductive toxicity study. Therefore, there is no concern for fertility and **conclusion (ii)** is drawn.

Developmental toxicity

In relation to developmental toxicity, a NOAEL of 29 mg/kg/day is derived from a two-generation reproductive toxicity study with V6. Assuming 100% absorption by the oral route, this leads to an internal body burden of 29 mg/kg/day.

In line with the draft TGD (2005), the minimal MOS for developmental toxicity is 100. This is established by taking into account an interspecies factor of 10 (4 for metabolic size differences * 2.5 for sensitivity differences) and intraspecies factor of 10.

The body burden for the combined local exposure is 2×10^{-2} mg/kg, which when compared with the internal body burden of 29 mg/kg results in a MOS of 1,450. The margin of safety is sufficient and so **conclusion (ii)** is drawn.

With respect to the combined regional exposure, the body burden is 2.1×10^{-3} mg/kg, which leads to a MOS of 13,809. There is no concern for regional exposure and so **conclusion (ii)** is drawn.

Summary of risk characterisation for the combined exposure

Conclusion (ii) is drawn for the combined exposure for all endpoints.

4.2 HUMAN HEALTH (PHYSICO-CHEMICAL PROPERTIES)

4.2.1 Exposure assessment

Exposure potentially occurs in the workplace during the manufacture of V6 and during the manufacture of PUR foam containing V6.

4.2.2 Effects assessment: Hazard identification

4.2.2.1 Explosivity

Explosive properties have not been tested. Based on its chemical structure and the known synthetic route of manufacture via an exothermic chemical reaction, there is no indication that the substance is thermodynamically unstable. The substance does not contain any of the more commonly known endothermic groups such as azides, cyano-, dienes, peroxide or chlorate. Therefore, the substance is not expected to possess explosive properties.

4.2.2.2 Flammability

Based on the known chemical and physical properties of V6 and its chemical structure, it is not expected to produce flammable gases in contact with water or damp air.

4.2.2.3 Oxidizing potential

Oxidising properties have not been tested. By reference to the structural formula, it can be seen that V6 contains highly electronegative atoms of chlorine; however, the fact that these elements are only bonded to carbon and/or hydrogen renders it unlikely that this will confer oxidising properties on the substance.

4.2.3 Risk characterisation

V6 gives no reason for concern to human health in relation to its physico-chemical properties. There is no need for further information and/or testing (**conclusion (ii)**).

5 RESULTS [17]

5.1 INTRODUCTION

The conclusions from the risk characterisation processes are brought together and summarised below.

5.2 ENVIRONMENT

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all compartments for all local life cycle stages, and at the regional scale in all compartments.

V6 does not meet all of the PBT criteria (it meets the screening criteria for P or vP).

5.3 HUMAN HEALTH

5.3.1 Human health (toxicity)

5.3.1.1 Workers

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all worker exposure scenarios in relation to all toxicological endpoints.

5.3.1.2 Consumers

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all consumer exposure scenarios in relation to all toxicological endpoints.

[17] Conclusion (i) There is a need for further information and/or testing.
Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.
Conclusion (iii) There is a need for limiting the risks; risk reduction measures which are already being applied shall be taken into account.

5.3.1.3 Humans exposed via the environment

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to both regional and local exposures in relation to all toxicological endpoints.

5.3.1.4 Combined exposure

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to combined exposure in relation to all toxicological endpoints.

5.3.2 Human health (risks from physico-chemical properties)

Conclusion (ii) There is at present no need for further information and/or testing and no need for risk reduction measures beyond those which are being applied already.

Conclusion (ii) applies to all endpoints.

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ABBREVIATIONS

ADI	Acceptable Daily Intake
AF	Assessment Factor
ASTM	American Society for Testing and Materials
ATP	Adaptation to Technical Progress
AUC	Area Under The Curve
B	Bioaccumulation
BBA	Biologische Bundesanstalt für Land- und Forstwirtschaft
BCF	Bioconcentration Factor
BMC	Benchmark Concentration
BMD	Benchmark Dose
BMF	Biomagnification Factor
bw	body weight / *Bw*, *b.w.*
C	Corrosive (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
CA	Chromosome Aberration
CA	Competent Authority
CAS	Chemical Abstract Services
CEC	Commission of the European Communities
CEN	European Standards Organisation / European Committee for Normalisation
CMR	Carcinogenic, Mutagenic and toxic to Reproduction
CNS	Central Nervous System
COD	Chemical Oxygen Demand
CSTEE	Scientific Committee for Toxicity, Ecotoxicity and the Environment (DG SANCO)
CT_{50}	Clearance Time, elimination or depuration expressed as half-life
d.wt	dry weight / dw
dfi	daily food intake
DG	Directorate General
DIN	Deutsche Industrie Norm (German norm)
DNA	DeoxyriboNucleic Acid
DOC	Dissolved Organic Carbon
DT50	Degradation half-life or period required for 50 percent dissipation / degradation
DT90	Period required for 50 percent dissipation / degradation
E	Explosive (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
EASE	Estimation and Assessment of Substance Exposure Physico-chemical properties [Model]
EbC50	Effect Concentration measured as 50% reduction in biomass growth in algae tests

EC	European Communities
EC10	Effect Concentration measured as 10% effect
EC50	median Effect Concentration
ECB	European Chemicals Bureau
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
ECVAM	European Centre for the Validation of Alternative Methods
EDC	Endocrine Disrupting Chemical
EEC	European Economic Communities
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EN	European Norm
EPA	Environmental Protection Agency (USA)
ErC50	Effect Concentration measured as 50% reduction in growth rate in algae tests
ESD	Emission Scenario Document
EU	European Union
EUSES	European Union System for the Evaluation of Substances [software tool in support of the Technical Guidance Document on risk assessment]
F(+)	(Highly) flammable (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
FAO	Food and Agriculture Organisation of the United Nations
FELS	Fish Early Life Stage
FR	Flame retardant
GLP	Good Laboratory Practice
HEDSET	EC/OECD Harmonised Electronic Data Set (for data collection of existing substances)
HELCOM	Helsinki Commission -Baltic Marine Environment Protection Commission
HPLC	High Pressure Liquid Chromatography
HPVC	High Production Volume Chemical (> 1000 t/a)
IARC	International Agency for Research on Cancer
IC	Industrial Category
IC50	median Immobilisation Concentration or median Inhibitory Concentration
ILO	International Labour Organisation
IPCS	International Programme on Chemical Safety
ISO	International Organisation for Standardisation
IUCLID	International Uniform Chemical Information Database (existing substances)
IUPAC	International Union for Pure and Applied Chemistry
JEFCA	Joint FAO/WHO Expert Committee on Food Additives
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
Koc	organic carbon normalised distribution coefficient

Kow	octanol/water partition coefficient
Kp	solids-water partition coefficient
L(E)C50	median Lethal (Effect) Concentration
LAEL	Lowest Adverse Effect Level
LC50	median Lethal Concentration
LD50	median Lethal Dose
LEV	Local Exhaust Ventilation
LLNA	Local Lymph Node Assay
LOAEL	Lowest Observed Adverse Effect Level
LOEC	Lowest Observed Effect Concentration
LOED	Lowest Observed Effect Dose
LOEL	Lowest Observed Effect Level
MAC	Maximum Allowable Concentration
MATC	Maximum Acceptable Toxic Concentration
MC	Main Category
MITI	Ministry of International Trade and Industry, Japan
MOE	Margin of Exposure
MOS	Margin of Safety
MW	Molecular Weight
N	Dangerous for the environment (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC
NAEL	No Adverse Effect Level
NOAEL	No Observed Adverse Effect Level
NOEL	No Observed Effect Level
NOEC	No Observed Effect Concentration
NTP	National Toxicology Program (USA)
O	Oxidizing (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
OECD	Organisation for Economic Cooperation and Development
OEL	Occupational Exposure Limit
OJ	Official Journal
OSPAR	Oslo and Paris Convention for the protection of the marine environment of the Northeast Atlantic
P	Persistent
pKa	negative log of the acid dissociation constant
PBT	Persistent, Bioaccumulative and Toxic
PBPK	Physiologically Based PharmacoKinetic modelling
PBTK	Physiologically Based ToxicoKinetic modelling

PEC	Predicted Environmental Concentration
pH	logarithm (to the base 10) (of the hydrogen ion concentration $\{H^+\}$
pKa	logarithm (to the base 10) of the acid dissociation constant
pKb	logarithm (to the base 10) of the base dissociation constant
PNEC	Predicted No Effect Concentration
POP	Persistent Organic Pollutant
PPE	Personal Protective Equipment
PUR	Polyurethane
QSAR	(Quantitative) Structure-Activity Relationship
R phrases	Risk phrases according to Annex III of Directive 67/548/EEC
RAR	Risk Assessment Report
RC	Risk Characterisation
RfC	Reference Concentration
RfD	Reference Dose
RNA	RiboNucleic Acid
RPE	Respiratory Protective Equipment
RWC	Reasonable Worst Case
S phrases	Safety phrases according to Annex III of Directive 67/548/EEC
SAR	Structure-Activity Relationships
SBR	Standardised birth ratio
SCE	Sister Chromatic Exchange
SDS	Safety Data Sheet
SETAC	Society of Environmental Toxicology And Chemistry
SNIF	Summary Notification Interchange Format (new substances)
SSD	Species Sensitivity Distribution
STP	Sewage Treatment Plant
T(+)	(Very) Toxic (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
TDI	Tolerable Daily Intake
TG	Test Guideline
TGD	Technical Guidance Document [1]
TNsG	Technical Notes for Guidance (for Biocides)
TNO	The Netherlands Organisation for Applied Scientific Research
UC	Use Category
UDS	Unscheduled DNA Synthesis
UN	United Nations
UNEP	United Nations Environment Programme
US EPA	Environmental Protection Agency, USA

UV	Ultraviolet Region of Spectrum
UVCB	Unknown or Variable composition, Complex reaction products of Biological material
vB	very Bioaccumulative
vP	very Persistent
vPvB	very Persistent and very Bioaccumulative
v/v	volume per volume ratio
w/w	weight per weight ratio
WHO	World Health Organization
WWTP	Wastewater Treatment Plant
Xn	Harmful (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)
Xi	Irritant (Symbols and indications of danger for dangerous substances and preparations according to Annex III of Directive 67/548/EEC)

Appendix A: Life Cycle of V6 - Supporting information

Information in this Appendix was originally presented in Section 2 of the risk assessment. For purposes of readability, it has been removed to this Appendix to make section 2 more concise.

In general it is assumed that the reader has already studied the relevant section(s) of the main RAR. Sources cited in the text are referenced in full in the main reference list.

1 FLEXIBLE FOAM PRODUCTION

Slabstock foams[18]

Polyurethanes are step addition polymers made by reacting isocyanate compounds with compounds containing active hydrogen groups, usually hydroxyl groups, on the ends of long polyether or polyester chains. The isocyanate groups can also react with water to form carbon dioxide and this reaction is used as the principal source of gas for blowing the foam, as well as a source of heat for the expansion and curing of the foam. Other blowing agents may also be added to the foam. The density of the foam can be progressively reduced by increasing the water content of the formulation and adding sufficient isocyanate to react with it. This also leads to a stiffening of the polymer and so the density of the foam can be reduced without greatly reducing the load-bearing properties of the foam. However, the exothermic heat of reaction effectively limits the amount of water in the formulation to about 4.6-5.5 parts of water to 100 parts of the polyether polyol, depending on the scale of manufacture, rate of heat dissipation, amount of excess isocyanate present and many other factors.

Since the foam product is a good thermal insulator, overheating of the foam can sometimes occur due to the heat release from reactions during its production and/or curing (for example, excess isocyanate in the foam could react with atmospheric moisture during curing, releasing heat). In some situations, the temperature of the interior of the foam can rise until the polyether chains begin to oxidise and produce more heat. In extreme cases, the foam may spontaneously ignite. The first sign of overheating is the formation of a yellow-brown discoloration in the centre of the foam. Typically, antioxidants are added to the polyether polyols used in flexible foam production to minimise these "scorch" effects (Woods, 1982). The most common type of halogenated flame retardants used in polyurethane foams are halogenated phosphorus based chemicals. However, these types of flame retardant can contribute to scorch problems, particularly in some low density flexible foams.

Flexible polyurethane foams can be manufactured in continuous or batch processes, with cross-sections of up to about 2.2 m wide by 1.25 m high. In a typical process the initial ingredients (mainly water, isocyanate, polyether polyols and any other additive such as a flame retardant) are mixed together at around 20^{o}C and placed into a mould. There then follows an induction period ("cream time") before bubbles appear and the foam begins to rise. The maximum temperature in the system occurs 30 minutes to 1 hour after the end of the foam rise, with the internal temperature remaining near this maximum temperature for 1-8 hours, depending on the block size. In a typical low density foam, the temperature of the interior could be around 160°C. The foam is then left to cure for around 48 hours (Woods, 1982). The blocks may for example be up to 60 metres long or alternatively they may be cut down to lengths of about 2 metres (HMIP 1995).

[18] The majority of the description of foam production presented in this section is taken from the ESR risk assessment for pentabromodiphenyl ether (EC 2000a).

Slabstock foam is usually made by continuously metering all the foam reactants to a mixing head, where they are mechanically mixed and immediately applied to the bottom lining of a continuously moving trough formed by a horizontal bottom paper or foil and two vertical side papers or foils. If the top of the foam is unrestrained, a continuous "domed" block is formed. As the final users usually require foam in sheets of uniform thickness, a domed top is often undesirable as it increases the amount of scrap foam during trimming. Several processes are used in order to reduce this effect such as: a) constraining the rise of the foam by using a paper or foil on the top of the mould; b) distributing the foam mixture onto a shaped base plate that allows foam to expand downwards; c) using a vertical process (Woods, 1982).

Continuous foaming machines can produce polyurethane foam at rates up to 500 kg/minute. The density of the foam produced is generally in the range 10-60 kg/m^3, with most being in the range 15-27 kg/m^3 (Woods, 1982).

The foaming section of the process is enclosed within a tunnel fitted with extraction for removal of di-isocyanate vapours and blowing agent emissions (HMIP, 1995).

Moulded foams

Moulded PUR products can be produced from TDI (toluene di-isocyanate) and also from a mixture of TDI and MDI (methylene diphenyl di-isocyanate). In polyurethane moulding processes the catalysts and other certain additives may be premixed into the polyol and blowing agents may be added to the di-isocyanate stream. Alternatively, components may be fed separately into multi-component mixing heads (HMIP, 1995).

A PUR mould has to perform the following functions (BASF undated):

- receive and distribute the reaction mixture
- maintain the correct reaction temperature and remove the heat of reaction
- absorb the reaction pressure
- seal against loss of material (flash)
- vent air
- locate inserts and reinforcing materials.

Depending on the properties required in the PUR foam, moulding may be carried out with the application of heat or alternatively under ambient conditions (cold cure process). Industry has indicated that cold cure moulded foam does not contain flame retardants (pers. comm. 31st July 2002, producers and downstream users). Hot cure foams result in lower densities and a higher hardness than cold cured foams.

Hot cure foaming is believed to account for 20% of flexible foam production and is used in the production of foams for automotive seating, aircraft seating and office furniture. The process is almost universally employed for the production of moulded automotive seating foams.

With hot cure moulding formulations the blowing is by carbon dioxide generated in situ by incorporation of water into the reaction mixture. With cold cure moulding carbon dioxide is also the normal means of expansion but some formulations may also employ a volatile organic compound as a secondary blowing agent (HMIP, 1995).

Predetermined quantities of mixed reactants are automatically or manually dispensed discontinuously into moulds, which may be stationary or continuously circulating on a track

(HMIP, 1995 and BASF undated). The moulds are normally temperature conditioned prior to filling (HMIP, 1995) to around 40^{o}C.

After the mixture of reactants has been dispensed, the lid of the mould is closed and foaming takes place. Alternatively the mixture is injected into a closed mould with defined vents. With cold cure formulations the foam becomes tack free at ambient temperature. With hot cure moulding, the moulds are heated to temperatures typically in the range 150^{o}C to 230^{o}C (HMIP, 1995).

Moulding allows inserts and fabrics, for example, to be added at the moulding stage to form an integral part of the moulded product. Also, components containing more than one foam composition such as car seat cushions can be produced by dispensing different formulations into different parts of the mould (HMIP, 1995).

On completion of the curing cycle, the moulds are opened and the moulded shapes are removed for trimming and finishing. Some moulded items are subject to a crushing stage or vacuum treatment in order to break open the closed cells in the moulding. The crushing operations may lead to the release of volatile compounds such as amines from within the cell structure of the foam (HMIP, 1995).

After removal of the moulded article the mould is cleaned by removal of residual foam material from the lid and from vents, etc. The mould is then treated with a mould release agent such as a wax which may be in organic solvent or in aqueous dispersion (HMIP, 1995).

Polyether versus polyester foams

Slabstock foam exists in both polyether and polyester form, depending on the nature of the polyol used (i.e. polyetherols or polyesterols). Polyether foams are different from polyester because of their greater flexibility and their homogeneous density. Polyester foams are more brittle and generally more difficult to produce than polyether foams (EC, 1997).

There is a large variety of polyether and polyester foams that serve several applications. In general terms two main branches can be identified, being comfort polyether foam for the furniture and bedding industry, and technical foam (mainly in polyester form) for various industrial purposes (EC, 1997). 80% to 90% of the polyols used today are polyetherols (BASF undated).

Polyether PU foam is a standard commodity product, sourced by customers depending on price (EC, 1997). Foam production plants are generally located close to their markets, as the product's high volume and low weight do not allow for economic transport over long distances (Europur, 2002). The market for comfort foam is influenced by downstream producers moving production to Eastern Europe, and by excess in production capacity for all producers (EC, 1997).

2 RECYCLING OF PUR FOAMS

The European Diisocyanate and Polyol Producers Association (ISOPA) has produced a number of publications on PUR recycling and recovery. Two publications from the mid 1990s summarise the desirability and status of the various technologies at that time:

- Evaluating the Options (ISOPA 1994): describes PUR uses, identifies possible recycling options and evaluates these using a multi-criteria scoring and weighting technique. For a given use, options are rated as of high, average or low desirability or of no relevance
- Options in Practice (ISOPA 1995): reports on the extent to which the technology options for PUR recycling are available and used in practice. For a given use, identifies whether options are commercially available, developmental or still in a pilot stage.

A description of the range of PUR recycling options currently available is given in **Table A.1**. Further information on recycling for furniture and automotive applications is given in sections 2.2.2.1.5 and 2.2.2.1.6 of the main risk assessment report, respectively.

Table A.1 PUR recycling options

Option	Description
Re-use	Reusing the same piece of PUR for the same or a similar application. Some use across the range of applications e.g. second hand furniture, sale of cars seats by dismantlers, re-use of sandwich panels on building sites
Rebonding	Rebonding chopped flexible PUR foam into new products together with a polyol/di-isocyanate. Mainly for scrap foam generated during the cutting of slabstock foams. Used in office furniture, low-end grade furniture, sound insulation in cars, carpet backing, high-density mattresses. (ISOPA 2003, Bürgi, D., (BAG), (2002))
Loose crumb	Flexible PUR foam is shredded but not reformed. Mainly for scrap foam generated during the cutting of slabstock foams. Main use in the EU is for garden furniture (see section 2.2.2.1.4 of the main risk assessment report, also ISOPA 2001a).
Adhesive pressing	PUR is granulated and blended with 5% to 10% polymeric MDI and formed into boards/mouldings at temperatures up to 200°C and under pressure (20 to 200 bar). Products are finished by sawing and sanding or by applying additional facings. Mainly for production trim from rigid block foam and panel production where composition is known. Also for production trim or used PUR from some automotive parts (e.g. thermoformable foam from headliners, flexible integral skin foam from steering wheels, flexible foam backed car carpets). Main applications are furniture in kitchens and sailing boats because virtually unaffected by water, also for flooring e.g. in gymnasiums which needs to have a certain elasticity (see ISOPA 2001b).
Use of particles	Oil binders: PU powder and larger particles obtained from cutting and shaping rigid foam for building and construction applications in the factory are used to absorb spilled liquids. Includes production of pressboards for use in windy conditions and hoses containing particles for use in containment of spills on water (see ISOPA 2001c). Insulating mortar: particles of rigid foam production scrap from building and construction applications are one of the main raw materials in insulating mortar used on construction sites for thermal and acoustic insulation (see ISOPA 2001c)
Regrind/ Powdering	PU foam scrap is ground into fine particles (0.05mm to 0.2 mm) and added as a filler to virgin systems in the production of PUR foam. Can be used for production trim or post consumer parts. Technologies in development (see ISOPA 2001d).

Option	Description
Chemolysis	PUR molecules are broken down into smaller building blocks for re-assembly into polymers suitable for the production of further PUR products. Preferable to process feedstock of known composition to obtain consistent and predictable regenerated products, e.g. production waste. Hydrolysis: PUR reacted with water under pressure at elevated temperature. Process developed up to pilot plant stage. Aminolysis: PUR reacted with amines such as dibutylamine under pressure at elevated temperature. Process at the research stage. Glycosis: PUR reacted with diols at elevated temperatures (200°C) with cleavage of covalent bonds. Processes developed for a range of PUR inputs to pilot and commercial scales. Single phase glycosis is currently applied industrially. For flexible foams it yields polyols which can replace up to 90% of the virgin polyols in semi-rigid foams, bringing the recycled content of "old" foam in the "new" foam to 30% (see ISOPA 2001e)
Feedstock recycling	For PUR in mixed waste streams. Many of the developing technologies are uneconomic at present. Pyrolysis: mixed plastics heated in an inert atmosphere. Liquid and gaseous hydrocarbons formed used as feedstock in other petrochemical processes. Pilot plant in the UK. Gasification: In a two stage process, mixed plastics are heated, then combined with air or oxygen. Product can be used in refinery processes and in production of methanol, ammonia and oxo-alcohols. Likely to be of most interest to PUR. Hydrogenation: plastics treated with hydrogen under high temperature and pressure. Liquid and gaseous hydrocarbons formed are used in refineries and chemical plants. Existing plants for packaging waste streams. Trials for non-packaging waste streams. Steel industry: up to 35% of the heavy oil or coal dust used as a reducing agent in blast furnaces can be replaced with mixed plastics. Operational at a German furnace (see ISOPA 2001f)
Energy recovery	Incineration with energy recovery, mainly in the combustion of municipal solid waste (MSWC). New markets under development, e.g. in power stations where PUR is used as a co-fuel and substitute for coal, as a co-fuel in cement kilns and as a co-fuel for industrial boilers (see ISOPA 1996 and 2001g). MSWC varies across European from around 80% of MSW in Denmark to as low as 12 % in the UK. Option recommended for recovery of rigid foams from demolition (ISOPA 2001b)

Regardless of the recycling technology employed, two factors play a key role in determining the technical and commercial feasibility of recycling polyurethane materials (ISOPA 2001h):

1. densification of low density, voluminous PUR foams, allowing for cost-effective transportation from collection point to recycling operation
2. size reduction of PUR articles (mattresses, car seats, insulation panels, etc.) making them suitable for treatment.

More than 100,000 tonnes of PUR is recycled and recovered each year (ISOPA undated 2), most via the rebonding of scrap from flexible foam production (see section 2.2.2.1.4 of the main risk assessment report). The majority of PUR is collected as mixed plastic waste or as municipal waste (ISOPA 1994).

