HERA

Human & Environmental Risk Assessment
on Ingredients of Household Cleaning Products

Isopropanol

CAS No 67-63-0

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Abstract

Isopropanol (IPA, CAS No 67-63-0) has been widely used as an industrial solvent and is a component of industrial and consumer products. HERA applications include laundry detergents, hand dishwashing liquids and various hard surface cleaners.

The HERA risk assessment has shown that the use of IPA in HERA applications results in environmental risk characterization ratios less than one, indicating no concern, for all environmental compartments.

For human health, a margin of exposure of about 3800 has been calculated for the total aggregate consumer exposure. This MOE has been considered very large, large enough to account for the inherent uncertainty and variability of the database and inter and intra-species extrapolations, which have been considered by an assessment factor of 100 or greater. It can be concluded that the use of Isopropanol in household cleaning products raises no safety concern for consumers.

The outcome of this HERA risk assessment focussing on the specific uses of IPA in household cleaning detergents is fully consistent with that of the OECD HPV review which looked at all global uses of IPA. The SIDS initial assessment profile (SIAP) concluded that IPA has been considered of low priority for further work and poses no concern for the environment or human health.

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1. Introduction

Isopropanol (IPA) or 2-Propanol (CAS No 67-63-0) is a high production volume (HPV) chemical which is used as an industrial solvent, a component of industrial and consumer products. Uses in household cleaning products, the scope of HERA, include laundry detergents, hand dishwashing liquids and various hard surface cleaners.

This HERA report therefore covers the human and environmental risk assessment of the use of IPA in household cleaning applications building on the physico-chemical and hazard information provided in the OECD Screening Information Data Set (SIDS) (OECD, 2000) and the International Uniform Chemical Information Database (IUCLID) profile (ECB, 2000). The analysis of the hazard data for the environmental and human health risk assessment has been based on the comprehensive and complete hazard review provided in the IUCLID and SIDS.

As part of the larger effort of OECD countries to co-operatively undertake initial hazard assessments of HPV chemicals, a SIDS has been developed for IPA. This SIDS on IPA contains an internationally agreed and harmonized data set providing general substance information and summarizing data on

- Exposure and use;
- Physico chemical properties;
- Environmental fate and pathways;
- Ecotoxicity data; *and*
- Human health data.

To characterise and assess the risks associated with the use of IPA in household cleaning detergents to human health and the environment according to the HERA methodology, the information provided in existing data profiles was supplemented by data from the HERA IPA substance team on habits and practices of uses of detergents and IPA volumes used in the various household cleaning applications in Western Europe. Respective hazard summaries and calculations of PEC/PNEC ratio and Margin of Exposures (MOE) and their underlying data which form the basis for this risk assessment are annexed to this report.

2. Substance Characterisation and Uses in Household Cleaning Applications

IPA is a secondary alcohol which largely goes into the solvent market either directly or via conversion to acetone or one of acetone's derivatives. IPA's major solvent use includes inks, coatings, cosmetics, pharmaceuticals and household cleaners such as laundry detergents, hand dishwashing liquids and various hard surface cleaners.

Since the 1940s, the dominant manufacturing process is the weak acid process in which propene gas is absorbed in, and reacted with, 60% sulfuric acid. The resulting sulphates are hydrolyzed in a single step process. IPA is stripped and refined from the condensate which contains di-isopropyl ether, acetone, and polymer oils of low molecular mass. Another major current manufacturing process is catalytic hydration of propene with water. Hydration can be gas-phase with a phosphoric acid catalyst, mixed phase with a cation-exchange resin catalyst or liquid phase using a tungsten catalyst.

In line with the objectives of the HERA initiative, this assessment will focus on the use of IPA in household cleaning products. Table 1 lists household cleaning applications and typical finished product concentration ranges of IPA used in household products.

Table 1: Household applications and finished product concentrations of IPA (AISE, unpublished data)

Product application	Range of IPA level in finished product
Regular laundry detergents	0.0 – 0.3 %
Compact laundry detergents	0.0 – 2 %
Fabric conditioners	0.4 -2.56 %
Laundry additives	0.0 -10.0 %
Hand dishwashing detergent	0.0 – 3.0 %
Surface cleaners	0.0 – 15.0 %

3. Environmental Assessment

Environmental Exposure

Tonnage Scenarios

Total use of IPA in Western Europe (to include both HERA and non HERA uses) has been estimated at 619,000 tonnes per annum (SRI International, 1996). In HERA applications it has been estimated that an annual tonnage of 12,600 of IPA has been used which has been calculated according to data received from a survey conducted among detergent formulator companies, for the uses shown in Table 1. This data is representative for the volume being consumed in the European Union 15+3 Countries (+ 3 being Iceland, Switzerland and Norway) and this value has been estimated to cover greater than 80% of the tonnage used within the HERA applications. Calculations of the predicted environmental concentration (PEC) in this assessment, therefore, have been based on 15,700 tonnes per annum to ensure that conservative estimates of 100% or greater of the tonnage used are employed to derive PEC_{HERA} values. This tonnage estimate in HERA use categories represents only 2.5% of the total use of IPA in Europe.

Physico-Chemical Properties

The most important physico-chemical properties to estimate a PEC value are aqueous solubility, vapour pressure, and the octanol/water partition coefficient. Details of the physico-chemical properties that have been used in this assessment for IPA are shown in Annex 1.