ISOPA (1994) does not give figures for actual recycling levels in Europe and reported that "in the absence of a viable market, incineration with energy recovery … (was then) the most realistic and cost effective recycling option for PUR post consumer waste". Industry has confirmed that foam is still not recycled in large volumes in Europe (Pers. comm. 16th October 2001).

The Rebonding Process – further information

Bonded foam, or rebond, is a moulded polyurethane product made from pieces of shredded flexible polyurethane foam, held together with a binder. Foam pieces from various sources – production trim and post-consumer waste – can be suitable for rebonding, although in practice production trim and cuttings are by far the most commonly processed (ISOPA 2001a). Rebonding is not relevant to moulded foams as the foam is pre-formed and thus not cut.

Granulators and flock-mills are normally used to shred the foam into pieces approximately one centimetre in diameter. There are other technologies available to handle large foam pieces by cutting them into very thin strips, which can then be reduced into smaller pieces (ISOPA 2001a). This type of process is deemed to be 'dust-free'. In the UK, modern equipment is of the 'turbine cutting' type, which produce particles of a controlled size and are designed to minimise production of dusts, which are in themselves a fire hazard. Some older types of equipment shred the foam by tearing, and produce more dust. This is commonly removed by air filters and disposed of to landfill; however, FR-containing foam is not processed by this method (Pers. comm. 29th April 2004).

The rebonding technologies used vary according to the market requirements and the final use of the rebond articles. Rebonding of polyurethane foam can be carried out through batch or through continuous moulding. The foam blocks are further processed to fabricate parts and articles, resulting in trim which in turn can be reused in the process. Rebonding is also applied in the moulding-to-final-shape technology which allows processors to optimise material use and cost (ISOPA 2001a).

Use of Rebonded Foam – further information

A number of reports make reference to current levels of rebonding in Europe, and all provide different information:

- more than 40,000 tonnes of bonded foam were produced in Europe in 1999, of which more than half was associated with flooring applications. A further 60,000 tonnes of scrap foam (production waste) was sent to the USA for carpet underlay. There is a trend towards lower export from Europe to the US (Mark and Kamprath 2000)
- world-wide, about 400,000 to 500,000 tonnes of foam is recycled on a yearly basis. In Europe that figure is of the order of about 60,000 tonnes (EUROMOULDERS 2002)
- an estimated 80,000 tonnes of PUR in the form of process trim is currently collected in Europe for further use (ISOPA 1994)
- up to 50 000 tonnes of rebonded foam are processed each year in Western Europe (ISOPA 2001a)
- foam scrap is often recycled into carpet underlay (rebond), particularly in the United States. The EU is an exporter of scrap foam (around 40,000 tonnes/year) to the United States for this use (ENDS 1998 in EC 2000).

Overall, between 40,000 and 80,000 tonnes of scrap foam is rebonded in Europe each year with a further 40,000 to 60,000 tonnes shipped to the US. However, discussions with a UK cutter indicate that the situation at present is somewhat different, the US market being "pretty closed" at the current time. Some of this scrap foam will contain V6.

Scrap foam sent to the US is used to make 'rebond', a carpet padding used between carpet and hard flooring surfaces such as concrete and wood. The carpet rebond is not attached to the carpet, thus the padding (rebond) is a separate material from the carpet itself. Carpet is laid over the rebond to provide a cushion effect and helps in minimising carpet wear (RPA 2000). Scrap foam exported to the US will include some foam that contains V6. Traditionally in the EU foam-backed carpet (latex) and latex underlay is used. It is understood that carpet rebond is not imported into Europe and thus this will not affect exposure to V6 in the EU.

3 AUTOMOTIVE USE: USE A

Production and use

V6 is typically recommended for the production of flame retardant foam required to resist ignition from low intensity flame sources such as those described in Federal Motor Vehicles Safety Standard No. 302 (Rhodia 2000). This is the accepted standard for the interiors of motor vehicles in the United States. This states that, for individual components, the rate of flame spread must not exceed 101.6 mm/min (4 in/min). This is a small-scale test regulated by the US Department of Transportation. This is also the standard recommended in the UK Society of Motor Manufacturers and Traders' (SMMT) TEC 811/1989 guideline. However, there is a UN standard which requires only 254 mm/min (10 in/min) (RPA 2000)

1n 1997 alone, more than 300,000 tonnes of PUR were used in applications in Western European cars. A typical car of 1,000 kilograms (kg) total weight contains 100 kg of plastics, of which about 15 kg are PUR. The main applications for PUR are: seat foam (7 kg per car), cushion overlay (fabric backing), carpet backing, door panels, sound absorption and vibration dampening, dashboards, steering wheels, bumpers, energy absorbers, headliners, airbag covers and window encapsulation (ISOPA and EUROMOULDERS undated). However, not all PUR car parts will be treated with flame retardants.

ISOPA data indicate that 100 foamers/moulders are involved in the production of automotive products from PUR foam in Europe each year, consuming 365,000 tonnes of polyurethane (ISOPA undated 1). However, only three or four European producers of moulded foam use flame retardants (pers. comm. 31st July 2002, producers and downstream users). Data have been provided by the producer of V6 and by companies using V6 in the production of foams for automotive applications. The number of sites using V6 is known.

End of Life – Current Situation

The following discussion of current and future levels of recycling of automotive PUR is taken from Mark F.E. and Kamprath A (2000) unless stated otherwise. This study presents data on conditions in Germany but indicates that other countries in central Europe e.g. the Netherlands has somewhat similar economic and market conditions.

Most cars at the end of life are delivered either to car dealers, where old cars are traded for new ones, or they may be delivered directly to an officially recognised dismantler or scrap dealer. At present very little dismantling takes place across the EU. The current situation in Germany and in many other countries, where there is no external funding for dismantling from the consumer, means that parts removal is not cost effective. Therefore only batteries and well functioning spare parts tend to be removed from cars.

Only in the Netherlands and Italy are small amounts of plastics and PUR currently removed from cars, with activities in the Netherlands being subsidised by the first owner of the car. For example in 1998, Auto Recycling Netherlands recovered 2,200 tonnes of PUR from the dismantling of seats (3% of the 70,000 tonnes of PUR available for recovery). This material was sent for recycling. Some scrap is used in the production of new parts for cars. For example, in the BMW 5, recycled polyol from glycolysed scrap is used in the manufacture of the warm air duct (Clausius R, undated).

In the vast majority of cases therefore, PUR seats remain in the end of life vehicle (ELV) which is sold to shredders for further processing. There are around 50 shredders in Germany.

After separation of the metal fraction of the shredded hulk, about 200 kg of ASR (automotive shredder residue) remains at the shredder site. The total ASR volume in Europe is a minimum of 1.5 million tons per year out of 6.7 million ELVs in Europe and about 200,000 tons out of 1.3 million ELVs in Germany.

Most ASR is currently disposed to landfill. There are many potential recovery operations for ASR but only recovery in municipal solid waste combustion (MSWC) is currently in use. Less than 70,000 tons of ASR (just under 5% of the 1.5 million tons per year) is used for energy recovery. This involves waste combustion to generate medium pressure steam (40 bar) used to drive a turbine for electricity generation or to provide medium to low pressure steam in district heating and industrial processes. An alternative source (pers. comm. 11th February 2003) suggests that incineration of ASR for energy recovery is widespread, and that it is only disposed of to landfill 'in exceptional cases'.

End of Life – Future Situation

The recycling and recovery of polyurethane and other car components is the subject of the End of Life Vehicles Directive 2000/53/EC. This came into force on 18th September 2000 and was to be transposed by Members States by March 2002. The Directive is intended to reduce the amount of waste arising from the scrapping of vehicles. It targets overall re-use, recycling and recovery rates at 85% by average weight per vehicle by 2006 and 95% by 2015, and to increase the rate of re-use and recycling over the same period to at least 80% and 85% respectively by average weight per vehicle and year. Another requirement of the Directive is for vehicle manufacturers to design products and cars with recycling and re-use in mind: expressed in the so called Type Approval of new vehicles as from 2005 (EURO-MOULDERS 2002), with the need for a minimum 95% of components of new vehicles to be reusable/recoverable (pers. comm. 11th February 2003).

The result of this is that systems will need to be set up to ensure that end of life vehicles (ELVs) are collected into approved dismantling chains and that improved treatment standards will be established for vehicle dismantlers and scrap dealers to meet (EURO-MOULDERS 2002).

PUR seating is one of the large plastic parts in an ELV and it can be relatively easily dismantled. Thus it is one of the key targets for legislators and environmental authorities for dismantling (Mark F.E. and Kamprath A 2000). Future options for the recovery of automotive PUR are:

- as a fuel in the production of cement or lime, or in the steel industry
- re-bonding
- regrind/powdering
- chemical recycling, e.g. glycosis
- feedstock recycling, e.g. gasification
- recovery in municipal solid waste combustion (MSWC).

All bar the last two options require dismantling of the seat cushions.

Removal of the cover textiles, plastics and large metallic parts inside the seat module and shredding the foam to 5-10 cm pieces would allow use in cement kilns for secondary firing as a fuel replacement[19]. This option is not currently cost effective due to current low fuel prices. For use for primary flame fuel firing in cement kilns, the seat foam would need to be shredded to form <2 cm fluff. This would require total dismantling of the seats and full separation of non-PUR materials. This option would be more costly and not economic as cement producers do not have lower gate fees for primary fuel versus secondary fuel replacement.

The use of PU seating as a fuel in steel (pig iron) furnaces is being seriously considered in Japan and studied in North America. However, the relatively high gate fee and additional treatment cost compared to MSWC make this route less attractive than that option.

Rebonding (see section 2.2.2.1.4 of the main risk assessment report) is widely used for scrap foam from slabstock foam production. It is estimated foam from ELVs could produce 70,000 to 80,000 tonnes of foam each year, which would double the size of the current EU market. The current market is not considered large enough to absorb this additional tonnage.

In laboratory tests, new moulded foam seats have been made containing 15% to 20% reground/powdered foam and exhibiting excellent processing characteristics. The investment cost of the first generation equipment limits the operational potential of this technology to slabstock (ISOPA, 2001d). This option is not operating on a commercial scale.

The polyols resulting from glycolysis although of similar costs to virgin materials are not suitable for seat production and can only be used in the production of rigid PUR foams. PUR from ELVs would generate around 200,000 tons of recycled polyols each year, about 50% of the current market for polyols in systems[20] for rigid foam production in 1999 (IAL, 2000). Thus the market is not big enough by far to take this additional input. More generally, viable chemical recycling routes for mixtures of PUR materials from ELV's seats do not exist at present at sufficiently large scale.

ASR can be used as an input for gasification plants that produce methanol via synthesis gas treatments (EUROMOULDERS 2002).

Use in MSWC does not require pre-treatment of waste as incinerators can take ASR. Alternatively bales of seat foam can be dropped into the bunker as they are delivered from the dismantler after the baling wires are cut.

The lowest cost option for the future disposal of an ELV is reported to be shredding followed by fuel substitution. Other favourable routes depend on regional circumstances. In general terms, seat dismantling is currently uneconomic and contaminants in the PUR from shredder residue prevent the use of other options such as rebonding. Also, because of the various qualities of the ELV PUR foams used for many years (10 to 15 years) in cars, special and costly cleaning and treatment methods would need to be found to produce recyclates with acceptable and stable characteristics (EUROMOULDERS 2002).

As fuel substitution in cement kilns is not currently economic, MSWC is at present the only viable option. It is however viewed by legislators as inferior to other material recycling or recovery routes.

[19] It is assumed that the small steel wires inside the foam cushion would not need to be removed on the basis that tyres are used for secondary firing with the steel cord left inside the tyre.

[20] See the TCPP risk assessment for a discussion of polyols and systems for rigid foam production.

All other use scenarios are described in detail in the Confidential use pattern and exposure Annex.

Appendix B: A new assessment of the release of flame retardants from polyurethane foam

Authors: Peter Fisk, Louise McLaughlin, Ros Wildey

This report was prepared by Peter Fisk Associates, largely under contract to the Environment Agency, as part of three environmental risk assessments being carried out under the ESR programme. Some parts were conducted independently by Peter Fisk Associates.

1 Introduction

The context of this report is the Existing Substances Regulation (ESR) risk assessments of the substances TCPP, TDCP and V6; its purpose is to review measured data supplied by industry and from the literature, which can help assessment of the rates of release of substances from a polyurethane (PUR) matrix. There are several complex areas of application of the data for the environmental risk assessment. There are various laboratory or simplified tests of release, and taken together at face value they do not reach an immediately obvious consistent set of conclusions. Therefore, in order to aid interpretation it has been necessary to develop a mathematical model of how fast additives are lost from polymer matrices, applied to polyurethane in particular. In order to achieve this objective it has been necessary to draw upon a somewhat wider set of source literature than that on PUR alone.

The proposed areas of application for the model are discussed below. The starting point of this study is the description of flame retardant releases in the Emission Scenario Document (ESD) for Plastics Additives (OECD, 2004).

The draft ESR risk assessments contain much of the background, and that is not repeated here. Losses from foam are relevant to the following processes identified to date:

- Foam production and storage
- Foam processing, recycling
- In-service loss
- Waste remaining in the environment
- Release from foam within landfills (where degradation of the polymer may also be important).

The above life cycle stages are also described in the ESR assessments of several brominated diphenyl ethers, although the extent of information now available, and the higher tonnages of the present substances in use means that the present treatment and these older ones are not identical, although broadly compatible.

The structure of this document in the subsequent sections is:

2. Review of measured data
3. A new mathematical model
4. Conclusions for the ESR RAR developments.

Some of the more detailed data and arguments are developed in Sections 2 and 3. The key findings for the current risk assessments are given in Section 4.

Whilst the models developed are based on a number of assumptions, and there are developments that would be necessary for a more complete picture, the work brings together several studies into a consistent whole, sufficient for the present purpose.

The authors are grateful for useful comments from Environment Agency and industry reviewers, and from Professor Gary Stevens of the University of Surrey.

2 SUMMARY OF MEASURED DATA

Polyurethane foams intended for use in construction or furniture are frequently treated with flame retardants (FRs), including TCPP and TDCP. Typical applications of this type of foam are insulation panels, one or two-component spray foams for professional or consumer use (e.g. for *in situ* application to roofs or as fillers), mattresses and upholstery foam, including for automotive applications.

During the storage, handling, service life, recycling and disposal of such foams, it is possible that the FR may be released due to diffusion through the polymer, followed by volatilisation or washing from its surface. For the purposes of risk assessment, it is important to quantify these releases in order to determine exposure to both humans and the environment. The main focus of this document is the environment, although the emission rates described could be used to estimate human exposure.

Several studies have been published relating to both flame retardant levels in indoor environments and the measurement of releases from various polymers, including polyurethane. Details of some key studies relevant to releases of TCPP and TDCP from foam are summarised in Section 2.1, and the results are discussed in Section 2.2. A brief review of studies relating to indoor measurements is given in Section 2.3.

When a fresh piece of foam is used in a study, such variables as air flow rate, foam size, chamber size affect concentrations measured in the air and on the walls of the chamber, and remaining in the foam. There might typically be a rapid loss rate as the outer surface of the foam loses flame retardant and as the receiving environment becomes saturated; thereafter the rate may slow. These factors are explored in more detail through this report.

2.1 MEASURED RELEASES FROM FOAM

2.1.1 BAM study

Researchers at the Federal Institute for Materials Research and Testing (BAM), funded by the Federal Environmental Agency in Germany, conducted chamber tests on different types of polyurethane foams, circuit boards and computer equipment (UBA, 2003). Sample materials were placed in either glass or stainless steel chambers under conditions that modelled real-life situations. Clean, dust-free air was passed through the chamber at a rate equivalent to 0.5 air exchanges per hour, at a temperature of 23°C and relative humidity of 50%. Sample sizes were selected such that the emitting surface area to chamber volume ratio modelled typical use patterns.

Emissions of TCPP to air were sampled via a pre-purified polyurethane foam plug fitted to the chamber air outlet. The foam plugs were extracted with acetone using ultrasonication and analysis by GC-MS was used to determine TCPP concentrations in the extract. In addition, at the end of some tests the chamber walls were rinsed with acetone and any losses of TCPP due to sink effects (condensation onto the chamber walls) were determined by GC-MS. The limit of detection was reported as 17 pg/µl and the limit of determination 55 pg/µl.

Three types of foam were tested, namely rigid insulation foam, rigid assembly foam and flexible furniture foam. Assembly foam is that which is used for adhesive/filling uses, referred to in the RARs as 1K. Within each group, other conditions such as foam density, FR (flame retardant) loading rate, ratio of emitting surface area to chamber surface area (source to sink ratio), and coverings were varied. TCPP was detected in all cases and the findings are summarised in **Table B.1**. Note that it appears that **Table B.1** contains original FR % b.w. concentrations that may have been supplied by manufacturers rather than determined by BAM for the sample sets they actually used. If this is the case there will be uncertainty in relating the release rates to the notional original concentrations. It was found that the air concentrations increased at the start of the tests, then reached a plateau air concentration or decreased slightly before the steady state concentration was reached. This concentration profile may be explained by the sink effect, where a certain time is required before equilibrium between air and the chamber walls is reached, or it may be due to migration of TCPP to the foam surface. A plateau air concentration also reflects saturation of the vapour phase, with a dynamic equilibrium between TCPP in the air on the surface of foam, and on the walls of the chamber.

Results were calculated as area-specific emission rates (SER), either on the basis of the equilibrium air concentration and area-specific air flow rate, or using the total amount of TCPP detected from both the air and chamber walls. Where there is close agreement between the two results, the test system is considered to be in equilibrium.

The observed emission rates were 0.3 to 0.7 µg $m^{-2}h^{-1}$ for insulation foams, 40 to 70 µg $m^{-2}h^{-1}$ for assembly foams, 36 to 77 µg$m^{-2}h^{-1}$ for upholstery foams and 12 ng $m^{-2}h^{-1}$ for a mattress.

Due to the variation in sample types and conditions used in the experiments, it is not possible to make direct quantitative comparisons between them. However, the researchers reached the following conclusions:

- In the test with insulation foams, a distinct sink effect was noted, with 25 and 33% of the total emitted TCPP being found on the chamber walls at the end of the test. Increasing the source to sink ratio was shown to reduce this effect since the measured equilibrium air concentration was higher when the source to sink ratio was increased for the Insulation I foam sample (PIR insulation foam welded in polyethylene foils, density 30 g/l). The higher concentrations in air are approaching theoretical upper limits based on the vapour pressure (202 000 ng/m^3), so it is not surprising that there would be some condensation onto any available surface.

- The increased emission of TCPP from the insulation foam with the smaller density is due to an increased interface between the polymer phase and air.

Table B.1 Results of BAM 2003

+ Based on total emission measured from PUR plug and walls of test vessel.

Sample	Density (g/l)	% TCPP *	Area-specific air flow rate ($m^3 m^{-2} h^{-1}$) Q	Source:Sink ratio (m^2/m^2)	Maximum Air Conc (ng/m^3)	Time to reach maximum (days)	Eqbm Air Conc (ng/m^3) Ceq	Time to reach equilibrium (days)	Overall Area-specific emission rate+ ($\mu g\ m^{-2} h^{-1}$)	Area-specific emission rate Ceq.q ($\mu g m^{-2} h^{-1}$)	Sink effect (%)
Insulation I	30	5	1.243	0.28	800	~37	480	~50	0.70	0.60	25
Insulation I	30	5	1.243	0.40	1800	~35	780	50 – 60			
Insulation II	80	2.5	1.243	0.28	250	~35	170	~50	0.35	0.21	33
Assembly I	20	14	5.12	0.067	15000	~12	3000	~75	40	16	NR
Assembly II	25	14	5.12	0.037	15000	~12	3000		NR	NR	NR
Assembly III Smooth New	NR	18	5.12	0.037	10000 - 15000	~10	10000 - 15000	~10	NR	50	NR
Assembly III Smooth Old	NR	18	5.12	0.037	9500	~10	9500	~10	70	50	NR
Assembly III Sawn New	NR	18	5.12	0.037	10000 - 15000	~10	10000 - 15000	~10	NR	70	NR
Assembly III Sawn Old	NR	18	5.12	0.037	26500	~10	26500	~10	130	140	NR
Upholstered stool	NR	9	1.24	0.40	45000	100	41000	150	28	36	NR
Mattress	NR	2	1	0.21	100	10	10	20	NR	0.012	NR
Upholstery foam	27	2	1.1	0.13	70000	< 5	70000	< 5	NR	77	NR

*Nominal values based on manufacturing information for the foam samples.

NR – Not reported.

Insulation I: PIR insulation foam welded in polyethylene foils, density 30 g/l

Insulation II: PIR insulation foam welded in polyethylene foils, density 80 g/l

Assembly I: B2 PUR assembly foam with sawn surface, density 20 g/l

Assembly II: B2 PUR frame foam with sawn surface, density 25 g/l

Assembly III: I-C-PUR express pistol foam in aluminium form and either left smooth or cut off to give sawn surface. Tested immediately and after storage for 6 months

Upholstered stool: Upholstery foam covered with fabric

Mattress: Soft PUR foam inside fabric fleece and textile cover

Upholstery foam: Polyether-based PUR foam, uncovered

- In addition to the higher TCPP content, the markedly increased polymer/air interface in the assembly foams results in substantially higher emission rates than for insulation foams. This effect of increased surface area was further demonstrated by testing a one component assembly foam with both a smooth and sawn surface. When new, there was no significant difference between the two. However, after storage for six months, emissions were greater for the sawn foam. No explanation was given for the difference between new and aged foams.

- The presence of upholstery fabric appeared to increase the time required for the system to reach equilibrium, and was considered to be the reason for the difference in emission rate between the upholstered stool and the uncovered foam. No explanation was offered for the significantly lower emission rate from the mattress, but the same effect can be assumed to operate.

Further chamber tests were conducted using computer equipment, two typical workstations comprising a PC, keyboard, mouse and a single printer and monitor. Test conditions were the same as for the foam tests. TCPP was detected in emissions from one of the workstation tests at levels comparable to the other flame retardants present. The presence of TCPP was contrary to the manufacturer's data and was attributed to an unknown source of contamination, possibly packaging.

2.1.2 Elastogran study

In this test, a concrete plate was covered with a 10 cm thick layer of a rigid, closed-cell two-component spray foam, intended for indoor insulation purposes, containing 9% TCPP. The sample was placed in a test chamber with a surface area to volume ratio of 1.4 m^2/m^3, and the test conditions were 23°C, 50% relative humidity and 0.5 per hour air exchange rate, as for the mattress test. Volatile emissions were collected on Tenax TA and analysed by GC-MS. The limit of detection was reported as 1 $\mu g/m^3$. TCPP was not detected.

2.1.3 EUROPUR study

Chamber tests were conducted on behalf of industry, provided to the authors via Elastogran, sponsored by EUROPUR (EUROPUR 2001, later published in Cellular Polymers, 22 (4), 2003, although that later reference has not been reviewed). Three types of flexible PUR foam used in mattresses were tested. The samples were 2000 x 1000 x 120 mm of full depth foam (i.e. no springs), were uncovered and were reported to contain TCPP at the high end of the typical level for this application (reported to be 2.5 – 14%, 7 – 8% on average, based on industry data collected for the risk assessment of TCPP).

The mattresses were placed in a 3.2 m^3 test chamber at 23°C and relative humidity of 50%, with an air exchange rate of 0.5 per hour. Volatile emissions were collected on Tenax TA absorbent and analysed by GC-MS. The limit of detection was reported as 2 $\mu g/m^3$. Results are summarised in **Table B.2**.

The CME 33 mattress gave a measured steady state air concentration of approximately 16 $\mu g/m^3$ after 48 hours, while the measured air concentration from the HR mattress was continuing to decline at the end of the 160 hour measurement period, indicating that steady state had not been reached.

Table B.2 Summary results of EUROPUR (2001)

Mattress Type	Air Concentration (µg/m³)				
	24h	48h	72h	120h	160h
HR[1]	6.0	22	25	19	10
CME 33[2]	9.1	16	16	19	17
CMHR[3]	1.8	1.7	2	<1	<1

[1]HR = High resilience foam, 36 kg/m³, 1.5% TCPP
[2]CME = Combustion modified ether, 33 kg/m³.
[3] CMHR = Combustion modified high resilience foam, 35 kg/m³

2.1.4 BRMA study

A study of long-term flame retardant retention in foams was organised by the British Rubber Manufacturers' Association (BRMA, 1998 – 2005). Over a period of nearly eight years, six monthly samples of two flexible foams manufactured by Company A (containing TDCP) and Company B (containing TCPP) were analysed for total phosphorus and total chlorine content. Details of the method of analysis are available but not reported here.

A further test was carried out with separate foam samples, aged at 80°C for only 100 hours.

The pieces of foam were cushion-sized (47 cm x 47 cm x 20 cm) and stored uncovered in a general factory area, supported underneath. The results of the two test series are summarised in **Table B.3**.

Table B.3 Summary results of BRMA trial

Time (months)	Company A (TDCP)		Company B (TCPP)	
	% P	% Cl	% P	% Cl
0	0.75	2.6	0.40	1.3
80°C for 100 h	0.74	2.5	-	-
6	-	-	0.39	1.7
12	0.74	2.5	0.41	1.4
18	0.75	2.7	0.40	1.2
24	0.70	2.7	0.39	1.3
30	0.72	2.7	0.37	1.3
36	0.71	2.6	0.39	1.3
42	0.73	2.6	0.40	1.2
48	0.72	2.6	0.40	1.2
54	0.74	2.5	0.41	1.2
60	0.73	2.4	0.42	1.2
78*			0.44	1.42
84*			0.45	1.42
90			0.44	1.48

* Change of analytical laboratory

The conclusion in each test report, on the basis of these results, is that flame retardant retention in the foams is very good. Whilst this is evidently true, the method used is insufficiently sensitive to detect small losses and there is no need to convert the concentrations into total TCPP, at least at this point. The % P and % Cl values show, relative to time 0, a range from a loss of <1.5% of TCPP /year to a gain of 1%/year, so it is not possible to apply the values with confidence. The overall data set suggests very low losses. It is an important study in that it is both long term and used direct analysis of foam of typical size.

2.1.5 Consortium-sponsored study

On behalf of an industry consortium, a program of research has been undertaken by the Polymer Research Centre at the University of Surrey and the Bolton Research Institute (Univ. of Surrey, 2005). The purpose of this research was to develop realistic exposure models for the release of flame retardants from products, suitable for use in human health and environmental risk assessment. Phase 1 of the research, examining flame retardant release from foams, was published in February 2005.

Releases were measured using several methods under a variety of conditions relevant to human and environmental exposure:

1. Weight loss following thermal ageing at room temperature, 40°C and 60°C.
2. Analysis of flame retardant content following solvent extraction of foam aged at 60°C.
3. Analysis of flame retardant emissions in aqueous media designed to model dermal absorption (contact blotting tests) and chewing (head over heels tests).
4. Measurement of volatile emissions during thermal ageing in sealed vials.
5. Measurement of particle size distribution in the pounding test using samples of aged and un-aged foams.

Experiments 1, 2, 4 and 5 are relevant for estimation of volatile releases during storage and service life for the purposes of risk assessment. Experiment 3 (not discussed herein) could have relevance to contact of foam with any liquid medium. Experiment 5 (pounding tests) could be used to assess the loss of particulates due to wear and tear during service-life.

Three types of foam were tested:

1. A combustion modified (CM) ether foam containing 8.47% by weight TCPP.
2. A combustion modified high resilience (CMHR) foam containing 5.2% by weight TCPP.
3. An FR ether foam containing 5.5% by weight TDCP.

Melamine was also present in the TCPP-containing foams.

2.1.5.1 Experiment 1: Thermal ageing

Samples sizes of 100 x 100 x 50 mm ('large') and 50 x 50 x 15 mm ('small') were aged for up to six weeks in:

- an air-conditioned laboratory at 20°C and 75% relative humidity;
- temperature controlled ovens at 40 and 60°C and ambient relative humidity;
- an environmental chamber at 60°C and 75% relative humidity.

The bulk density of the foam tested was ~32 kg/m^3. The oven volumes were 150 or 350 litres, with 10 or 4.3 air changes per hour (considered by the authors to be a relatively fast rate). The foam was positioned on wire with enough space for free air movement to all surfaces. The results are summarised in **Table B.4**.

Table B.4 Percentage weight loss after ageing time of six weeks

	CM Ether Foam – TCPP		CMHR Foam - TCPP		FR Ether Foam – TDCP	
	Large	Small	Large	Small	Large	Small
20°C	0.11	0.26	0.02	0.18	0.11	0.18
40°C	0.44	1.86	0.52	1.47	0.17	0.24
60°C	3.21	7.12	2.18	3.99	0.16	0.17

Rates of loss are higher for the CM ether foam, reflecting the higher FR content. For foams containing TCPP, emissions increase with temperature and were found to obey an Arrhenius relationship; the size of the temperature effect suggests a higher activation energy than would be true for diffusion alone. The dimensions of the foam tested are also important, with higher percentage losses for the smaller block of foam. Results for TDCP were less predictable, but were in general lower than for TCPP, although the difference was small at ambient temperature.

Release rates in the environmental chamber at 75% relative humidity were lower than for the corresponding oven test. The report attributes this to the higher relative humidity inhibiting diffusion of hydrophobic additives. However, there is no evidence to support this, and other factors, such as different test chamber volumes or air-exchange rates could have contributed.

The result at 20°C is the one of most relevance to the ESR risk assessment.

2.1.5.2 Experiment 2: Solvent extraction of flame retardant from aged foam

Foam samples ('large') were aged at 60°C for 6 weeks. After ageing, small pieces of foam were cut from the block, extracted and analysed for residual flame retardant. Ten samples were analysed for each foam type.

The flame retardant content of aged foams was determined by extraction into toluene using Soxhlet extraction (over a period of 8 hours). Extracts were analysed by GC-MS. The extraction procedure was validated by spiking a piece of foam without flame retardant with known quantities of TCPP or TDCP. No description of how the spiked samples were prepared is given in the report. Recoveries are reported as 100 – 105.5% for TCPP and 100 – 111% of TDCP. However, analysis of un-aged foam samples gave results of 82.6% of nominal for CM ether foam with TCPP, 102.6% of nominal for CHMR foam with TCPP and 30% of nominal for FR ether foam with TDCP. No explanation is given for the low yield of TDCP. It seems possible that the FR could be strongly bonded into the foam in some way, although evidently not irreversibly.

Results were expressed as percentage of flame retardant lost, and as the equivalent weight loss for the piece of foam. Actual weight loss after ageing was also recorded. The results are summarised in **Table B.5**.

Table B.5 Results of FR extraction for thermally aged samples (six weeks, 60°C)

Foam Type	Analytical data		Measured % weight loss of foam
	% of FR lost	Equivalent % weight loss of foam	
CM Ether Foam - TCPP	38.6 39.5	3.3	3.14
CMHR Foam - TCPP	47.6 47	2.4	2.01
FR Ether Foam - TDCP	24.0 13	1.88 0.86	0.36

There is reasonable agreement between the measured weight loss and the flame retardant loss, indicating that most of the observed weight loss is due to flame retardant emission. However, it is expected that a concentration gradient would develop over time, as flame retardant diffuses through the foam block. Since only small pieces of foam were analysed, the part of the block from which they were cut could affect the concentration of flame retardant remaining. Since samples were taken from the inner part of the block, overall losses from the whole block could be underestimated, although because of redistribution within the block this is not a major issue.

Variation in the recovered flame retardant for replicate samples was 40.7 – 64.4% for CM ether foam, 40.2 – 93.1% for CMHR foam and 16.6 – 33.9% for FR ether foam.

The results of Experiment 2 seem to confirm those from Experiment 1, although TDCP loss rates were higher in Experiment 2.

2.1.5.3 Experiment 4: Measurement of volatile emissions during thermal ageing

Samples of foam were placed in septum sealed glass vials and stored in temperature-controlled ovens at 60°C, 40°C and room temperature for a period of 4 months. Headspace samples were collected using a syringe and analysed by GC-MS and sample weight loss was also recorded. The results obtained are summarised in **Table B.6**.

Table B.6 Volatile emissions from thermally aged foam in sealed vessels for 4 months

Temperature	CM Ether Foam		CMHR Foam		FR Ether Foam	
	Weight loss (%)	TCPP Released (% w/w)	Weight loss (%)	TCPP Released (% w/w)	Weight loss (%)	TDCP Released (% w/w)
60°C	1.4	0.26	0.8	0.3	0.2	0.064
40°C	0.06	0.11	0.4	0.059	0.4	0.023
Room temperature	-0.45	$<9.5 \times 10^{-5}$	-0.3	$<8.6 \times 10^{-5}$	-0.25	$<8.9 \times 10^{-5}$

The measured flame retardant release in this case is considerably lower than the recorded weight loss and in the case of room temperature samples, a slight weight increase was observed. The authors attribute this weight increase to possible water absorption. The weight loss at 40 and 60°C is also less than that measured in the first thermal ageing experiment.

The lack of flame retardant detected in the headspace of the vials is attributed to the enclosed nature of the vial leading to re-absorption to the foam. The lack of air flow through the vial means that air saturation would certainly have been reached, thus preventing any further diffusion from the foam surface. The sample volume used was 50 cm^3 (20 mm x 50 mm x 50 mm) and the vial volume was 73 – 160 cm^3.

In experiments at room temperature no flame retardant was detected above the limit of detection of the analytical method. This is an important finding when considering potential releases from foam used in enclosed areas such as insulation panels.

2.1.5.4 Experiment 5: Pounding tests

This study will not be reviewed in detail. Two foam types, CM ether and CMHR, were subjected to pounding tests using un-aged and aged foams. The diameter of particles emitted from aged foam (30 nm to 0.1 μm) was typically smaller than for the un-aged foam (100 nm to 6.5 μm), and particle size decreased with increasing length of the test. From the available information, it is not possible to relate these results to typical conditions during service life. Further work is being undertaken to characterise the physical and chemical nature of the particles.

Volatile emissions of TCPP were not detected during the pounding tests. This implies a release rate of less than 36 and 10 μg/kg/h for unaged and aged foam respectively.

2.1.6 Losses from very small sized pieces of foam

2.1.6.1 Experimental details

A study (Hall, 2005) was commissioned by the industry to examine the loss of TCPP over time from small particles of polyurethane foam. This study is particularly important as a key to understanding the whole data set so is dealt with in some detail.

A small block of combustion modified polyether urethane foam was received from routine UK manufacture for GC-MS analysis to investigate the loss of TCPP over time. The foam was first analysed for the content of TCPP by extraction with dichloromethane. The foam was then blended into three different particle size ranges and 10 sets of 1 g of each range were weighed into Petri dishes. The samples were left in the open for different time periods of 0, 1, 3, 7, 10, 15, 30, 45, 60 and 90 days. After reaching the allotted time period the samples were analysed for the TCPP content.

The three particle size ranges were:

1. Dust (diameter less than 1 mm)
2. Small crumbs (diameter 3 mm to 1 cm)
3. Large crumbs (diameter 1 to 3 cm).

The crumbs were produced using a blending machine whilst the dust was produced by cooling the foam in liquid nitrogen prior to blending for 2 minutes.

The room where the samples were left measured 310 cm x 370 cm x 290 cm with an archway measuring 98 cm x 207 cm linking to a second room of 290 cm x 370 cm x 280 cm. This gives a total volume of 63 m^3 with a maximum sample loading of 27 g on day 0 reducing by 3 g at each of the sampling periods. There was no air flow monitoring of the room, however the air turnover is believed to be greater than total volume per day. Boards were placed up against the windows to stop light entering, which could affect the foam.

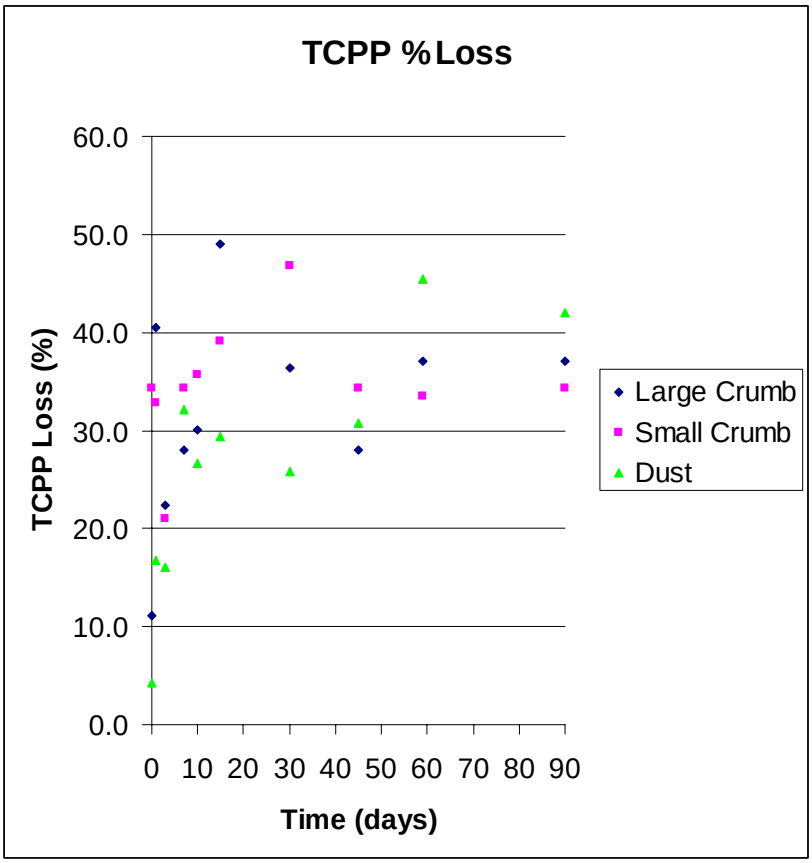
2.1.6.2 Results

Results of the study are presented in **Table B.7** and **Figure B.1**.

Table B.7 Data for loss of TCPP from three sizes of foam particles

Time (days)	Large Crumb		Small Crumb		Dust	
	% TCPP	% loss	% TCPP	% loss	% TCPP	% loss
	14.3		14.3		14.3	
0	12.7	11.2	9.4	34.3	13.7	4.2
1	8.5	40.6	9.6	32.9	11.9	16.8
3	11.1	22.4	11.3	21.0	12.0	16.1
7	10.3	28.0	9.4	34.3	9.7	32.2
10	10.0	30.1	9.2	35.7	10.5	26.6
15	7.3	49.0	8.7	39.2	10.1	29.4
30	9.1	36.4	7.6	46.9	10.6	25.9
45	10.3	28.0	9.4	34.3	9.9	30.8
59	9.0	37.1	9.5	33.6	7.8	45.5
90	9.0	37.1	9.4	34.3	8.3	42.0

Figure B.1 Graph of loss of TCPP from three sizes of foam particles



2.1.6.3 Interpretation and conclusions

The experiments showed a TCPP loss from the particle size ranges of between 34% and 42% at the end of the 90 day period with the general trend being an initial loss of approximately 30% over the first 10 days and subsequently a slower rate of loss to the final value. The greatest loss was observed in the dust size range with a final value of 42%, for the large crumb sample a loss of 37.1% was observed whilst the small crumb sample showed the least final value loss of 34.4%. Despite some experimental variability, there is a clear trend associated with the results which indicates the dust range samples has a slightly higher rate of loss than the large and small crumbed samples.

There is an initial rapid loss followed by approach to a plateau at around 40% loss. The fact that the release reached a definite plateau, rather than merely slowing, supports the view that releases of TCPP had stopped rather than being slowed or limited by some external factor. The rate of air turnover in the experimental system was unchanged and the lack of continued release therefore demonstrates that the plateau was not caused by any saturation effect. The initial rates correlate with particle size (discussed further in section 3). It is possible that rates over the first two days are as high as 20% per day. Given that only 40% of the TCPP is available, this could be seen as a loss of 50% per day of that which is available to be lost.

It is necessary to consider whether there being an 'unavailable fraction' has a physicochemical explanation. It is possible that polar interactions between urethane functions and the flame retardant (FR) will exist. It is also possible that the FR could be physically entrapped. A recent paper, (Levchik *et al.*, 2005) shows that TDCP can react chemically with free NH_2 groups derived from decomposition of the isocyanates used to make PUR. The amount of these forms depends on the precise ingredients used to make the foam. This would be an essentially irreversible process. Therefore, it is reasonable that not all the TCPP was released from the particles used in the study.

2.2 DISCUSSION OF RESULTS

2.2.1 Large pieces of foam

From the information included in the two EUROPUR studies, it is possible to calculate area-specific release rates in the same manner as used by BAM.

For a piece of mattress foam with dimensions 2000 x 1000 x 120 mm, a surface area (A) of 2.72 m^2 was available for emission (i.e. one large face excluded). The chamber surface area was 13.12 m^2, its volume was 3.2 m^3 and the air exchange rate was 0.5 per hour, giving a volumetric air flow rate (V°) of 1.6 m^3h^{-1}. The area-specific air flow rate (q) is then calculated as:

$q = V°/A = 0.59\ m^3\ m^{-2}\ h^{-1}$

For the CME 33 foam, an equilibrium air concentration (Ceq) of approximately 16 μgm^{-3} was attained, therefore the area-specific emission rate (SER) is calculated from:

$SER = Ceq \times q = 9.4\ \mu g\ m^{-2}h^{-1}$

From the BAM study, the SER for a piece of uncovered upholstery foam was determined to be 77 $\mu g\ m^{-2}\ h^{-1}$ under the similar test conditions in terms of temperature, humidity and area-specific air flow rate.

The mattress tested by BAM gave an area-specific emission rate of 12 ng m^{-2} h^{-1}, much lower than that measured by EUROPUR, although this mattress was covered which could have reduced emissions.

To illustrate how these emission rates can be used to estimate losses during service life, consider the emission rate of 5.44 µg $m^{-2}h^{-1}$. For a mattress with dimensions 2 x 1 x 0.12 m (one face excluded) the annual emission would be:

Normalised rate per unit area and time x Area x Time

2.72 m^2 x 5.44 µg $m^{-2}h^{-1}$ x 24 h/d x 365 d/y x 1E-09 kg/µg = 1.3E-04 kg/y or 130 mg/y

Assuming a foam density of 27 g/l (as the upholstery foam used in the BAM study), then the foam weight is 6.48 kg and assuming that the loading rate of TCPP is 10% (actual value not reported), this equates to an initial TCPP loading of 0.65 kg. A loss of 1.3E-04 kg/y is therefore equivalent to approximately 0.017% per year.

The highest emission measured by BAM was for an uncovered upholstery foam containing 2% TCPP, which gave an area-specific emission rate of 77 µg$m^{-2}h^{-1}$. The weight of a block of foam with the same dimensions as for the EUROPUR test is 6.48 kg, containing 0.13 kg TCPP. The annual emission is 3.18E-03 kg/y, equivalent to 2.4% per year.

The results of the Elastogran test on a closed-cell rigid insulation foam showed no emission of TCPP up to the detection limit of 1 µg/m^3. However, treating this upper limit as a worst case emission, the SER for this product can be calculated. The surface area to volume ratio is reported as 1.4 m^2/m^3 and the air exchange rate is 0.5 per hour, therefore:

q = 0.5/1.4 = 0.36 $m^3m^{-2}h^{-1}$

SER = Ceq x q = 0.36 x 1 = 0.36 µg$m^{-2}h^{-1}$

The foam tested had a density of 30 kg/m^3, was 10 cm thick (high for practical applications and considered an upper limit), and contained 9% TCPP. Assuming an emitting surface area (one face only) of 1 m^2, and hence a volume of 0.01 m^3, the weight of foam would be 0.3 kg, containing 0.027 kg TCPP. At an emission rate of 0.36 µg$m^{-2}h^{-1}$ the total amount release per year is 3.15 mg TCPP or around 0.01% per year.

The worst-case release from an insulation foam tested by BAM was 0.70 µg$m^{-2}h^{-1}$ for a foam of density 30 g/l and containing 5% TCPP. A block of the same dimensions as tested by EUROPUR would therefore contain 0.015 kg TCPP and the overall release would be around 0.04% per year.

Higher emission levels (up to 70 µg$m^{-2}h^{-1}$) were measured by BAM for assembly foams of density 20 – 25 g/l and containing 14 – 18% TCPP. However, it is not clear whether these samples were covered or uncovered, and the relevance of sawn surfaces in real applications is not known. Again assuming an emitting surface of 1 m^2 and a volume of 0.01 m^3, the block would contain 0.045 kg TCPP and the overall release would be around 1.4% per year.

These results are summarised in **Table B.8**, but should be treated with caution due to the variety of test conditions used.

Table B.8 Summary of annual release rates (excluding Surrey studies)

Sample	Study Reference	Estimated Annual Release (% per year)
Uncovered mattress foam	EUROPUR 2001	0.03
Uncovered upholstery foam	UBA 2003	2.4
Insulation foam (one side uncovered)	Elastogran 2002	0.01
Insulation foam (both sides covered)	UBA 2003	0.04
Assembly foam (sawn surface)	UBA 2003	1.4
Flexible cushion foam	BRMA 2001-2005	~0

The BAM and EUROPUR studies had generally similar conditions, although the latter had larger foam pieces and a larger chamber.

The research carried out on behalf of BRMA is based on the residual levels of flame retardant in foam, determined by measurement of total phosphorus and total chlorine, and reports that FR concentrations are stable over time.

The results of Experiment 1 at 20°C from the University of Surrey study are of most relevance to the service-life of polymers. Over a 6 week period, losses of 0.02 - 0.11 and 0.18 - 0.26% (by weight) were measured foam containing TCPP (large and small pieces respectively), while for foam containing TDCP, losses of 0.11 and 0.18% by weight were measured for large and small pieces respectively. The results of Experiment 2 suggest that this loss can be attributed mainly to release of flame retardant. **Table B.9** shows the equivalent flame retardant loss based on the assumption that the weight loss is due entirely to emission of TCPP or TDCP. However, extrapolating a 6-week experiment to an annual weight loss introduces some further uncertainty.

Table B.9 Results of University of Surrey Experiment 1 expressed as annual loss

Foam type	% FR	% loss (by weight, 6 weeks)	Equivalent % FR loss	% FR loss [1] (y)
CM Ether Large	8.47	0.11	1.3	11.3
CM Ether Small	8.47	0.26	3.1	26.9
CMHR Large	5.2	0.02	0.38	3.3
CMHR Small	5.2	0.18	3.5	30.3
FR Ether Large	5.5	0.11	2.0	17.3
FR Ether Small	5.5	0.18	3.3	28.6

[1] Assumes that the rate of loss will remain constant over the year – this assumption has not been tested.

In conclusion, the BAM, Elastogran and EUROPUR studies show estimated annual release rates in the range 0.01% to 2.4%, and one further study with the loss below the limit of detection. No unambiguous explanation for the evident variability is available, although various possibilities are explored. Significantly higher release rates were measured in the University of Surrey study, although this finding is consistent with the smaller dimensions of the pieces of foam tested and the high air-turnover rate used in the experiments. The loss rates

from the very small particles are considerably higher, again showing the importance of the size of the piece of foam.

2.2.2 Dust and loose crumb

The interpretation of these data for small foam pieces/particles will be returned to alongside the findings of Section 3.

2.3 FLAME RETARDANT LEVELS IN INDOOR ENVIRONMENTS

Separate to the model experiments described in Sections 2.1 and 2.2, a number of studies have been conducted measuring flame retardant levels in real indoor environments such as homes, offices, factories and automobiles. Concentrations have been measured in both air and dust.

These data are reported in the main RAR and are not reproduced here. They serve to show that TCPP and TDCP are widely found and underline the need to be able to explain realistically both the mechanisms by which the substances come to be found, and the concentrations.

2.4 APPLICATION TO ENVIRONMENTAL RISK ASSESSMENTS

2.4.1 Losses during curing and storage

After production, blocks of foam are routinely kept in storage at the production site until completely cool. By the same process of diffusion, it is reasonable to assume that local emissions of flame retardant could occur during this storage period. From information gained on a site visit to a major producer, it is known that foam tends to be stored in large warehouses with little air circulation. There is relatively little space between the blocks. Under those circumstances, it is very likely that the air around the blocks will be saturated with the additive, and thus there will be very little loss from the foam. This is very difficult to quantify.

2.4.2 Losses during service life

Service life losses are associated with diffusion through the polymer, followed by volatilisation or washing from the surface. It can reasonably be assumed, in the UK at least, that most domestic homes, offices, institutional or civic buildings will contain furnishings or insulation treated with TCPP and/or TDCP. From the studies reviewed, it can be concluded that losses from large pieces of foam during service life can occur.

2.4.3 Waste remaining in the environment

Waste remaining in the environment (WRITE) is dust and foam fragments generated by some form of physical attrition. It is also likely to be a very important contributor to measured environmental concentrations.

2.4.4 The importance of the receiving compartment

It is useful to summarise here factors that relate to this topic:

- The ESD on Plastics Additives (OECD, 2004) does not discuss this other than to suggest a 50% split between air and water for service life losses.

- The results and the models (discussed further in Section 3) show that the size of a piece of plastic or foam and the rate of air movement above it are very significant influences on the % emission rate, although it has less influence on the absolute rate, which is area dependent.

- The new studies demonstrate a 'sink' effect, i.e. the receiving compartment properties are important. This makes modelling difficult because the number of possible physical locations of foam is enormous. The development of a generic containment model should be possible and subject to validation, but has not been attempted in the present study.

- It could reasonably be assumed that in a closed compartment containing only PUR and air, should the air become saturated then the rate of emission from polymer will eventually equal the rate of redeposition (or readsorption)

- Given the known vapour pressure of TCPP (and hence its saturated concentration in air), it can be calculated from the rate of release (obtained using the diffusion models described in section 3.2) that a closed compartment of 1 m^3 in contact with 1 m^2 of PUR would become saturated in about an hour and the rate of release will drop to zero if a release-readsorption equilibrium is established.

3 A MATHEMATICAL MODEL FOR LOSS OF FLAME RETARDANT FROM FOAM

Mathematical modelling of the rate of diffusion of non-polymer molecules within plastics has been used to aid interpretation of available data, support some very clear assertions (e.g. about the importance of the size of pieces of plastic) and to compare with measured rates.

For the purpose of clarity, modelling performed in this section assumes that all FR present in the plastic is available for release.

3.1 FUNDAMENTALS

There are several basic premises to the approach set out in the following sections:

1. A polymer is seen as a continuous matrix, not subject to physical or biological degradation. Such processes are important but are not the subject of the present text. Given the properties of foam, some adjustments will be needed. Foam is not a continuous matrix since it contains air cells, therefore the effective thickness of polymer is less than the thickness of the foam block itself. It is assumed that there is

no barrier to the migration of flame retardant through the air cells. The effective polymer thickness will be controlled by the cellular wall structure.
2. Additives are initially uniformly distributed through the polymer, without there being 'domains' of additive at very high concentration; and that redistribution occurs as a result of surface loss.
3. Additives are not chemically bound to the polymer, the only interactions being weak (non-specific physical interactions or weak hydrogen bonds). This assumption is critical, because if stronger forces such as strong hydrogen bonds are formed, then the basis of the diffusion model is flawed. However, studies of temperature dependence can give insights as to whether such bonding is occurring.
4. In the modelling, the concentration of an additive in the receiving compartment (usually air) is assumed to not be influential; however, this is an important factor, which is considered qualitatively. A containment model would need to be developed to account for this and is outside of the scope of this study.
5. A containment barrier model is also required for those cases where the foam is covered by a fabric or other layers that might constrain the additive at or close to the interface between the foam and the barrier, and prevent air flow over the surface. This is also dealt with by a quantitative estimation.

Under such conditions, an additive molecule at the surface of a polymer may evaporate from it or be washed from it. This process can continue, and, if the rate of escape from the surface is faster than the rate of diffusion (which there is every reason to believe is the case) then, in time, a concentration gradient near the surface of polymer can arise, of a scale much larger than molecular (microns to millimetres in size, perhaps).

Diffusion of solutes in liquid solution is known to depend primarily on molecular size, temperature, and viscosity of the solvent. The diffusion coefficient ***D*** is the primary descriptor of rate, as expressed in Fick's laws of diffusion. Fisk and Jonathan (1999) have provided a review of the prediction of diffusion coefficients in solution. In practice, diffusion in homogeneous solution can only be measured easily where a concentration gradient exists. At a boundary between phases (e.g. aqueous and non-aqueous immiscible solutions), molecules generally cross the interface freely, particularly where this partitioning process is favoured by the position of equilibrium and the relative concentrations in the two phases.

Considering polymers, the situation is more complicated because they are not very mobile, and therefore molecules can move less easily within the polymer than they can in solution. Nevertheless, many of the same principles apply. At the polymer-air interface, it could be envisaged that the additive could accumulate on the surface, but it may be assumed that where air is circulating freely, the concentration of the additive in air will be effectively zero, and that molecules of additive reaching the surface will evaporate rapidly. The consequence is that a diffusion gradient will be established within the polymer. A further uncertainty is that in cellular foams a different mechanism may exist due to the cellular structure and the establishing of a cellular-volume/external-atmosphere exchange mechanism (Note: this is akin to the cell wall acting as a gas/vapour transport membrane rather than a semi-infinite slab (as assumed herein, applying Fickian and Case I and Case II diffusion).

3.2 DEVELOPMENT OF THE MODEL

Sections 3.2.1 and 3.2.2 develop some simple equations that can readily be applied to the migration of additives in polymers. Sections 3.2.3 to 3.2.5 demonstrate the influence of

varying different parameters on the outputs of the model, while application of the model to scenarios relevant for polyurethane foams and comparison with measured data are discussed in Sections 3.3 and 3.4.

The mathematics of diffusion in solution and polymers is complex and so some major simplifications have to be made just to generate some practical numbers.

Migration of substances in polymers has received considerable attention in respect of studies for food contact approval, and whilst there are standard tests to meet regulatory targets, a reasonable body of more fundamental research has been carried out, and is still ongoing. This field of research is useful as a source of data, but it is beyond the present scope to review it. The equations used are similar, and the papers obtained contain measured diffusion coefficients.

Migration in polymers is sufficiently slow that it can be readily assumed that molecules that reach the polymer surface can volatilise or dissolve in any solvent there much faster than the diffusional rate (Fisk *et al*., 1999). It at least represents a reasonable worst case.

The sources of the equations used are such standard sources as Crank, 1975.

3.2.1 Initial rates

Fick's second law of diffusion deals with diffusion which is time-dependent, i.e. during the period between time zero and the establishment, if it occurs, of a steady state.

Consider a newly formed polymer containing evenly-distributed additive at concentration C_0. If the area of surface exposed to a sink for the substance is A, then Fick's second Law can be solved such that, for small amounts of loss (up to approx. 20%), the number of moles lost N is given by:

$$N = 2AC_0\left(\frac{Dt}{\pi}\right)^{0.5}$$

where D is the self-diffusion coefficient. This equation predicts that rate will slow with time, which is a consequence of the physical fact that the molecules near the surface will escape first, and then it takes more time for the deeper ones to reach the surface and escape. It also shows that the rate of loss is proportional to area and concentration, which seems entirely reasonable.

The diffusion coefficient represents the rate at which a molecule can diffuse through a medium. Diffusion coefficients depend on temperature, molecular size, and the viscosity of the solvent, and they can be predicted relatively easily (Fisk and Jonathan, 1999). Workers on diffusion in polymers give similar results (see Section 6, and in particular Reynier *et al*., 2001). Reynier *et al*. did not carry out an *ab initio* prediction, they simply sought correlation of some molecular size and shape parameters obtained from a molecular dynamics code with actual diffusion measurements in a single type of semicrystalline polypropylene at 40°C. The authors commented that these would not necessarily generalise to other conditions, or to other polymers. Such correlation approaches can however be very useful and could be constructed for PUR foams with appropriate experimental work.

3.2.2 Steady state rates

Eventually the initial rate of movement slows. The achievement, if it occurs, of a steady state implies that a linear concentration gradient is established over some depth ***L*** of the polymer. Again assuming that a single surface is exposed, with a concentration ***C*** in the interior of the polymer, then

$$\frac{N}{t} = \frac{ACD}{L}$$

This equation again shows that the rate of loss from the matrix is proportional to area and concentration.

Whether the initial rate model or the steady state model is most appropriate in the present context is explored below.

3.2.3 Application of the models

Application of the models requires a mixture of reasonable assumptions and measured values for the input data. These are described in **Table B.10**.

Table B.10 Input parameters for models

Constant	Meaning	Comment
A	Exposed area (m^2)	Reasonable assumptions can be made
C	Concentration of additive (%)	Usually known
t	Time scale (y)	Usually known
D	Diffusion coefficient (m^2/s)	Measurements for diffusion rates of additives in polymers are known, and a number of predictive methods are available (see Section 6)
L	Thickness of polymer over which a steady state is established (m)	This may well not be known; since it is only needed for the steady state equation, it may not be relevant.

3.2.4 Use of the Initial Rate Model

For the 'demonstration' calculations, the model was set up using the following parameters, reasonably representative of polymers but not intended to be specific.

Substance molecular weight: 300 g/mol

Temperature: 25°C

Diffusion coefficient: 3×10^{-15} m^2/s

Concentration of additive: 5%

Density of polymer: 1100 kg/m^3 – this assumes the bulk density to be consistent throughout.

These values were kept constant while the initial investigation was carried out.

3.2.4.1 Large flat pieces of plastic

3.2.4.1.1 Model outputs

The influence of surface area and timescale on the output of the initial rate model was investigated. To simplify calculations, it is assumed that only one surface is available for diffusion. This might be justified since during service life, the surfaces of polyurethane foam blocks are covered in some way e.g. by upholstery fabric in flexible foam for sofas or mattresses, or sandwiched between plastic or metal for rigid foam in construction applications.

For a piece of plastic with thickness 0.1 m, the surface area available for diffusion was varied from 0.0001 m^2 to 5 m^2 over timescales of 5, 10 and 20 years. The model outputs in grams are presented in **Table B.11**.

Table B.11 Amount of additive lost (grams) as a function of surface area and timescale

Timescale (y)	Surface area (m^2)									
	0.0001	**0.0005**	**0.001**	**0.005**	**0.01**	**0.1**	**1**	**2**	**3**	**5**
5	0.00427	0.0213	0.0427	0.213	0.427	4.27	42.7	85.4	128	2.13E+02
10	0.00604	0.0302	0.0604	0.302	0.604	6.04	60.4	121	181	3.02E+02
20	0.00854	0.0427	0.0854	0.427	0.854	8.54	85.4	171	256	4.27E+02

This demonstrates that the amount of substance released varies linearly with surface area and is dependent on the timescale considered. Expressed as a percentage loss averaged over time, as in **Table B.12**, there is no dependence on surface area since the initial amount of additive present also varies linearly with surface area for a rectangular block.

Table B.12 Average annual percentage loss (thickness = 0.1 m)

Timescale (y)	Average percentage loss %/y
0.1	1.1
1	0.35
5	0.16
10	0.11
20	0.08

The magnitudes are discussed below. **Figure B.2** shows the total amount lost versus timescale for a 1 m^2 x 0.1 m block of foam, while **Figure B.3** shows annual percentage loss as a function of timescale. While the total amount lost clearly increases over time, this relationship is not linear, as the rate of loss decreases with time. This also means that when considering average annual losses, e.g. for regional risk assessment calculations for in-service loss, the expected lifetime of the product is an important consideration

For this initial rate model, the total amount of substance lost is independent of the thickness of the polymer block. **Table B.13** shows the model outputs for a block with surface area 1 m^2 and varying thickness, over a 10-year timescale. Percentage loss is inversely proportional to

thickness, since the initial amount of additive present is dependent on thickness but the net amount lost remains constant.

Table B.13 Amount lost as a function of thickness
(surface area = 1 m^2, timescale = 10 years)

Thickness (m)	Total amount lost (g)	% lost over total time	Average percentage loss (%/y)
0.005	60.4	22	2.2
0.01	60.4	11	1.1
0.05	60.4	2.2	0.22
0.1	60.4	1.1	0.11
0.5	60.4	0.22	0.022

Figure B.2 Total amount lost as a function of timescale (surface area = 1 m2)

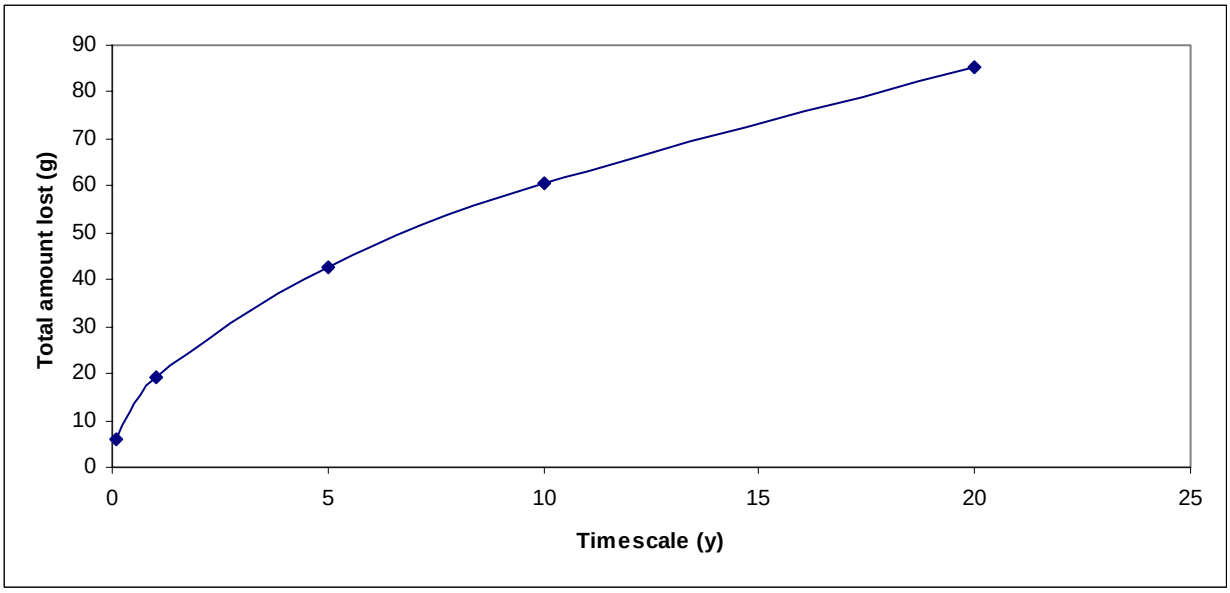
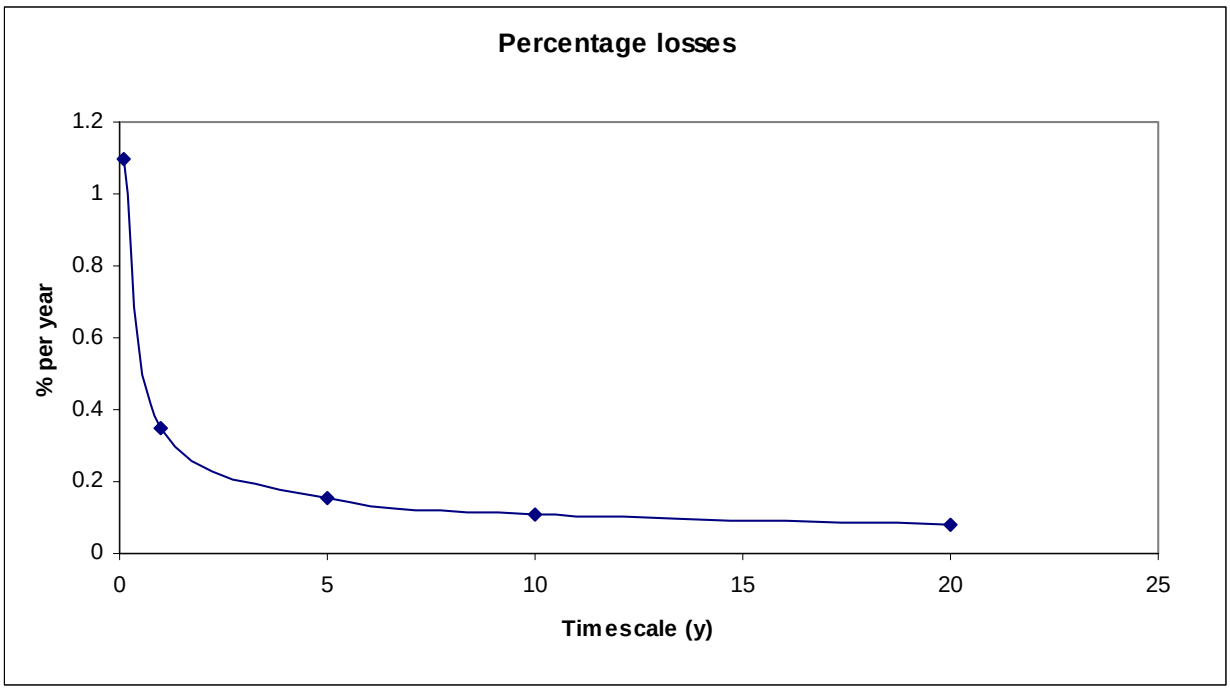


Figure B.3 Annual average percentage loss as a function of timescale (thickness = 0.1 m)



3.2.4.1.2 Applicability to polyurethane foams

Due to the nature of foams, the bulk density of a foam block is considerably lower than the density of the polymer itself. Typical flexible foams for use in furniture have a bulk density of 10 – 60 kg/m^3 (Woods, 1982). For the purposes of modelling, it can be assumed that there is no limitation to the diffusion of an additive through 'air cells' in the foam. Since it is already assumed that diffusion is occurring from one surface only, the "effective" thickness of polymer can therefore be determined if both densities are known and the available surface area remains constant:

Effective thickness = Actual thickness x (Bulk density of foam/Density of polymer)

As described in the risk assessment reports for TCPP, TDCP and V6, blocks of foam are stored on-site during the curing process. Curing time is typically 48 hours and temperatures can be as high as 150°C in the middle of a large block, although at the surface temperatures will be close to ambient. There is therefore potential for volatile emissions at this stage of the life-cycle.

3.2.4.2 Small particles

As well during the service life of polyurethane foam articles, losses due to diffusion should also be considered for two other scenarios. Waste remaining in the environment (WRITE) arises from physical abrasion of a polymer due to weathering and wear. For polyurethane foams, such losses may occur in addition to the in-service losses associated with use in furniture foam and result in small particles (e.g. 10-100 µm in size) of polymer collecting, for example, in dust. On this scale it could be assumed that no correction is required for bulk density of the foam.

A further life-cycle stage which may be of relevance is the production of rebonded or loose crumb foam from scrap foam produced as a result of cutting blocks into the required shapes. Scrap foam is shredded into pieces approximately 1 cm in diameter and, taking into account the correction for bulk density, there may be potential for significant volatile losses from these small pieces during the process. Once incorporated into rebonded foam or loose crumb furniture, it could be assumed that the diffusion behaviour is equivalent to that of a larger solid block.

In both cases, the assumption that diffusion occurs from only one surface is not valid, as the particles are likely to be approximately spherical. A correction for the increased surface area is therefore required.

For a spherical particle with diameter 100 μm, the surface area is calculated from $4\pi r^2$ and the volume is $4\pi r^3/3$ (r = radius = 50 μm), therefore the area is 3.14E-08 m^2 and the volume 5.24E-13 m^3. Inputting these values the model gives a percentage loss of 100% in less than a day, indicating that all additive would be lost over a very short timescale. Under conditions of low air movement, this loss may be ameliorated. The loss may seem surprising but reflects the small particle size. It should be borne in mind, however, that the model assumes a polymer that would have no specific interactions with any additive. Given that polyurethane is frequently used as an adsorbent in analytical chemistry, this assumption may be invalid.

The initial rate model is only strictly valid for up to about 20% loss of the substance from the polymer. At losses up to 50% the steady state model is therefore preferred because its parameters would reflect the physical reality of the concentration gradient present. If complete loss is predicted, this is outside the scope of both models but the results are still useful qualitatively, as an indication of the order of magnitude.

For a particle of 1 cm diameter, as applicable for producing rebonded or loose crumb foam, a correction for bulk density is required. The surface area available for emission remains at $4\pi r^2$ (3.14E-04 m^2), but the "effective" volume can be calculated by:

Effective volume = Actual volume x (Bulk density of foam/Density of polymer)

Assuming that the foam has a bulk density of 30 kg/m^3, the effective volume is therefore 1.43E-08 m^3 and the effective thickness is 1.5E-03 m. Inputting these values into the model with a timescale of 1 day gives an emission of over 100%. This indicates that volatile losses of additive during the production of rebonded foam could potentially be significant. Controls in these locations may not be so stringent as those in place at foaming locations where isocyanates are in use. However, it should be noted that typical industry practice is to carry out granulating processes within contained equipment, therefore actual rates of loss are anticipated to be much lower than the modelled results.

3.2.4.3 Impact of varying other parameters

To investigate the dependence of releases on parameters other than the dimensions of the piece of plastic, a fixed size of 1 m^2 surface area and 0.1 m thickness was used in the model with a 10 year timescale. Unless stated otherwise, other values used were as described in section 3.2.4.

3.2.4.3.1 Molecular weight

A number of measured diffusion coefficients in polymers are available, but a predictive equation is also available (Reynier *et al*., 2001). Predicted diffusion coefficients are dependent on the molecular weight (MW) of the additive according to the relationship:

$$D\ (m^2/s) = 10^{(-7.83 - 0.0062MW)} / 10000$$

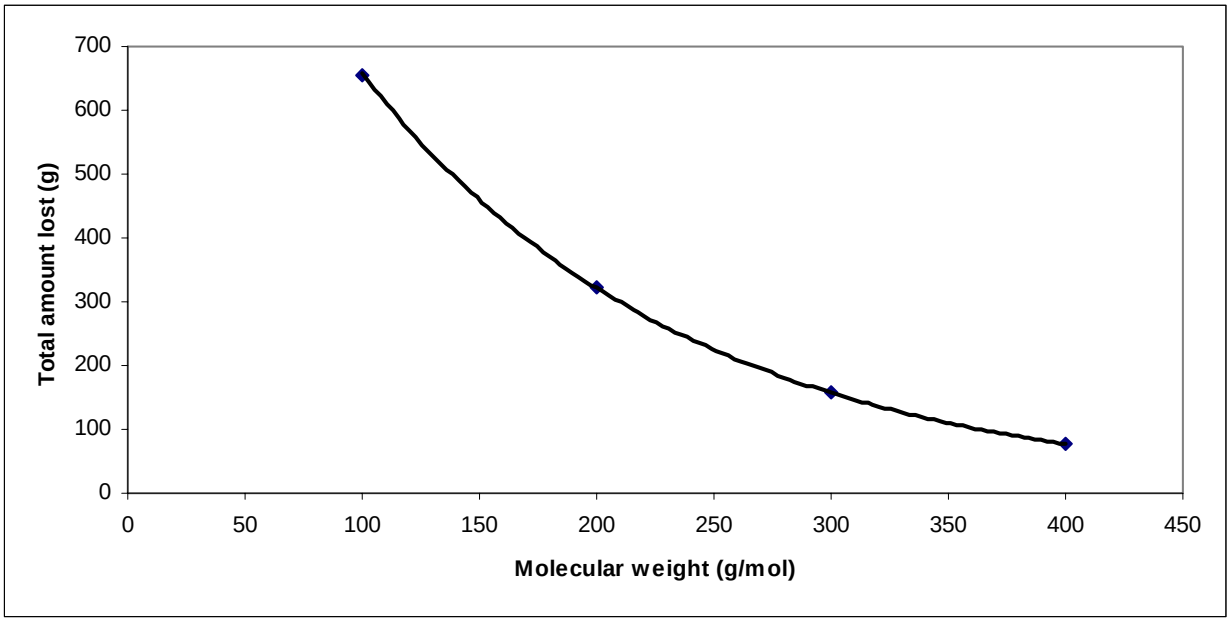
Using diffusion coefficients predicted by the model, releases for varying molecular weights are shown in **Table B.14** and **Figure B.4**.

Table B.14 Amount lost as a function of molecular weight

Molecular weight (g/mol)	Predicted diffusion coefficient (m^2/s)	Amount lost over 10 years (g)	Average annual loss (%)
100	3.548E-13	656	1.2
200	8.511E-14	322	0.585
300	2.042E-14	157	0.287
400	4.898E-15	77	0.14

It can therefore be seen that, as might be expected, the amount of additive lost increases exponentially with decreasing molecular weight. This approach is much less sensitive than the use of vapour pressure as a guide, as described in the ESD; vapour pressure changes very rapidly with changing molecular weight, whereas the diffusion model is less sensitive.

Figure B.4 Amount lost as a function of molecular weight



3.2.4.3.2 Temperature

Predicted diffusion coefficient, and hence release rate, is also dependent on temperature according to the relationship (many references, reviewed in Fisk and Jonathan, 1999):

$D(X°C) = [D(25°C) \times (X + 273)]/298$

This is shown in **Table B.15** and **Figure B.5**. The equation used here is only applicable at fixed viscosity of polymer (i.e. a thermoset polymer such as PUR, rather than a thermoplastic one).

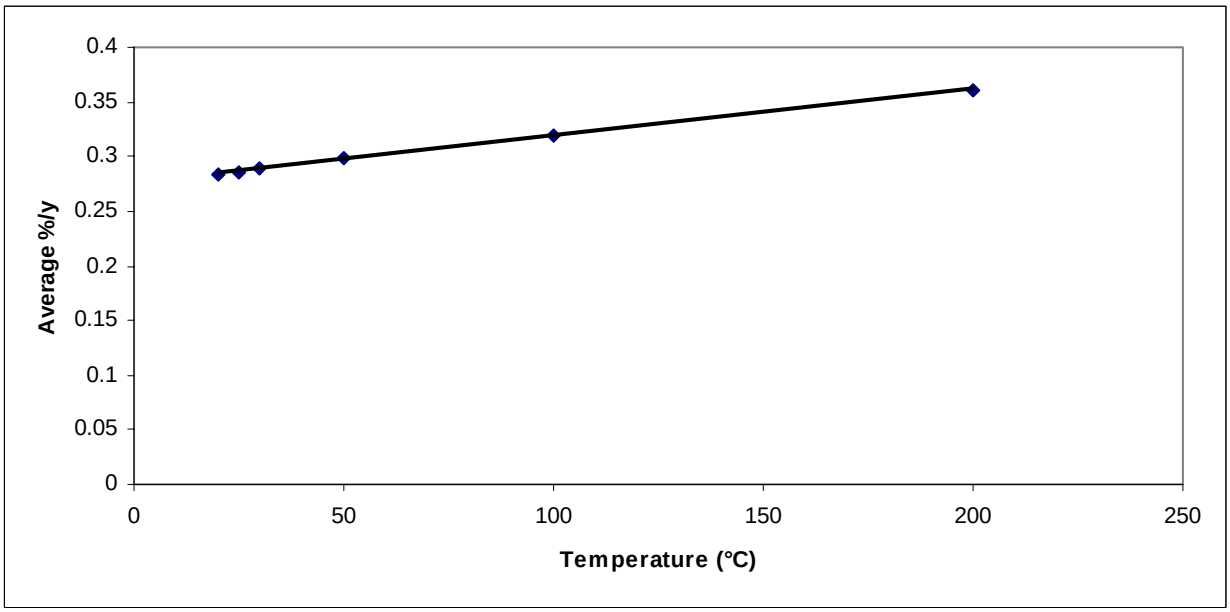
Table B.15 Amount lost as a function of temperature

Temperature (°C)	Predicted diffusion coefficient (m2/s)	Amount lost over 10 years (g)	Average annual loss (%)
20	2.007E-14	156	0.284
25	2.042E-14	157	0.286
30	2.076E-14	159	0.289
50	2.213E-14	164	0.298
100	2.556E-14	176	0.320

Although the difference made by temperature is small, this could become more significant for high or low-temperature applications.

The effect of temperature is small; this is a very useful result because the Plastics Additives ESD does not deal with this issue. For thermoplastics, the temperature dependence would be a little higher, since the viscosity of the polymer will change with temperature, but that is not described herein as it is not applicable to polyurethane foams.

Figure B.5 Amount lost as a function of temperature



3.2.5 Use of the Steady-state model

The initial rate model is only strictly valid for up to about 20% loss of the substance from the polymer. At losses up to 50% the steady state model is preferred on theoretical grounds. In some instances (very small particles) complete loss is predicted, which is outside the scope of both models but the results are still useful qualitatively, as an indication of the order of magnitude. The steady-state model refers to the point at which a linear concentration gradient has been established within the polymer block. At this stage both surface area and thickness are important for determining the amount of substance lost, but expressed as a percentage per year, the rate of loss is dependent only on thickness.

The release rates predicted by the steady-state model are lower than the initial rate model. In the extreme scenario of very thick pieces of polymer, percentage loss values will be very low indeed, as shown in **Table B.16**.

Table B.16 Percentage loss per year as a function of thickness (surface area 1m^2)

Thickness (m)	% per year
0.5	3.78E-05
1	9.46E-06

3.3 APPLICATION OF THE INITIAL RATE MODEL TO PUR FOAMS CONTAINING TCPP

3.3.1 Model Parameters

The initial rate model was tested for various scenarios relevant to the life cycle of TCPP. The following parameters were fixed in the model, which are representative of the properties of foams for which measured data are available, as described in Section 2.

Substance molecular weight: 328 g/mol

Concentration of additive: 5%

Density of polymer: 1100 kg/m^3

Bulk density of foam: 30 kg/m^3

The diffusion coefficient (3E-15 m^2/s) obtained from the literature was used.

3.3.2 Life cycle Stages

The outputs from the model are given in **Table B.17**.

3.3.2.1 Losses during curing

At foam production sites, large blocks of foam (typically with dimensions 60 x 2.2 x 1.25 m) are stored on-site while curing takes place. Temperatures in the interior can reach up to 150°C, but at the surface the temperature will be near ambient.

Inputs to the model were therefore as follows:

Surface area: 132 m^2

Thickness: 0.034 m (correcting for density)

Temperature: 25°C

Timescale: 2 days

3.3.2.2 Losses during service life

A typical application of PUR foam containing TCPP is in furniture such as sofas. Dimensions of a piece of such furniture foam could be, for example, 2 x 0.5 x 0.1 m. The temperature of a typical room is 23°C.

Inputs to the model were therefore as follows:

Surface area: 1 m^2

Thickness: 2.7E-03 m (correcting for density)

Temperature: 23°C

Timescale: 10 years

3.3.2.3 Waste Remaining in the Environment

Waste remaining in the environment (WRITE), for the present purpose, refers to small particles of foam produced from weathering and wear during service life, separate to volatile releases from the foam block itself. Volatile releases can also be expected from such particles. Applying the scenario to TCPP, the inputs were as follows:

Surface area:3.14E-08 m^2

Thickness: 50 µm

Volume: 5.24E-13 m^3.

Temperature: 23°C

Timescale: 1 day

3.3.2.4 Production of rebonded and loose crumb foam

The following inputs were used for TCPP:

Surface area: 3.14E-04 m^2

Thickness: 1.36E-04 m

Mass of additive present: 1.572E-05 kg

Temperature: 23°C

Timescale: 1 day

Table B.17 Releases of TCPP from typical life cycle stages

Lifecycle Stage	Percentage loss
Curing	0.076% in two days using initial rate model
In-service	1.3% per year before accounting for any covering, using steady state model
WRITE	100% loss in a few days (both models)
Rebonded foam	Maximum of 13% in one day predicted by initial rate model

These results are subject to a number of approximations and assumptions, and should not be over-interpreted.

3.4 COMPARISON OF MODEL WITH MEASURED VALUES

Table B.7 summarises the annual emissions derived from available studies in the literature.

An uncovered upholstery foam tested by EUROPUR in 2001 showed a measured release rate of 0.03% per year, whereas in a test by UBA in 2003, a release rate of 2.4% per year was measured. Since the exact dimensions of the foam tested by UBA are not known, it is not possible to directly compare the output from the model with this result. However, the result is not inconsistent with the model prediction of 1.3% per year for in-service loss.

In practice, some amelioration of the model results is to be expected since in practice, foams used in most applications are covered in some way e.g. upholstery fabric for furniture foams, steel panels for insulation foams.

Experiment 1 from the University of Surrey study is the one of most importance, because it included ambient conditions. Emission rates were found to be highly dependent on the dimensions of the piece of foam. Higher temperatures lead to higher diffusion rates and hence higher emissions. The results of this experiment were used to test the new model, as described below. It should be noted that during the air turnover period, the ovens used in this test may have become partially saturated.

For CM ether foam containing 8.47% TCPP, density 32 kg/m^3, size 50 mm x 50 mm x 15 mm ('small'), the initial rate model at 20°C predicts 7.78% loss over 6 weeks from one face of 50 mm x 50 mm, which should be multiplied by 3.2 for the whole surface area of the block, giving 24.9% loss of TCPP, or 2.1% of the total weight. The measured weight loss at this temperature is 0.26%. Note: a factor of 8 difference may seem high but this may be due to containment effects.

For pieces of size 100 mm x 100 mm x 50 mm the initial rate model gives, at 20°C, 2.34% loss over 6 weeks from one face of 100 mm x 100 mm, which should be multiplied by 4 for the whole area, giving 9.36% loss of substance, or 0.79% of the total weight. The measured weight loss at this temperature is 0.11%.

Experiment 2 from this study indicates that the observed weight loss is mainly due to loss of flame retardant.

The data for loss from dust and foam show a plateau at around 40% loss, preceded by rapid (and hence facile) loss. The modelling predicts that all the FR should be lost very quickly. This suggests that 60% of the FR is unavailable to be lost from the foam to its surroundings.

The model seems to predict values of the right order of magnitude, and the relative rates for pieces of different sizes are dealt with well. The pieces used were all small relative to foam in actual use. Results are expressed in various forms in **Table B.18**; it must be borne in mind that these results do not reflect the loss that might occur with larger (or smaller) pieces.

Table B.18 Comparison of model predicted emissions with measured total weight loss (CM ether foam)

			Total Weight Loss (%)	
Temperature (°C)		**Predicted**	**Measured**	
	Small	Large	Small	Large
20	2.1	0.79	0.26	0.11
60		0.84	7.12	3.21
			TCPP Loss (%/d)	
Temperature (°C)		**Predicted**	**Measured**	
	Small	Large	Small	Large
20	0.59	0.22	0.07	0.031
60		0.24	2.0	0.90
			TCPP Loss (%/y)	
Temperature (°C)		**Predicted**	**Measured**	
	Small	Large	Small	Large
20	100	80.3	26.7	11.3
60		100	100	100

At 60°C the model predicts total weight loss of 0.84% for a large piece of foam, while the measured data show a loss of 3.21%. This temperature dependence is much higher than expected for weak intermolecular forces, due to an activated process not accounted for in any diffusional model. The magnitude of the temperature dependence suggests some kind polar interaction with the polymer. Indeed, it is known that both substances adsorb moderately strongly to soil, which whilst being a very different medium, contains polar and non-polar domains just as polyurethane does. However, an irreversible chemical reaction is not implied by the data. The model predicts relatively small diffusional differences between TCPP and TDCP under conditions of high air turnover; this was found at 20°C. However, since air turnover is in fact important, then the lower loss rate of TDCP would be consistent with its lower vapour pressure, TDCP may also have a greater propensity than TCPP to associate with the PU foam.

3.5 CONCLUSIONS

3.5.1 Outcome of modelling

The modelling shows several important findings, the implications of which may need further work, not necessarily within the present project:

- Loss rates from pieces of foam of dimensions 1 cm and below are predicted to be very fast, and, in a receiving compartment of sufficient size, complete loss can occur over a period of hours. The measured data show this to be correct, but modified for a value of around 60% of the FR which is not lost at all.

- Loss rates from large thick pieces of plastic are predicted to be very much slower than the predicted values for flame retardants from the Plastics Additives ESD. However, even large blocks of foam contain a relatively small amount of polymer, and predicted rates are of the same order as measured values.

3.5.2 Comparison with Emission Scenario Document for Plastics Additives

The current Emission Scenario Document for Plastics Additives (OECD 2004) gives generic emission factors for losses of additives during the service life of plastic goods. For indoor service life, a default release of 0.05% to air over the service life for an additive of moderate volatility. Typical service life varies from 5 to 20 years depending on the application. For an additive with high volatility, the loss rate is increased by a factor of 5.

As demonstrated in Section 3.2, the total amount and percentage of additive lost through diffusion is dependent on the dimensions of the plastic, and the rate of loss is not constant during the service life of an article. While the default loss rates given in the ESD are within the range of values predicted by the model (e.g. **Table B.12**), there are grounds to suggest that a review is needed.

The Plastics Additives ESD approach to in-service loss does not take into account:

- The concentration of additive in the polymer (although this will not change the rate when expressed as a % of initial concentration).
- The mechanism of additive loss and the effect of containment.
- The effect of polymer matrix type and structure on diffusion rates.
- The relationship between molecular size and rate of diffusion.
- Time-dependence of average annual release rates.
- Time-temperature profile at different points in the life cycle.
- Influence of the dimensions of the piece of plastic, which is probably the most important variable.
- The significance of the air exchange rate, and the potential for saturation of the receiving air in contained situations – most practical situations are “contained”.
- The presence of any fabric or other barrier at the surface.
- The ESD sets a fixed rate of in-service loss, modified according to volatility. In practice, the key variable (D) is related to molecular size; volatility is also related to size.

4 DERIVATION OF RELEASE RATES FOR USE IN THE ENVIRONMENTAL RISK ASSESSMENTS

For application of the above findings for the purposes of risk assessment, a 'reasonable worst case' interpretation of the various sources has been applied.

Table B.19 sets out the basis of treatment of these releases to be used in the RAR. The rates presented in the table relate to TCPP. It must be noted that the % figures **have all been multiplied by a fraction**, representing that which is 'available' for release, i.e. is not very strongly bound. This fraction is estimated to be 0.4 for TCPP (from the data) and 0.1 for TDCP and V6 (an estimate from a very limited amount of data).

Table B.19 Conclusions of the modelling related to life cycle stages in the risk assessment of TCPP, TDCP and V6

Application area	Conclusions
FLEXIBLE FOAM	
Foam production	It is considered that the only source of releases from large foam production sites will be from curing and storage (see below for more details). At small sites, a handling release is also included, in line with the published ESD. Additional releases associated with the generation of foam dusts due to cutting of foam blocks at the site must also be considered, since modelling now shows that FR contained in foam dusts will very rapidly be volatilised (see WRITE (Waste Remaining In the Environment) below). Since high levels of control are known to apply at these sites, it is considered adequate to assume that this release is negligible and contained within the curing/storage losses (see below).
Curing and storage at foam production sites	Rates of release to air are calculated from the in-service loss rate, and loss rates of 2.4% per year (worst-case emission from the BAM study) could apply. However, blocks are large and the air around them at the production site would probably be saturated for most of the time. The effect of air saturation on release rates is demonstrated in Experiment 4 of the University of Surrey study where at 60°C a release of 0.11% TCPP was measured over 4 months in a sealed vial, compared with 39.5% loss in 6 weeks in an oven test with air movement. The release rate of 2.4% is therefore considered to be too high for the conditions at the production site, and reduction by a factor of 100 is proposed. The proposed rate is therefore 0.024% to air, per year. This fraction applies to the fraction of product actually in storage at any one time, estimated in the RAR at 2.5%, giving an overall loss of **0.0006% per year to air**, for all sites. 50% is assumed to adsorb to surfaces and reach wastewater due to cleaning. While some internal parts of the foam blocks reach a high temperature during curing, this is not expected to have a significant influence on the release rate (as discussed in section 3.3.2.1). Correcting for availability, the release rates used in the risk assessment are: TCPP: 1.2E-04% to air and 1.2E-04% to wastewater TDCP: 3E-05% to air and 3E-05% to wastewater V6: 3E-05% to air and 3E-05% to wastewater

Application area	Conclusions
Further processing (i.e. at cutters' and furniture manufacturers' sites)	Cutters (termed 'converters' by the industry) and furniture manufacturers will store foam and cut it. The data and models indicate that there must be volatile losses from such locations. The same rate as for curing and storage at producers' sites should be applied for such stages. Additional releases associated with the generation of foam dusts must also be assessed, since modelling shows that FR contained in foam dusts will be volatilised very rapidly (see WRITE below). While it is known from consultation that dusts are collected at the point of cutting by extractors attached to the blade, it could still be the case that a small proportion of dusts and small pieces of foam are exposed to air and hence that some FR could be released on a local scale. A study has established that up to 0.1% of foam is lost as dust and non-recycled offcut pieces (EUROPUR, 2005), and it is herein assumed that 1% of this material is not collected by the extractor systems. These pieces of FR foam could then release FR into the workplace air and could reach the environment via air and also wastewater (via adsorption and cleaning). A release rate of **0.0005% to air and 0.0005% to water per year** is therefore proposed. Correcting for availability, the release rates used in the risk assessment are: TCPP: 2E-04% to air and 2E-04% to wastewater TDCP: 5E-05% to air and 5E-05% to wastewater V6: 5E-05% to air and 5E-05% to wastewater
In service loss for flexible foams (covered upholstery foams, mattresses, automotive furnishing & sound insulation; including rebonded foam)	For uncovered foams, the % loss rate could be as high as 2.4%/year. However, given that the air surrounding the foam is likely to be slow moving, and the foam is covered in service by fabrics and upholstery, then it is proposed to reduce the rate by 10 x for each of these two release-limiting factors. This is an estimate that is justified pragmatically on the basis of workplace monitoring data, and the fact that FR performance is not dramatically lost over time. An annual rate of release of **0.024% per year** to air is proposed for TCPP. For TDCP and V6, which have much lower volatility, a rate correction of ~25 is appropriate to allow for the slower rate of release at moderate air turnover, which is consistent with the ESD. Therefore the annual rate of release for TDCP and V6 is proposed as **0.001% per year**. Please note that this correction refers to *slower speed of release*, and is separate from the correction for lower *total amount available for release* for these substances compared with TCPP. Please refer to the discussions of different air turnover scenarios below the table. Correcting for availability, the release rates used in the risk assessment are: TCPP: 9.6E-03% to air TDCP: 1E-04% to air V6: 1E-04% to air
Loose crumb	The rate for loose crumb, used mainly in outdoor furnishing, with covering, is set to 0.24% for TCPP, 0.01% for TDCP and V6. Correcting for availability, the release rates used in the risk assessment are: TCPP: 0.096% to air TDCP: 1E-03% to air V6: 1E-03% to air

Application area	Conclusions
Recycling of flexible foams: loose crumb and rebonding	Both methods involve the generation of foam granules. Granule sizes are typically around 1 cm and therefore the model shows that losses of FR could be as high as 13% per day. However, the granulation and rebonding processes are contained within equipment, therefore rates of loss are anticipated to be much lower. Granulating machines are fitted with dust extraction equipment. Taking the same approach as for cutting at furniture manufacturing sites, it could be estimated that up to 0.1% of foam is lost as dust, and that 1% of this material is not collected by the extractor systems and could be released to the local air compartment. Releases are therefore 0.001% to air. Correcting for availability, the release rates used in the risk assessment are: TCPP: 4E-04% to air TDCP: 1E-04% to air V6: 1E-04% to air
RIGID FOAMS	
Rigid foam (production of panels)	As proposed in earlier work (Dec 03), it is considered that the only source of releases from large foam production sites will be from curing and storage (see below for more details). At small sites, a handling release is also included, in line with the published ESD. Additional releases associated with the generation of foam dusts due to cutting of panels at the site must also be considered, since modelling shows that FR contained in foam dusts will be volatilised very rapidly (see WRITE below). Since high levels of control are known to apply at these sites, it is considered adequate to assume that this release is negligible and contained within the curing losses (see below).
Curing and storage at foam production sites	Rates of release should now be calculated from the in-service loss rate of an uncovered foam. Loss rates of 2.4% per year could apply, equating to 0.0066% per day. However, blocks are large and the air around them would probably be saturated, as discussed previously for flexible foams, so this rate is estimated to be 100 x too high. The presence of facing panels will be an important additional retarding factor, say 10 x. The proposed rate is therefore 6.6E-06**%** to air per day. This fraction applies to the fraction of product actually in storage at any one time. This is not estimated in the RAR but could be around 1%, giving an overall loss of **2.4E-5% per year to air**, for all sites. Correcting for availability, the release rate used in the risk assessment is: TCPP: 4.8E-06% to air and 4.8E-06% to wastewater
1K foams – releases from foaming *in situ*	Release from foaming *in situ* (e.g. during building work) is based on the rate of release in service. Based on an uncovered foam (at the time of spraying) the loss rate should be as calculated for uncovered flexible foam, reduced by an estimated 10 x due to the enclosed nature of the application, giving 0.00066% per day. The formation of a 'skin' on spray foam may make this a slight over-estimate. Correcting for availability, the release rate used in the risk assessment is: TCPP: 0.096% to air
Spray foams – releases from foaming *in situ*	Release from foaming *in situ* (e.g. insulation of roofs) is based on the rate of release in service. Based on an uncovered foam (at the time of spraying) the loss rate should be as calculated for uncovered flexible foam, reduced by 10 x due to the large volume of the foam produced, giving 0.00066% per day. Correcting for availability, the release rate used in the risk assessment is: TCPP: 0.096% to air
In-service loss (sandwich panels; 1K foam; spray foam)	All of these foam types are in highly enclosed environments in service, and the rigidity of the foam would be a further retarding factor. Given the use in buildings where there will be very limited air circulation around the exposed foam and edges of panels, it is proposed to now set these rates of release to zero.

Application area	Conclusions
BOTH FOAM TYPES	
WRITE – weathering and wear in service, via abrasion and creation of small foam particles	The present approach is to assume complete release of the available fraction from small particles. The modelling suggests, however, that this will occur very rapidly, and dust reaching landfill will no longer contain the additive FR in a form that is available for release. Correcting for availability, the release rates used in the risk assessment are: TCPP: 0.8% to air TDCP: 0.2% to air V6: 0.2% to air
Release within landfill	It is not realistic to attempt to model losses from landfill. However, the Environment Agency has made measurements of TCPP and TDCP in leachate from a number of landfills, and these will be used to set up a general approach to releases.

TDCP and V6

The rates (before correction for the 'available' fraction) to be applied in the risk assessments for TDCP and V6 require further consideration. It should not be assumed that vapour pressure is a perfect indicator of volatility (it is a guide), because vapour pressure relates to the equilibrium of a vapour with an excess of the pure substance, e.g. as a liquid phase. Three scenarios can be identified:

- Where there is **very low air turn over**, all three substances will give saturation of the air and hence almost the same rate of loss, which would be very low, controlled by the air turn over. This applies to storage of foam.
- Where there is **high turn over**, diffusion in the polymer controls and the rates for TDCP and V6 will be only very slightly lower than those of TCPP. This applies to small particles.
- In the situation of **moderate air turn over** the air saturation is reached quickest for lower volatility, since it requires less substance, and hence the loss rate will be slower for TDCP and V6, although it is hard to estimate by how much. This applies to in service loss of flexible foam, including furniture and automotive foam. The ESD applies a factor of 25 x lower rate for TDCP and V6 relative to TDCP, for all stages; it seems appropriate to use this factor for these applications, although it is empirical.

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6 LITERATURE SEARCH RESULTS FOR DIFFUSION OF ADDITIVES IN POLYMERS

Diffusion coefficients of additives in polymers. I. Correlation with geometric parameters
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Publication Source
Journal of Applied Polymer Science (2001), 82(10), 2422-2433
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JAPNAB

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John Wiley & Sons, Inc.
Abstract
Diffusion coeffs. of a broad range of mols. (mol. wt. 100-800 g/mol) were measured in polypropylene by solid/solid contact methods at 40°. The behaviors of the various mols. are compared to those of linear alkanes. The diffusion coeffs. are correlated to parameters describing size, shape, and flexibility of the mols. The concept of weighted fractionated vol. is introduced using mol. modeling. It enables the classification of the mols. according to modes of mol. displacement (crawling, jumps, or dual mode).
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Language
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Accession Number
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Document Number
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Title
Prediction of worst case migration: presentation of a rigorous methodology
Author
Reynier, A.; Dole, P.; Feigenbaum, A.
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Publication Source
Food Addit. Contam. (1999), 16(4), 137-152
Identifier-CODEN
FACOEB
ISSN
0265-203X
Publisher
Taylor & Francis Ltd.
Abstract
An improvement of the Piringer model, allowing the prediction of a worst case migration from packaging to food is presented here. The authors are proposing other consts. for the calcn. of the upperbound value of the diffusion coeff., using exptl. data detd. by a film to film method. Considering the plasticizing effects of food simulants, a model involving the variation of the diffusion coeff. vs. space and time must be used. Future fields of investigation are discussed: the relationship between

diffusion coeffs. and the vol. of the migrant (instead of molar mass), and the variation of diffusion coeff.
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Language
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Accession Number
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Search: polymer and volatil* NOT doctype: p NOT determination AND language: english AND migrat* AND
doctype: gr
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ANSWER 6 ©2002 ACS
Title
The **migration** of non-**volatile** additives from plastics: New concepts from further experiments with model systems
Author
Adcock, L. H.
Organization
PIRA, Leatherhead, UK
Publication Source
Lect. - Int. Symp. Migr., 4th (1983), 245-65 Publisher: Dtsch. Unilever GmbH, Hamburg, Fed. Rep. Ger.
Identifier-CODEN
51LFA6
Abstract
A review and discussion with no refs. on the **migration** of additives from polymers into food in the absence of **polymer** swelling.
Document Type
Conference; **General Review**
Language
English
Accession Number
1984:422051 CAPLUS
Document Number
101:22051
Search: polymer and (leach* or migrat*)* NOT doctype: p
Search: polymer and (leach* or migrat*) NOT doctype: p
Search: polymer and (leach* or migrat*) NOT doctype: p AND additive*
Display from CAplus database
ANSWER 20 ©2002 ACS
Title

Polymer additive migration to foods-a direct comparison of experimental data and values calculated from **migration** models for polypropylene
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Taylor & Francis Ltd.
Abstract
To reduce the amt. of compliance testing for food contact polymers the use of **migration** modeling is under discussion and being evaluated by an EU Commission funded project (Evaluation of **Migration** Models No. SMT4-CT98-7513). The work reported in this paper was exclusively funded by industry to provide data for the independent evaluation of a diffusion based model using eight different samples of polypropylene (PP) covering the range of polymers specification and five commonly used plastics **additive**s. One hundred and fifty exptl. **migration** data have been obtained in triplicate and used to evaluate a Fickian-based **migration** model in the prediction of specific **migration** of five **additives** into olive oil. All tests were conducted using olive oil, representing the most severe case for fatty foods, with test conditions of 2 h at 121°, 2 h at 70° and 10 days at 40°, representing short term exposures at high temps. and room temp. storage. Predicted **migration** values were calcd. using the Pringer "**Migratest** Lite" model by entering the measured initial concn. of **additive** in the polymers(Cp,0) in to the equations together with known variables such as **additive** mol. wt., temp. and exposure time. Where necessary the data generated in this study have been used to update the model. The results indicate the Piringer **migration** model, using the "exact" calcns. of the **Migratest** Lite program, predicted **migration** values into olive oil close to, or in excess of, the exptl. results for >97% of the **migration** values generated in this study. For all measurements, the predicted **migration** from the **Migratest** Lite program was greater than 70% of the obsd. value. This study has identified the possibility that random co-polymers of propylene and ethylene give higher **migration** than other grades of polypropylenes and could be treated as a sep. case. However, further work on more samples of random co-polymers is required to confirm this finding.
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Title

Comparison of techniques to measure **additive** diffusivity in **polymer** films
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Publication Source
Annu. Tech. Conf. - Soc. Plast. Eng. (2000), 58th(Vol. 3), 3497-3501
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Publisher
Society of Plastics Engineers
Abstract
The surfaces of a **polymer** film can be modified by allowing **additives** within the film to diffuse to the surfaces and accumulate there. To model the diffusion/accumulation process, it is necessary to accurately measure the diffusion coeff. of the **additive** in the **polyme**r. We have attempted to characterize the diffusivity of erucamide in LLDPE through several means: mass sorption ("diffusion in") and surface washing and ATR-FTIR ("diffusion out"). Expts. demonstrate that surface washing can provide inconsistent results. Mass sorption and ATR-FTIR provide comparable results, although emphasis is placed on the ATR-FTIR technique because the **migration** process more closely mimics the behavior of com. films.
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Title
Loss of high molecular weight, sterically hindered amines from polypropylene
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Abstract
The loss from polypropylene (PP) of sterically hindered amines with mol. wt. ranging from 1364 to 2758 in heptane, chloroform, and methanol at room temp. was studied. The **additives** leak from **polymer** in heptane and in chloroform and some residual concn. remains in the **polyme**r; the stabilizers show slight **migration** in methanol. The rate of loss increases with **additive** concn. in the **polyme**r. The effect of solvent during washing out could be explained by its different soly. in PP resulting in changes in **polymer** chain mobility and **additive migration** from the **polyme**r.
Document Type
Journal
Language
English
Accession Number
2000:42106 CAPLUS
Document Number
132:181354
Cited Reference or Reference
(1) Al-Malaika, S; Toxicological implications associated with loss of antioxidants from plastics for use in food-packaging applications; Free Radicals and Food Additives 1991, P151
(2) Baner, A; Alternative fatty food simulants for polymer migration testing: experimental confirmation; J Polym Eng 1995-1996, V15, P161
(3) Billingham, N; Oxidation Inhibition of Organic Materials 1990, V2, P249
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(5) Malik, J; Physical loss of hindered amine light stabilizers from polyethylene; Polym Degrad Stab 1992, V35, P125
Display from CAplus database
ANSWER 45 ©2002 ACS
Title
The estimation of partition coefficients, solubility coefficients, and permeability coefficients for organic molecules in polymers using group contribution methods
Author
Baner, A. L.
Organization
Friskies R and D Center Inc., St. Joseph, MO, 64503, USA
Publication Source
ACS Symp. Ser. (2000), 753(Food Packaging), 37-55
Identifier-CODEN
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American Chemical Society
Abstract
Partition, soly. and permeability coeffs. of org. substances are necessary for modeling mass transfer phenomena (aroma permeation and scalping, **polymer additive migratio**n) in polymeric food packaging systems. The uncountable no. of different **polyme**r/org. mol./food system combinations of interest coupled with the laborious and difficult exptl. work needed for measurement makes it desirable to explore the use of semiempirical thermodynamically-based group contribution methods to est. these parameters. The accuracy of partition, soly. and permeability coeffs. estns. using the UNIFAC, GCFLORY, ELBRO-FV, Regular Soln. and Retention Indexes methods are compared with exptl. data for aroma compds. and **polymer additives** in polyolefin, PET, nylon-6 and PVC polymers.
Document Type
Journal
Language

English
Accession Number
2000:336335 CAPLUS
Document Number
133:104009
Cited Reference or Reference
(1) Abrams, D; Statistical thermodynamics of liquid mixtures. New expression for the excess Gibbs energy of partly or completely miscible systems; AICHe Journal 1975, V21, P116
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(4) Baner, A; The application of a predictive migration model for evaluating the compliance of plastic materials with European food regulations; Fd Addit Contam 1996, V13, P587
(5) Baner, A; Food Packaging and Preservation 1994
Display from CAplus database
ANSWER 69 ©2002 ACS
Title
Polymer additive migration to foods-a direct comparison of experimental data and values calculated from
migration models for high density polyethylene (HDPE)
Author
O'Brien, Anthony; Goodson, Anne; Cooper, Ian
Organization
Pira International, Surrey, KT22 7RU, UK
Publication Source
Food Addit. Contam. (1999), 16(9), 367-380
Identifier-CODEN
FACOEB
ISSN
0265-203X
Publisher
Taylor & Francis Ltd.
Abstract
To reduce the amt. of compliance testing for food contact polymers the use of **migration** modeling has been proposed. This study was conducted to provide valid data for the independent evaluation of two such diffusion-based models using a range of different high d. polyethylene (HDPE) polymers and plastics **additive**s. Seventy-two exptl. **migration** data were obtained in triplicate and used to evaluate two Fickian-based **migration** models in the prediction of specific **migration** of four HDPE **additives** into olive oil. All tests were conducted using olive oil, representing the most severe case for fatty foods with test conditions of 2 h at 70°C, 6 h at 70°C, 10 days at 40°C representing short term exposures at high temps. and room temp. storage. Predicted **migration** values were calcd. by inserting the measured initial concn. of **additive** in the polymers (Cp,0) into the equations together with known variables such as **additive** mol. wt., temp. and exposure time. The results indicate that both models predict **migration** values into olive oil close to, or in excess of, the exptl. results. The Piringer **migration** model, using the "exact" calcns. of the **Migratest** Lite program, gave an overestimation for 83% of the **migration** values generated in this study. The highest overestimation was 3.7 times the measured value. For all measurements, the predicted **migration** from the **Migratest** Lite program was greater than 50% of the obsd. value. The FDA model was found more accurately to predict **migration** in most situations but underestimated **migration** more frequently. Differences in the **polymer** specification had little effect on specific **migration** of the **additives** investigated.
Document Type
Journal
Language
English
Accession Number
1999:574969 CAPLUS

Document Number
131:285593
Cited Reference or Reference
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Appendix C: Comparative property data Table for TCEP, TCPP, TDCP and V6

Reliabilities recorded in the table ('R') use the standard Klimisch code system.

IUCLID ref	Endpoint	TCEP	R [a]	TCPP	R	TDCP	R	V6	R	Comment on the data, QSAR or read-across
Physicochemical properties										
	Molecular weight	285.49		327.57		430.91		583.00		
2.1	Melting/freezing	<-70	1	<-20	1	<-20	1	<-50.5 (freezing point)	1	Not possible or necessary to obtain an exact value
2.2	Boiling	320 (decomp)	1	ca. 288 (decomp)	1	ca. 326 (decomp)	1	252 (decomp)	2	
2.3	Density at 20°C	1.4193 at 25°C	1	1.288	1	1.513	1	1.473	1	
2.4	Vapour pressure (Pa, 25ºC)	0.00114	1	1.4×10^{-3}	1	5.6×10^{-6}	1	*2.75 x 10-6*		Value predicted for V6: EPIWIN[b] Version 3.05, modified Grain method
2.6.2	Surface tension	-	ND	-	ND	-	ND	-	ND	-
2.6.1	Water solubility (mg/l, 20ºC)	7820	1	1080		18.1	1	232	1	Data make a self-consistent set
2.5	Octanol-water partition coefficient	1.78	1	2.68		3.69	1	2.83	1	
2.7	Flashpoint (closed cup)	200°C	1	No flash up to 245°C, then decomposes	1	-	ND	191°C [c]	1	Read across could be considered for TDCP
2.9	Flammability, Pyrophoric properties	-	ND	-	ND	-	ND	-	ND	Not possible or necessary
2.10	Explosivity	-	ND	-	ND	-	ND	-	ND	Not possible or necessary
2.8	Autoignition temperatureºC	480	1	>400	1	513 [d]	4	>400 [c]	1	
2.11	Oxidising properties	-	ND	-	ND	-	ND	-	ND	Not possible or necessary

IUCLID ref	Endpoint	TCEP	R [a]	TCPP	R	TDCP	R	V6	R	Comment on the data, QSAR or read-across
Environmental fate and behaviour										
3.5	Ready biodegradability	No	1	No	2	No	2	No (not GLP)	2	Weight of evidence is that none is readily biodegradable
3.5	Inherent biodegradability	No (based on two tests, one of short duration)	1	Evidence of partial degradation	2	No	2	Evidence of partial degradation (not GLP)	2	A consistent picture of lack of ready degradability. The mono-chloro chain substances show some degradation after acclimation; it cannot be assumed that TDCP would behave similarly.
	Other biodegradation results	Not anaerobically biodegradable Not degraded by soil micro-organisms	1			Not degraded by soil micro-organisms	1			
3.7	Bioaccumulation in fish	0.6 - 5.1 (From 3 tests, with *Cyprinus carpio*, *Carassius auratus* and *Oryzias latipes*)	1	–0.8 – 4.6 *Cyprinus carpio*	2	0.3 – 89 (From 2 tests, with *Cyprinus carpio* and *Oryzias latipes*)	2	*50.8*		Value predicted for V6: Veith *et al*, 1979. Read-across not recommended due to possible importance of metabolism; no available evidence suggests that high BCF values are likely.
3.1.2	Hydrolysis pH 7	t1/2 >1 year	1	t1/2 >1 year	1	t1/2 >1 year	1	t1/2 >1 year	1	
3.3	Log Koc			2.24 (Koc = 174, calculated from TDCP value)	1	3.25 (OECD 106) (Koc = 1780)	1 1	2.39 (Koc = 245, calculated from TDCP value)	1	Full study more reliable than HPLC estimation.

IUCLID ref	Endpoint	TCEP	R [a]	TCPP	R	TDCP	R	V6	R	Comment on the data, QSAR or read-across
	Log Koc (estimated by HPLC method) (Estimated using TGD QSAR for TCEP)	*2.04* (Koc estimated from log Kow)	1	2.76	1	4.09		4.04	1	
Ecotoxicity (most sensitive values only reported, test species and test guidelines (where known) are reported in italics)										
4.1	Acute toxicity to fish (mg/l)	LC50 = 90 *Carassius auratus*	1	LC50 = 51 *P. promelas*	1	LC50 = 1.1 O. mykiss OECD 203	1	LC50 = 52 *O. mykiss* *OECD 203*	1	
	QSAR[b] (Esters) acute toxicity to fish (96 h LC_{50})	*36*	*2*	*21*	*2*	*8.1*	*2*	*32*	*2*	ECOSAR Program (v0.99h). The QSAR estimates are of the same order of magnitude as the measured data, but tend to over-predict toxicity slightly (with the exception of TDCP).
	QSAR[b] (Phosphate esters) acute toxicity to fish (96 h LC_{50})	*19*	*2*	*11*	*2*	*4.5*	*2*	*17*	*2*	ECOSAR Program (v0.99h). The QSAR estimates are of the same order of magnitude as the measured data, but tend to over-predict toxicity slightly (with the exception of TDCP).
4.2	Acute toxicity to invertebrates (48 h EC_{50} in mg/l)	EC50 = 235 (24 h) *D. magna*	1	EC50 = 131 *D. magna*	1	EC50 = 3.8 *D. magna* *OECD 202*	1	EC50 = 42 *D. magna* *OECD 202*	1	

IUCLID ref	Endpoint	TCEP	R [a]	TCPP	R	TDCP	R	V6	R	Comment on the data, QSAR or read-across
	QSAR[b] (Esters) acute toxicity to invertebrates (48 h LC_{50})	*230*	*2*	*63*	*2*	*9.9*	*2*	*81*	*2*	ECOSAR Program (v0.99h). The QSAR estimates are of the same order of magnitude as the measured data, but tend to under-predict toxicity slightly (with the exception of TCPP).
4.3	Acute toxicity to algae (72 h E_rC_{50} in mg/l)	ErC50 = 3.6 *Scenedesmus subspicata*	1	ErC50 = 82 *Pseudokirchneriella subcapitata* OECD 201	1	ErC50 = 2.8 *Pseudokirchneriella subcapitata* *OECD 201*	1	ErC50 = 35 *Pseudokirchneriella subcapitata* *OECD 201*	1	TCEP result appears out of line with the other results
	QSAR[b] (Esters) toxicity to algae (96 h EC_{50})	*2.9*	*2*	*1.8*	*2*	*0.69*	*2*	*2.6*	*2*	ECOSAR Program (v0.99h). The selected QSAR appears to over-predict toxicity in general
4.5.1	Chronic toxicity to fish (mg/l)	-	ND	-	ND	-	ND	-	ND	
	QSAR[b] (Esters) chronic toxicity to fish	*16*	*2*	*5.2*	*2*	*1.0*	*2*	*7.0*	*2*	ECOSAR Program (v0.99h)
4.5.2	Chronic toxicity to invertebrates (mg/l, 21-day repro test)	NOEC = 13 *D. magna*	1	NOEC = 32 *D. magna* *OECD 202*	1	NOEC = 0.5 *D. magna* *OECD 211*	1	NOEC $\geq$3.68 *D. magna* *OECD 211*	1	
	QSAR (Neutral organics) chronic toxicity to invertebrates			NOEC (reproduction) = 4.3	2	NOEC (reproduction) = 1.1	2	NOEC (reproduction) = 6.0	2	ECOSAR Program (v0.99h)

IUCLID ref	Endpoint	TCEP	R [a]	TCPP	R	TDCP	R	V6	R	Comment on the data, QSAR or read-across
4.3	Chronic toxicity to algae (72 h growth rate results in mg/l)	48h ErC10 = 0.65 *Scenedesmus subspicatus*	1	ErC10 (72hr) = 42 *Pseudokirchneriella subcapitata* OECD 201	1	ErC10 (72hr) = 2.3 *Pseudokirchneriella subcapitata* OECD 201	1	NOEC (96hr) = 10 *Pseudokirchneriella subcapitata OECD 201*	1	
	QSAR[b] (Esters) chronic toxicity to algae (96 h NOEC)	*2.2*	*2*	*1.4*	*2*	*0.55*	*2*	*2.1*	*2*	ECOSAR Program (v0.99h)
	Toxicity to WWTP micro-organisms (mg/l)	IC50 = 3200 Activated sludge OECD 209	1	IC50 = 784 Activated sludge ISO 8192	1	IC50 = >10000 Activated sludge OECD 209	2	IC50 = >1000 Activated sludge OECD 209	1	
4.6.1	Toxicity to sediment dwelling organisms (mg/kg dw)[e,f]					28 d NOEC = 10.6[g] (10)[2.2] 28 d NOEC = 8.8[h] (8.3)[1.8] 28 d NOEC = 3.9[i] (3.7)[0.8] *Chironomus riparius OECD 218*	1			
	Toxicity to higher plants (mg/kg dw)	EC50 = 64 NOEC = 10 *Avena sativa Modified OECD 208*	1	NOEC = 17 *Lactuca sativa OECD 208*	1	NOEC = 19.3 *Sinapis alba OECD 208*	1	NOEC = 17 (Read-across from TCPP)		
	Toxicity to earthworms (mg/kg dw)[j]	14 d NOEC = 580 *Eisenia andrei*	1	14 d LC50 = 97 (33) OECD 207 56 d NOEC = 53 (18) *Eisenia foetida OECD draft guideline (January*	1	14 d LC50 = 130 (44) OECD 207 57 d NOEC = 9.6 (3.3) *Eisenia foetida OECD draft guideline (January*	1	14 d LC50 >1000 (>340) 14 d NOEC >1000 (>340) (not GLP) *Eisenia foetida OECD207*	1	

IUCLID ref	Endpoint	TCEP	R [a]	TCPP	R	TDCP	R	V6	R	Comment on the data, QSAR or read-across
				2000): Earthworm Reproduction Test		*2000): Earthworm Reproduction Test*				
	Toxicity to other soil invertebrates (mg/kg dw)	28d LC50 = 66.5 (mortality) 28d LC10 = 19.3 (mortality) 28d EC10 = 44.6 (repro) (*Folsomia candida* springtail)	1	-	ND	-	ND	-	ND	
	Toxicity to soil micro-organisms	Inhibition 15-42% at 5-50 mg/kg dw in various soils.	1	28 d NOEC = ≥128 mg/kg ww Nitrifying micro-organisms in sandy loam soil (Read-across from TDCP)		28 d NOEC = ≥128 mg/kg ww Nitrifying micro-organisms (species not stated) in sandy loam soil OECD 216	1	28 d NOEC = ≥128 mg/kg ww Nitrifying micro-organisms in sandy loam soil (Read-across from TDCP)		
	Toxicity to birds (g/kg)	Neurotoxicity not observed at 14.2 g/kg *Gallus domesticus*	1	-	ND	-	ND	-	ND	

Notes:

ND – not determined (no data available)

a The TCEP ESR RAR does not state data reliabilities. It has been assumed here that values used in the risk assessment must be considered to be of high reliability. This is useful to provide a point of reference for comparison with the reliability of available data on the other three substances.

b SRC Syracuse Research Corporation programs for estimating properties

c subject to clarification of test substance composition

d Industry considers result to be invalid but reason is unknown

e Values in (parentheses) have been corrected to standard organic matter content of 5.0%

f Values in [parentheses] have been corrected to standard organic matter content of 5.0% and expressed as wet weight

g Based on initial (day 0) measured exposure concentrations in sediment

h Based on geometric mean of measured exposure concentrations in sediment on days 0 and 3

i Based on geometric mean of measured exposure concentrations in sediment on days 0 and 28

j Values in parentheses have been corrected to standard organic matter content of 3.4%

Appendix D: V6 – Carcinogenicity endpoint

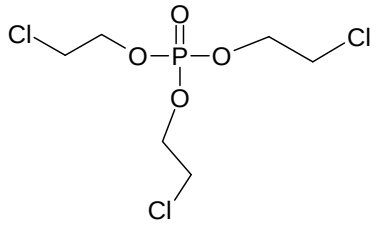
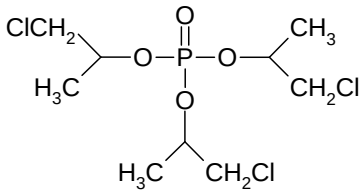
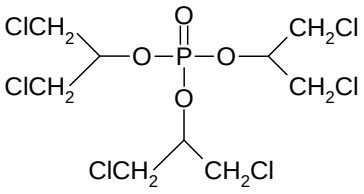
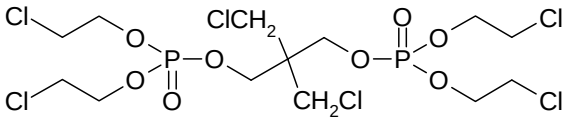
There are no carcinogenicity data available for V6.

V6 is a chlorinated alkyl phosphate ester. Three other chlorinated alkyl phosphate esters, which have related structures to V6, are TDCP, TCEP and TCPP. TDCP and TCEP are non-genotoxic carcinogens and are classified as Carc Cat 3 R40[21]. A discussion of the possible qualitative read-across from TCEP and TDCP for the endpoint of carcinogenicity of V6 is presented in this appendix.

1. Structure

V6 contains two phosphate groups, each covalently linked to two chloroalkyl chains. The two phosphate groups in V6 are linked via a chloroalkyl bridge. TDCP, TCPP and TCEP all contain a single central phosphate group covalently linked to three chloroalkyl chains. The structures of all four substances are presented in **Table D.1** below.

Table D.1 Structures of V6, TCEP, TCPP and TDCP

Tris(2-chloroethyl) phosphate (TCEP) 	Tris(2-chloro-1-methylethyl) phosphate (TCPP) 
Tris[2-chloro-1-(chloromethyl)ethyl] phosphate (TDCP) 	2,2-Bis(chloromethyl)trimethylene bis(bis(2-chloroethyl)phosphate) (V6) 

The V6 molecule could be described as a dimer of the TCEP molecule, linked via a chloroalkyl bridge. As it is a bulkier molecule than TDCP, TCPP and TCEP, it may be expected that the reactivity at the P=O groups in V6 would be lower than the less sterically hindered P=O in the other three substances.

It is thought that the electronegative chlorine atoms of V6, TDCP, TCPP and TCEP may have an effect on the lability of the phosphate ester groups to differing degrees. It is expected that the abundance of chlorine atoms in V6 will create a strong ⁻I-effect, and as a result, the phosphate ester group of V6 may be expected to be more labile than the phosphate ester group of TDCP, TCPP or TCEP.

[21] Commission Working Group on the Classification and Labelling of Dangerous Substances Meeting on the Health Effects of Pesticides, Existing Chemicals & New Chemicals, November 14-18, 2005.

Based on this structural assessment, although V6 is bulkier than the other three substances, there are some similarities between V6 and TDCP, TCPP and TCEP. These similarities are based on the nature of the chloroalkyl chains surrounding the central phosphate group in all four molecules. However, it is acknowledged that TDCP, TCPP and TCEP are more closely aligned.

The four substances were also evaluated using a hierarchical clustering with the QSAR data-mining tool, Leadscope (Patlewicz *et al*., 2007). This analysis was made available to the Rapporteur. The modified Tanimoto index within the tool was used as a means of comparing the substances for structural similarity. The Tanimoto index is used to quantitatively relate two or more chemicals together on the basis of the commonality of features between those chemicals. In addition, the model also compares the absence of structural features. When the cluster threshold distance (i.e. a cut-off value to determine whether a chemical belongs to one cluster or another) was set to the default value recommended for similar substances, all four substances were found to be in the same cluster and thus very similar to each other. When the substances were then clustered based on structural features, TCEP and TCPP were found to be most structurally similar, and thus clustered together. TDCP and V6 were both clustered separately (Patlewicz *et al.,* 2007). The results of this analysis indicate that TCEP, TCPP and TDCP are most similar to each other, with V6 considered generally to be similar to this group.

2. Physical Chemical Properties

The key physical chemical properties of each are presented in **Table D.2** below.

Table D.2 Physical chemical properties of V6, TCEP, TCPP and TDCP

Name	V6	*TCEP	**TCPP	***TDCP
Molecular weight	583	285.49	327.57	430.91
Physical state	Liquid	Liquid	Liquid	Liquid
Melting /freezing point	<-50.5 ^{0}C	<-70 ^{0}C	<-20 ^{0}C	<-20 ^{0}C
Boling point	252°C, (decomp.)	320 ^{0}C (decomp)	Ca. 288 ^{0}C (decomp)	Ca. 326 ^{0}C (decomp)
Relative density	1.473 at 20°C	1.4193 at 25 ^{0}C	1.288 at 20 ^{0}C	1.513
Vapour Pressure	2.75 x 10^{-6} Pa at 25°C (estimated)	1.14 x 10^{-3} Pa at 20 ^{0}C (extrapol)	1.4 x 10^{-3} Pa at 25 ^{0}C	5.6 x 10^{-6} Pa at 25 ^{0}C
Water solubility	232 mg/l at 20°C	7820 mg/l at 20 ^{0}C	1080 mg/l at 20 ^{0}C	18.1 mg/l
Log Kow	2.83	1.78	2.68 ± 0.36	3.69 ± 0.36

* Values taken from BAUA, 2006

**Values taken from HSA/EA 2008a

*** Values taken from HSA/EA 2008b

All four substances are liquid at room temperature. V6 has the highest molecular weight of all the substances, being approximately twice that of TCEP. The boiling points and relative densities of all the substances are comparable. There are differences in the water solubilities of the substances, with V6 falling within the range of values of the other three substances. All four substances have log Kow within the range 1-4, indicating favourable absorption. The vapour pressure of V6 is comparable with TDCP. However, the vapour pressures of all four substances are not considered to be toxicologically significant. Although there are some

minor differences in the physical chemical properties, the four substances can be considered relatively comparable.

The physiochemical similarity of the substances was also evaluated using Leadscope software (Patlewicz *et al.,* 2007). Clustering analysis was conducted based on physicochemical descriptors: lipophilicity (log P and water solubility) and molecular size (including molecular mass and molecular refraction). TDCP and TCPP were found to be most similar to each other based on the chosen physical chemical parameters, and thus clustered together, with TCEP and V6 each clustered separately. When the cluster threshold distance was increased, TDCP, TCPP and TCEP were clustered into one group, with V6 in a separate cluster (Patlewicz *et al.,* 2007).

3. Toxicokinetics

Absorption, distribution & excretion

Following a single oral low or high dose of ^{14}C-V6 to male and female rats, radioactivity was absorbed slowly, with the highest concentrations in the blood found at 8 hours post dosing (TNO Quality of Life, 2008). ^{14}C-V6 was almost completely absorbed from the gastrointestinal tract. The total retention of radioactivity was around 2.5% after the low dose and 0.8% after the high dose, with most of the radioactivity excreted within 3 days. The elimination half life was 102-111 hours. Excretion occurred mainly by the biliary route (approx. 60%), with excretion in urine at approximately 20% and a small amount of radioactivity exhaled as $^{14}CO_2$. Volatile radioactivity could not be detected. The percentage radioactivities recovered up to 7 days post dosing are presented in table A.3 below.

In a study conducted by Minegishi *et al*. (1988), the comparative absorption, distribution and excretion of ^{14}C-TCPP, ^{14}C-TDCP and ^{14}C-TCEP were evaluated following a single oral dose in rats (reported in HSA/EA 2008a). All three substances are well absorbed from the gastrointestinal tract. The percentage radioactivities recovered after 7 days are presented in **Table D.3** below.

Table D.3 Percentage recovery of radioactivity in rats following oral administration of ^{14}C -V6, ^{14}C -TCEP, ^{14}C -TCPP and ^{14}C -TDCP

	Percentage recovery of radioactivity			
	V6*	**TCEP****	**TCPP****	**TDCP****
Urine	15.28 – 23.49 %	93%	67.2%	43.2%
Faeces	52.32 – 65.92 %	5.6%	22.2%	39.2%
Expired air	0.85 – 3.01 %	1.7%	7.7%	16.24%
Carcass	0.83 – 2.74 %	0.8%	0.7%	2.51%
Total	78.05 – 90.18 %	101.5%	97.8%	101.8%

*TNO Quality of Life, 2008

**Minegishi *et al*., 1998, reported in HSA/EA 2008a

From the table above, V6 appears to be excreted to a lower degree in urine and a higher degree in faeces than the other substances. The distribution of radioactivity between urine and faeces is more evenly balanced for TDCP. For TCPP, the excretion profile appears to be the opposite of V6, with the majority of TCPP (67%) excreted in urine but a significant amount

(22%) is also excreted in faeces. Like the other substances, very little V6 was retained at 7 days post dosing; up to 2.7 % for V6, versus 0.8%, 0.7% and 2.51% for TCEP, TCPP and TDCP, respectively.

The biliary excretion of radioactivity for TDCP and TCPP was found to be comparable, 40% for TDCP and 45% for TCPP (compared with 25% for TCEP). The biliary: faecal ratios at 48 hours for TCEP, TCPP and TDCP were determined to be 4.62, 2.23 and 1.04, respectively. A ratio of greater than 1 indicates re-absorption of biliary metabolites from the gastrointestinal tract and therefore it is anticipated that that some degree of enterohepatic re-circulation of TCEP occurs, and to a lesser extent with TCPP. This would prolong the half-life of both substances in plasma. TDCP, in comparison, is expected to exhibit only limited enterohepatic recirculation and would therefore be expected to have a shorter half-life. The biliary: faecal ratio was not calculated for V6, and therefore no conclusion can be drawn on the re-absorption potential for biliary metabolites. However, V6 was predominately excreted via the biliary route.

At 7 days post ^{14}C-V6 dosing, the highest concentrations of radioactivity were found n the liver, kidney, adrenals and abdominal skin in both sexes. The lowest radioactivity was found in brain, plasma and fat, the latter indicating no bioaccumulation of V6 (TNO Quality of Life, 2008). Minegishi *et al.,* 1988 (reported in HSA/EA 2008a) found that at 72 hours after oral administration, the distribution of TCEP in tissues was kidney > liver > blood > spleen. TCPP and TDCP had similar distribution profiles: liver > kidney > lung for TCPP and liver > kidney > adipose > blood for TDCP. At 7 days after dosing, the tissue distribution for TCEP was comparable to the other two substances: liver > kidney> blood=lung. In a study by Nomeir *et al*. in 1981 (HSA/EA 2008b), the distribution of TDCP 24 hours following oral administration was kidney > liver > lung > blood > muscle. Therefore, for all four substances, no specific target organs, other than the organs of elimination were found.

Overall, all four substances are well absorbed from the gastrointestinal tract and almost completely excreted by 7 days post dosing. No specific target organs, other than the organs of elimination, were identified for all substances. All substances were excreted by the biliary route, although the extent of the excretion differed between the substances. However, the distribution of metabolites between urine and faeces for V6 was different when compared with the other substances, indicating a difference in excretion pathways. Therefore, with respect to toxicokinetics, based on the above, it is considered that TDCP, TCPP and TCEP are closely comparable, with V6 similar to this group.

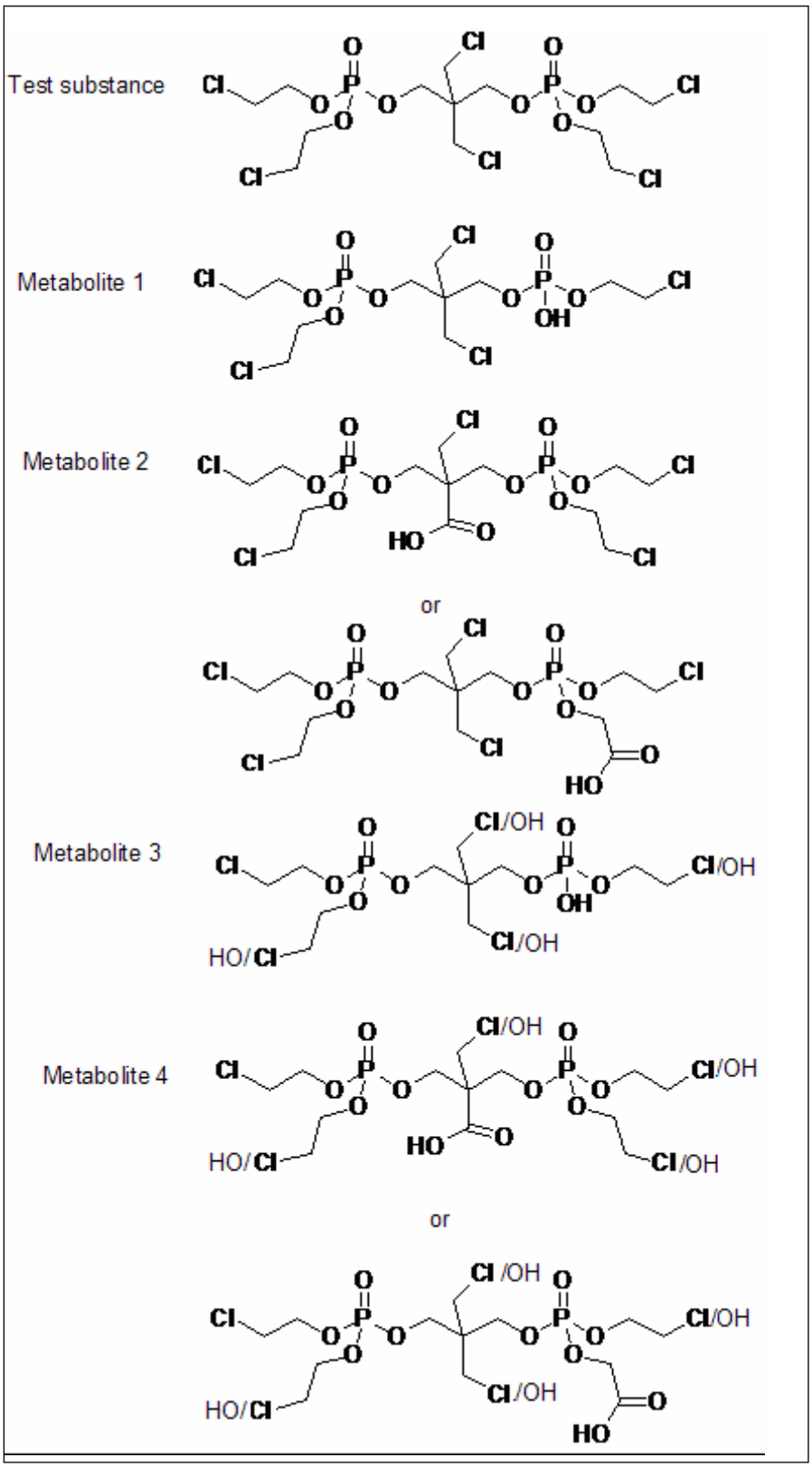
Metabolism

Phosphate esters behave similarly to carboxylic acid esters and as such can undergo several main reaction mechanisms such as: hydrolysis at the acyl carbon (or "P=O" bond), which can be acid catalysed or base promoted, nucleophilic substitution at the acyl carbon, as well as alkylation reactions via S_N2 at the alkyl C adjacent to the ester O.

As discussed in section 4.1.2.1.1 of the main report, metabolic profiling and metabolite identification following oral administration of ^{14}C-V6 to rats was conducted as part of the study by TNO Quality of Life (2008). Metabolic profiling in pooled urine showed one major metabolite (up to 5% of the administered dose), at least 11 minor metabolites and no parent compound. The early retention time of this metabolite in the HPLC column points to a small polar compound, such as: 2-chloroethanol, ethylene glycol, acetic acid or 2-hydroxy acetic acid. In addition, this metabolite could not be identified using LC-MS, further indicating that is probably of low molecular weight. One of the minor metabolites found in female urine

(present at 2-5%) was also the major metabolite identified in faeces. Pooled faeces contained at least 14 metabolites, with four of them major metabolites which were higher than 5% of the administered dose: Metabolite 1 at up to 30%; metabolite 2 at up to 20%; and metabolites 3 and 4 at up to 9%. Based on elemental compositions, proposed structures of metabolites 1-4 are presented in **Figure D.1** below. The exact structure of metabolites 2, 3 and 4 could not be elucidated. A small amount (< 1%) parent compound was found in faeces, but only up to 48 hours post dosing. Deconjugation experiments showed that conjugated metabolites were either not present, or present only in very small amounts.

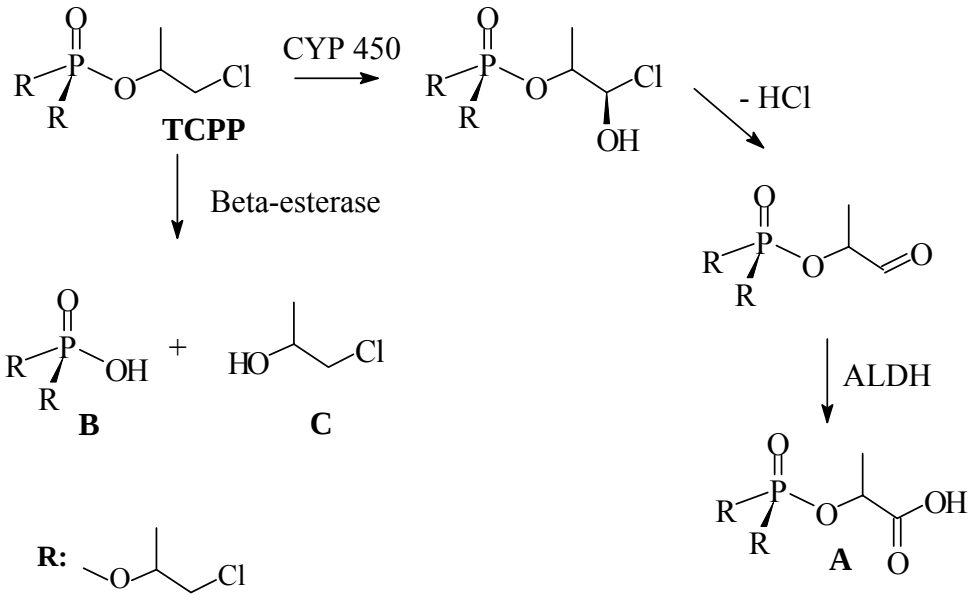
Figure D.1 Proposed structures of the major metabolites of V6 identified in faeces



It is noted that the proposed metabolites of V6, presented in **Figure D.1**, above, are either missing a chloroethyl moiety or the chlorine has been replaced by hydroxyl group, and further oxidised to a carboxyl group. When looking at possible metabolic pathways of V6 it should be borne in mind that the metabolites of V6 have not been definitively identified.

Following oral administration to rats, TCPP was extensively metabolised prior to excretion in urine and faeces, with unchanged TCPP representing less than 2% of the administered dose. The metabolites identified were 0,0-[bis(1-chloro-2-propyl)]-0-(2-propionic acid)phosphate (> 50%), bis(1-chloro-2-propyl)monophosphoric acid (12%) and 1-chloro-2-propanol (not quantified) (Stauffer Chemical Co, 1984, reported in HSA/EA 2008a). A proposed metabolic pathway for TCPP is shown in **Figure D.2** below.

Figure D.2 A proposed metabolic pathway for TCPP



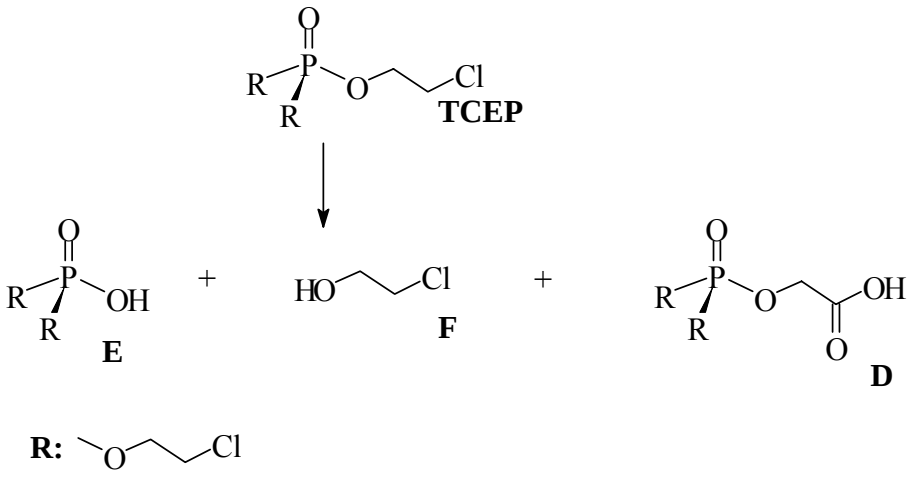
A: 0,0-[bis(1-chloro-2-propyl)]-0-(2-propionic acid)phosphate (>50%)
B: bis(1-chloro-2-propyl)monophosphoric acid (12%)
C: 1-chloro-2-propanol (not quantified)

From the metabolites identified it can be postulated that β-esterases catalyse the hydrolysis of TCPP to form metabolites B and C, while a second pathway mediated by cytochrome P450 enzymes results in aldehyde dehydrogenase (ALDH) oxidation reaction to form metabolite A.

When the metabolites of TCPP are compared with the postulated metabolites of V6, some similarities can be seen. A similar hydrolysis reaction for V6 is plausible, resulting in V6 metabolite 1 (and 2-chloroethanol, which is possibly the small polar metabolite observed in urine), and oxidation type reaction to form V6 metabolites 2 and 4.

The metabolism of TCEP has been investigated both *in vivo* and *in vitro* (BAUA, 2006). Following oral administration of ^{14}C-TCEP to rats and mice the following metabolites in urine were identified but not quantified: bis(2-chloroethyl)carboxymethylphosphate, bis(2-chloroethyl)hydrogen phosphate and bis (2-chloroethyl-2-hydroxyethyl-phosphate glucuronide (BAUA, 2006). The structures and a proposed similar metabolic pathway to TCPP (and possibly V6) are presented in **Figure D.3** below. The presence of metabolites bis(2-chloroethyl)carboxymethylphosphate and bis(2-chloroethyl)hydrogen phosphate indicates that a similar metabolic pathway to TCPP and possibly V6 may operate for TCEP: acyl-like hydrolysis at "P=O" bond cleaving a chloroalkyl chain and also metabolism via Cytochrome P450 enzymes.

Figure D.3 A proposed metabolic pathway for TCEP



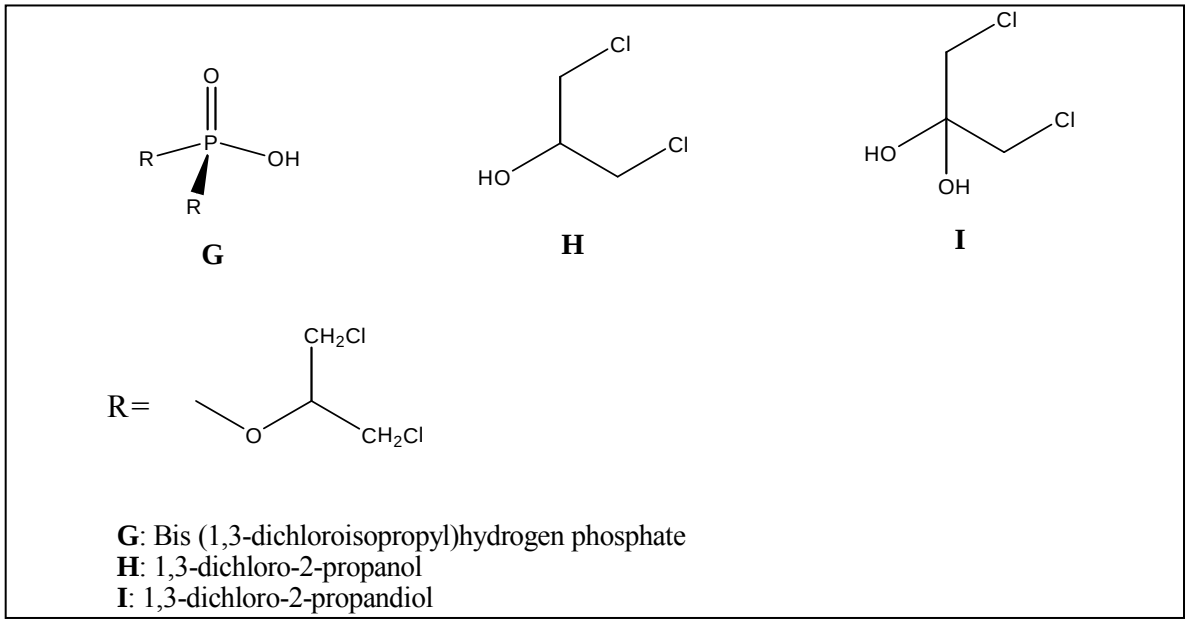
D: Bis(2-chloroethyl)carboxymethyl phosphate
E: Bis(2-chloroethyl)hydrogen phosphate
F: 2-chloroethanol

In *in vitro* metabolism studies of ^{14}C-TCEP in liver slices and liver microsomes, bis(2-chloroethyl)hydrogen phosphate and 2-chloroethanol were identified as the main metabolites (BAUA, 2006) again supporting the hypothesis that a similar metabolic pathway to TCPP, and possibly V6, exists for TCEP.

No analogue of the TCEP metabolite bis (2-chloroethyl-2-hydroxyethyl-phosphate) glucuronide was identified in the *in vivo* metabolism studies with V6 or TCPP. This indicates that in addition to the similarities outlined above, there may be some differences in the metabolism of the substances. However, as the metabolites of TCEP were not quantified it is not clear how significant this metabolite is.

The metabolism of TDCP has been investigated *in vitro* and also *in vivo* following intravenous administration (reported in HSA/EA, 2008b). *In vitro*, mixed function oxidases (MFO) in microsomes of rat liver homogenate appear to play an important role in the metabolism of TDCP. The metabolite bis(1,3-dichloroisopropyl)hydrogen phosphate accounted for 75% of the MFO-metabolised TDCP (reported in HSA/EA 2008b). TDCP was also shown to be metabolised by glutathione-S-transferase present in the soluble fraction of rat liver, and it appears that TDCP is directly conjugated with glutathione. In a separate *in vitro* study, the metabolism of TDCP in the soluble fraction resulted in almost exclusively in one metabolite, which is possibly a γ-glutamylcysteinyl conjugation product of the parent TDCP. The following metabolites were also generated by the microsomal fraction of liver homogenate: bis(1,3-dichloro-2-propyl) phosphate (64 % of total metabolites), 1,3-dichloro-2-propanediol (20%), 1,3-dichloro-2-propanol (5.7 %) and an unknown metabolite (11 %). The structures are presented in **Figure D.4** below.

Figure D.4 TDCP metabolites



G: Bis (1,3-dichloroisopropyl)hydrogen phosphate
H: 1,3-dichloro-2-propanol
I: 1,3-dichloro-2-propandiol

Following i.v. administration, the metabolites isolated from rat urine were bis(1,3-dichloro-2-propyl) phosphate (67.2% of total urine radioactivity), an unidentified polar metabolite (32%), 1,3-dichloro-2-propyl phosphate (0.29%) and un-metabolised TDCP (0.45%).

The presence of a glutathione conjugate of TDCP *in vitro* indicates a difference in the metabolism of TDCP, when compared with V6, TCPP or TCEP. However, the identification of bis(1,3-dichloro-2-propyl) phosphate, 1,3-dichloro-2-propanediol and 1,3-dichloro-2-propanol metabolites of TDCP points towards a similar acyl-like hydrolysis at "P=O" bond to that described for TCPP and TCEP, and possibly V6. However, there does not appear to be an equivalent CYP 450 mediated reaction for TDCP, as seen for TCPP, TCEP and possibly V6.

From the available information, it can be concluded that there is some similarity in the metabolic pathways of TDCP, TCPP and TCEP, although metabolism of these substances does not result in identical metabolites but rather analogous metabolites. Based on the proposed metabolites of V6, there appears to be some similarity in the metabolic pathway of V6 compared with this group of substances. However, the presence of conjugated metabolites (glurcuronide conjugate for TCEP and glutathione conjugate for TDCP) and no evidence of conjugated metabolites for V6 indicate that the metabolic pathways for the substances, while similar, are not identical.

4. Carcinogenicity

As discussed in section 4.1.2.7 of the main report, V6 is not genotoxic *in vivo*. There are no carcinogenicity data available for V6.

TCEP and TDCP are both classified as Carc. Cat 3 R40 "Limited evidence of a carcinogenic effect"[22]. No classification for carcinogenicity is proposed for TCPP (HSA/EA 2008a).

TCEP administered orally to rats and mice for 2 years resulted in an increased incidence of neoplastic lesions (BAUA, 2006). In rats, the main target organ was the kidney, where there

[22] Commission Working Group on the Classification and Labelling of Dangerous Substances Meeting on the Health Effects of Pesticides, Existing Chemicals & New Chemicals, November 14-18, 2005.

was an increase in the incidence of both proliferative lesions and adenomas of the renal tubule, which correlates with the distribution to this organ in the toxicokinetic studies. There was also an increased incidence of thyroid follicular cell neoplasms, which were possibly treatment related, and an increase in mononuclear cell leukaemia. In mice, the main target organ was the kidney, where there was a marginal increase in the incidence of renal tubule neoplasms in males at the highest dose (350 mg/kg). There was also an increase in Harderian gland adenomas in females. In an 18 month dietary study in mice, an increased incidence of renal tumours was observed, in addition to an increased incidence of tumours in the liver.

TCEP is not mutagenic *in vivo* and is therefore considered to be a non-genotoxic carcinogen (BAUA 2006). A number of possible mechanisms were hypothesized in the TCEP risk assessment report for the formation of kidney tumours observed in the carcinogenicity studies, including biotransformation of TCEP metabolites in the kidney to nephrotoxic species. However, the mode of TCEP tumour formation has not been elucidated (BAUA 2006). Of the identified metabolites of TCEP, carcinogenicity data are only available for 2-chloroethanol. In 2-year dermal studies in rats and mice, no evidence of carcinogenicity in either species was found (NTP 1985). Therefore, it is not possible to attribute the tumours observed following TCEP administration to one particular metabolite.

TDCP is also considered to be a non-genotoxic carcinogen. In a 2 year oral carcinogenicity study in rats an increase in the incidence of renal cortical and hepatocellular adenomas in both sexes were observed, in addition to benign testicular cell tumours and Leydig cell tumours in males. The LOAEL of 5 mg/kg/day derived from the study was based on the observed hyperplasia of the convoluted tubule epithelium of the kidney (HSA/EA 2008b). It is generally accepted that hyperplasia is a pre-neoplastic lesion, leading to tumour formation. However, it is not clear whether the hyperplasia observed following treatment with TDCP would progress to cancer or whether the kidney tumours observed with TDCP arise through a different mechanism. One possible mechanism of tumour formation involves the further metabolism of the glutathione conjugated metabolite by the brush border enzymes of the kidney to yield cytotoxic species. The resulting sustained cytotoxicity leads to compensatory tissue repair and cell proliferation, and the formation of renal tumours. However, this possible mechanism has not been confirmed for TDCP, although it is acknowledged that the absence of a similar glutathione conjugated metabolite for V6 precludes this mechanism applying to V6. No specific mechanisms have been identified for the formation of any of the tumours observed in the study.

Of the identified metabolites of TDCP, carcinogenicity data are available for 1,3-dichloro-2-propanol. Following administration in the drinking water of rats for 104 weeks, a statistically significant increase in the incidence of hepatocellular adenomas and carcinomas, squamous cell papillomas and carcinomas of the tongue/oral cavity and thyroid follicular cell adenomas and carcinomas were noted (NTP 2005). The available mutagenicity data is not sufficient to rule out a genotoxic mechanism for the induction of the tumours of the rat tongue, although it would appear that non-genotoxic mechanisms are responsible for the other tumours observed (COC 2004). 1,3-dichloro-2-propanol is listed on Annex I to 67/548/EEC as Carc. Cat 2 R45. There are no carcinogenicity data available for the other identified metabolites. Therefore, it is not possible to attribute the tumours observed in the study to one particular metabolite.

No carcinogenicity data are available for TCPP. Of the identified metabolites of TCPP, carcinogenicity data are available only for 1-chloro-2-propanol, which has been evaluated in 2-year carcinogenicity studies in both rats and mice. There was no evidence of a carcinogenic effect in either species (NTP 1998).

There are sufficient data available to conclude that TCEP and TDCP are non-genotoxic carcinogens. Although the target organs for TCEP and TDCP differ, no specific mechanism of tumour formation has been elucidated for either substance.

5. QSAR estimates

The carcinogenic potential of TCEP, TDCP, TCPP and V6 were estimated using a number of QSAR models – TOPKAT, Danish EPA QSAR database, OncoLogic™ and Derek for Windows (Patlewicz *et al.,* 2007). For TOPKAT, the prediction for V6 was outside the applicability domain of the model, and therefore unreliable. TCEP is in the NTP training set of the model and is predicted to be positive. TCPP and TDCP have conflicting species predictions. TDCP is predicted to be a carcinogen in male rat, but predictions in female rat and male mouse are outside the applicability domain of the model and therefore unreliable. TCPP is predicted to be a carcinogen in male species but not female species (Patlewicz *et al.,* 2007). Overall, the TOPKAT could not provide a valid prediction for V6 and the predictions for the other substances are unreliable.

MCASE carcinogenicity predictions were extracted from the Danish EPA QSAR database (Patlewicz *et al.,* 2007). Overall, predictions generated indicate that V6 is a carcinogen, although some (3 of 8) of the predictions were outside the model domain. TCEP is predicted to be a carcinogen, although it should be noted that it is possible TCEP is the training set of the model (this could not be verified). TCPP is not predicted to be a carcinogen. TDCP is predicted to be a carcinogen, although a number of the predictions were outside the model domain.

OncoLogic™, which was run in the default mode and, so did not make use of the available experimental data (e.g. mutagenicity, physical chemical properties) on the substances. Again, it was not possible to make a prediction for V6 as the structure contains a combination of structural elements unknown to the programme. It predicted the final level of concern for TCEP as "low-moderate", but again it should be noted that TCEP is in OncoLogic's training set. TDCP and TCPP both had predictions of "moderate" level of concern (Patlewicz *et al.,* 2007).

Derek for Windows produced "plausible" alerts for carcinogenicity (alkylating agent with – CH_2Cl), chromosomal damage (*in vitro*) and mutagenicity (*in vitro)* for all four substances, with little differentiation between the substances (Patlewicz *et al.,* 2007).

As there were some inconsistencies between the predictions generated by the different models, and also when the predictions were compared with the available experimental data for TCEP and TDCP, it is not possible to draw any definitive conclusions from these predictions with respect to the possible carcinogenicity of V6.

6. Quantitative read-across

As discussed above, there are no carcinogenicity data for V6, and it is accepted that V6 is not-genotoxic *in vivo*.

As described in section 4.1.2.9 of the main report, V6 has been tested in a 28-day repeated dose toxicity study and the effects on parental animals, as part of a two-generation reproductive toxicity study, is also reported. The main target organs following repeated oral exposure to V6 are the liver and thyroid. In the 28-day study, significantly greater absolute and relative liver weights were noted in females from the mid dose of 150 mg/kg/day and in

both sexes at the highest dose of 600 mg/kg/day, which correlated with histopathological changes observed: hepatocellular hypertrophy in females at 150 mg/kg and slight to marked centrilobular hypertrophy in both sexes at 600 mg/kg. A significant increase in absolute and relative thyroid weight was also noted in the high dose group, which correlated with evidence of thyroid hyperactivity (follicular cell hypertrophy, decreased diameter of the follicular lumen and decreased eosinophilic colloidal contents). A NOAEL for V6 of 15 mg/kg/day was derived from this study, based on the absolute and relative liver weight changes and the correlated liver histopathology.

In a 2-generation reproductive toxicity study, an increase in absolute and relative thyroid weight was observed in mid dose (86 mg/kg/day) males of the F0 generation, and high dose males and females (corresponding to 262 mg/kg and 302 mg/kg, respectively) in both generations. In the F0 generation, the increase in thyroid weight was accompanied by evidence of an activated state; follicular cell hypertrophy and a reduction in colloid in mid dose males and high dose animals. In both generations, there was an increase in relative liver weight in mid dose males and absolute and relative liver weight was increased in high dose males and females. In the F0 high dose animals this was accompanied by hepatocyte hypertrophy. The low dose of 29 mg/kg bw/day is considered to be the NOAEL for parental toxicity (males). This is based on effects on the thyroid at mid and high doses in males following at least 77 days exposure.

It is noted that in both studies with V6, there was no evidence of pre-neoplastic or hyperplastic lesions, which would indicate a concern for carcinogenicity.

When the repeated dose toxicity data for V6 is compared with studies of similar duration for TCEP, there is some difference in the potency and severity of the effects seen between the two substances. In a 16 week oral gavage study in rat with TCEP, the most relevant toxic effects observed were mortality at highest dose (350 mg/kg) and brain lesions in females at 175 mg/kg and above (BAUA 2006). Although an increase in relative kidney and liver weights was observed, no corresponding histopathological effects were seen in these organs. The NOAEL identified was 88 mg/kg, based on neuronal effects. In a second 3 month dietary study in rats, an increased incidence of regenerative hyperplasia in renal cortex was observed in both sexes at the highest dose (506 mg/kg males and 586 mg/kg females). The NOAEL identified was 192 mg/kg/day (BAUA 2006). Based on the above, there appears to be a difference in target organs and severity of effects between V6 and TCEP which would indicate that a direct quantitative read-across to data on TCEP is not appropriate.

No study of similar duration is available for TDCP, although in the 2-year carcinogenicity study, the liver and kidney were identified as target organ for TDCP (HSA/EA 2008b). The LOAEL of 5 mg/kg/day was based on hyperplasia observed in the kidney and testicular effects observed at this dose. The target organs of TDCP and V6 are not comparable and therefore, it is concluded that a direct quantitative read-across from TDCP is not possible.

A summary of the available repeat dose toxicity data for V6, TCEP, TDCP and TCPP is presented in **Table D.4** below.

7. Summary and conclusion

As discussed above, when compared with the group of chloroalkyl phosphates, TCPP, TDCP and TCEP, there are some differences in the toxicokinetics, metabolism and target organs for V6. Also, while V6 shares the same basic structure as the other three substances, it is a much

bulkier molecule than the other substances, and so possibly less reactive. Therefore, it is considered that V6 is not sufficiently similar to this group to support a quantative or qualitative read-across for the carcinogenicity endpoint.

In addition, V6 is not mutagenic and no pre-neoplastic or hyperplastic lesions were observed in the repeat dose toxicity studies for V6, which would indicate a concern for carcinogenicity.

Table D.4 Summary of the available repeat dose toxicity data for V6, TCEP, TCPP and TDCP

Study type	TCEP	TCPP	TDCP	V6
14-day (oral)				
Species	Rat	Rat	No study available	No study available
Dose	0,22,44,88,175, 350 mg/kg	417, 648, 1015, 1636 mg/kg (M) 382, 575, 904, 1517 mg/kg (F)		
NOAEL	350 mg/kg	1015 mg/kg		
Target organs/ effects:	-Increase kidney weight at ≥ 175 -Increase liver weight at 350	-Decrease bw gain		
14-day (oral)				
Species	Mouse			
Dose	0, 44, 88, 175, 350, 700 mg/kg			
NOAEL	175 mg/kg			
Target organs/ effects:	-ataxia and convulsive movements Days 1-3			

Study type	TCEP	TCPP	TDCP	V6
28-day (oral)				
Species	No study available	Rat	No study available	Rat
Dose		0, 417,648,1015, 1636 mg/kg (M) 0,382,575,904,1517 mg/kg (F)		0, 15, 150, 600 mg/kg (M&F)
NOAEL		10 mg/kg/day		15 mg/kg/day
Target organs/ effects:		- Increase in liver weight high dose & liver histopathology in mid and high - Decrease in ALAT at high		-increased liver weight mid & high dose & liver histopathology in high Increased in thyroid weight high dose & histopath indicating hyperactivity
90-day (oral)	(3mth dietary)			
Species	Rat	Rat	No study available	No study available
Dose	0,26,65,192,506 mg/kg (M) 0,30,75,215,586 mg/kg (F)	0,52,160,481, 1349 mg/kg (M) 0,62,171,570,1745 mg/kg (F)		
NOAEL	192 mg/kg (regenerative hyperplasia in kidney)	52 mg/kg (LOAEL)		
Target organs/ effects:	-Increase in kidney & liver wt at ≥ 192/215 mg/kg -Increase incidence of tubular hyperplasia at high dose - Decrease in gonad & brain wt at 2 highest doses -decreased heart wt at high dose	-Increase in liver weight in all treated males & liver histopath at high dose -Increase in kidney weight -Thyroid follicular cell hyperplasia		

Study type	TCEP	TCPP	TDCP	V6
90-day (oral) Species Dose NOAEL Target organs/ effects:	(3 mth dietary) Mouse 0,12,60,300 & 1500 mg/kg LOAEL 12 mg/kg - Decreased heart & testes wt at high dose - decreased kidney wt F at 1500 mg/kg -focal necrosis & vacuolation in liver -hypertrophy & hyperplasia of urinary tubule epithelium.			
16 weeks (oral) Species Dose NOAEL Target organs/ effects:	 Rat 0,22,44,88,175, 350 mg/kg 88 mg/kg -Increase kidney & liver wt (no histopath) at > 44 mg/kg (F) &350 mg/kg (M) - Increase in brain wt at 350 mg/kg - Neuronal necrosis hippocampus & thalamus at ≥ 175 mg/kg	No study available	No study available	No study available

Study type	TCEP	TCPP	TDCP	V6
16 weeks (oral)				
Species	Mouse			
Dose	0,44,88,175,350, 700 mg/kg			
NOAEL	350 mg/kg			
Target organs/ effects:	- Increase in liver wt F ≥ 175 mg/kg (no histopath) - Decrease in kidney wt M at ≥ 175 mg/kg - Histopath kidney proximal convoluted tubule - slight decrease in sperm count			
2-yr (oral)	(103 weeks)			
Species	Rat	No study available	Rat	No study available
Dose	0, 44,88 mg/kg		0,5,20,80 mg/kg	
NOAEL	44 mg/kg (LOAEL kidney; NOAEL brain)		5 mg/kg (LOAEL)	
Target organs/ effects:	- Increase in focal hyperplasia of renal tubule epithelium - degenerative lesions of brain stem & cerebrum		- Increase in kidney weight & hyperplasia in convoluted tubule of kidney - Increase in liver weight & liver histopath at mid & high dose - Increase in thyroid weight high dose female - Testis effects in all treated groups	

Study type	TCEP	TCPP	TDCP	V6
2-yr (oral)	(103 weeks)			
Species	Mouse			
Dose	0,175,350 mg/kg			
NOAEL	175 mg/kg (LOAEL kidney) No NOAEL for liver effects			
Target organs/ effects:	-Karyomegaly of tubule epithelium in kidney -Increased incidence of foci of cytologic alteration in liver at all doses (precursor of hepatocellular neoplasms)			

Study type	TCEP	TCPP	TDCP	V6
2-year carcinogenicity				
Species	Rat		Rat	
Route	Oral		Oral	
Dose	0, 44, 88 mg/kg		0,5,20,80 mg/kg	
NOAEL	None established		5 mg/kg (LOAEL)	
Target organs/ effects:	- Increase in incidence of neoplastic lesions in kidney (proliferative lesions & adenomas of the renal tubule). - Increased incidence of thyroid follicular cell neoplasms (possibly treatment related) - Increase in mononuclear cell leukaemia		- Hyperplasia of convoluted tubule in all treated males & high dose females - Increase in renal cortical adenomas in mid & high dose at 24 mths -Increase in benign testicular cell tumours at mid & high dose - Increase in Leydig cell tumours in mid & high dose males. - Increase incidence of hepatocellular adenomas at high dose.	
2-year carcinogenicity				
Species	Mouse			
Route	Oral			
NOAEL	None established			
Dose	0,175, 350 mg/kg			
Target organs/ effects:	- marginal increase in incidence of renal tubule neoplasms at 350 mg/kg (M) - Increase in Harderian gland adenomas at 175 mg/kg (F)			

Study type	TCEP	TCPP	TDCP	V6
2-year carcinogenicity				
Species	Mouse			
Route	Oral (dietary)			
Dose	0, 12, 60, 300, 1500 mg/kg			
NOAEL	Kidney: ≥ 12 mg/kg (LOAEL) Liver : 60 mg/kg			
Target organs/ effects:	- Increase in incidence of tumours in liver and kidney			

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The report provides the comprehensive risk assessment of the substance 2,2-bis(chloromethyl) trimethylene bis[bis(2-chloroethyl) phosphate] (V6). It has been prepared by Ireland (Human Health) and the United Kingdom (Environment) in the frame of Council Regulation (EEC) No. 793/93 on the evaluation and control of the risks of existing substances, following the principles for assessment of the risks to man and the environment, laid down in Commission Regulation (EC) No. 1488/94.

The evaluation considers the emissions and the resulting exposure to the environment and the human populations in all life cycle steps. Following the exposure assessment, the environmental risk characterisation for each protection goal in the aquatic, terrestrial and atmospheric compartment has been determined. The environmental risk assessment concludes that there is no concern for any of the environmental compartments. For human health the scenarios for occupational exposure, consumer exposure and humans exposed via the environment and the possible risks have been examined and no concerns have been identified.