Environmental Fate

Several reviews highlight that IPA is readily biodegradable. Aerobic biodegradation of IPA has been shown to occur rapidly under non-acclimated conditions based on a result of 49% biodegradation from a 5 day BOD test (OECD, 2000, ECB, 2000). Additional aerobic and anaerobic biodegradation data developed using standardised test methods show that IPA removal from the test medium has been 72% to 99% within 20 days (ECB, 2000). In surface soils IPA has been shown not to persist due to rapid evaporation (ECB, 2000). In the air, physical degradation of IPA has been shown to occur rapidly due to hydroxyl radical (OH) attack (OECD, 2000). Monitoring data for IPA in European surface water are not available. However, based on the above data IPA has been shown not to be expected to accumulate in aquatic habitats.

Predicted Environmental Concentrations (PEC) Calculations

The European Union System for the Evaluation of Substances (EUSES) version 2.03 calculated degradation of IPA in a waste water treatment model as 86.6% based on the fact that IPA has been determined to be readily biodegradable. The remainder of IPA partitioned between air (1.03%), water (12.4%) and sludge (0.013%). The EUSES report file has been included in Annex 2.

The HERA environmental risk assessment for IPA has been based on the Technical Guidance Document for new and existing substances (TGD, 2003). At the screening level it makes use of the EUSES programme (EUSES 2.03, 2005) to calculate the local and regional exposure to IPA (Table 2). The total IPA tonnage produced for, and used in detergents was assumed to follow the down-the-drain pathway to the environment. The production and formulation releases, at local level, were not considered because they fall outside the scope of HERA. For the calculation, the HERA exposure scenario (to assign 7% of the EU tonnage to the standard EU region, instead of the TGD default 10%, and to increase the emissions at local level by a factor of 1.5, instead of the TGD default factor of 4) has not been used, as the revised TGD has updated the default values for the regional emissions and the local input of substances used in household detergents, based on the experimental data submitted during the TGD revision process (Fox, 2001). More details and justification of these default values can be found in chapter 2.2.3 of the revised HERA methodology document (HERA, 2005).

As explained above the IPA volume used in HERA applications has been used to calculate all PECs, therefore the subscript HERA has been added to the calculated PECs to indicate that the HERA volume has been used. It should be stated that other releases of IPA to the environment cannot be ruled out but are outside the scope of this assessment. However, considering the fact that IPA has been shown to be readily biodegradable in all environmental compartments and has been classed as presenting a low potential exposure to aquatic and terrestrial biota (OECD, 2000) it has been justified using the local PEC_{HERA} in the environmental risk characterisation.

Table 2 PEC_{HERA}* estimates for IPA using EUSES

Local					**Regional**
PEC_{HERA} air	PEC_{HERA} surface water	PEC_{HERA} freshwater sediment	PEC_{HERA} soil 30d	PEC_{HERA} WWTP microorgs	PEC_{HERA} surface water
(mg/m^3)	(mg/L)	(mg/kg WW)	(mg/kg WW)	(mg/L)	(mg/L)
6.3 E-05	0.016	0.013	2.9 E-05	0.13	2.6 E-03

*it should be noted that the PECs calculated here are based on IPA volume used in HERA household applications and are as such denoted by the subscript HERA

Environmental Effects

Ecotoxicological data for IPA have been thoroughly reviewed in the context of the OECD HPV programme (OECD, 2000). A summary of those toxicological endpoints and considerations most relevant for the assessment of IPA in context of HERA are attached in Annex3.

Numerous studies have shown that IPA has a low order of acute aquatic toxicity with LC_{50} values ranging from 1,400 to 10,000 mg/L in 24 hour to 96 hour studies with freshwater and saltwater fish as well as aquatic invertebrates. The acute aquatic data did not show clear evidence of one taxonomic group being more sensitive then another. A chronic toxicity study with *Daphnia magna* has been used to derive the predicted no effect concentration (PNEC) for the aquatic compartment. In this case the Technical Guidance Document (TGD) (EC, 2003) recommends an assessment factor of 100 be applied to this value in the absence of any chronic toxicity data for species from other trophic levels. In a 21 day extended toxicity study with *Daphnia magna*, the no observed effect concentration (NOEC) was 30 mg/L and the resulting $PNEC_{aquatic}$ has been calculated at 0.3 mg/L.

The toxicity of IPA to various micro-organisms has been assessed in several studies and the toxicity threshold ranged from 104 to 4930 mg/L. The $PNEC_{microorganism}$ has been derived from a growth inhibition test with a ciliated protozoa (*Chilomonas paramecium*) where the toxicity threshold has been determined to be 104 mg/L. The toxicity threshold in this assessment corresponded to an EC3 and TGD recommends an assessment factor of 10 be applied to generate a $PNEC_{microorganism}$ of 10.4 mg/L.

Data on aquatic toxicity of IPA in the sediment compartment has not been available. The $PNEC_{aquatic}$ has been used to derive a $PNEC_{sediment}$ using equilibrium partitioning. The $PNEC_{sediment}$ has been calculated as 0.24 mg/kg WW using EUSES.

Similarly, data on toxicity to soil dwelling organisms have been lacking. In the absence of soil toxicity data the TGD recommends that a $PNEC_{soil}$ be derived from equilibrium partitioning data from the $PNEC_{aquatic}$ as an initial screen. The partition coefficient soil water ($K_{soil\text{-}water}$) has been determined by EUSES and the $PNEC_{soil}$ of 0.04 has been reported.

Based on IPAs low log Kow (0.05, Annex 1) there has been no evidence of bio-concentration potential of IPA in aquatic biota.

Environmental Risk Characterisation

The risk characterisation has been conducted by comparing the ratio of PEC_{HERA} derived from the EUSES calculation for the local worst case scenario based on the household HERA tonnage and the PNEC values for the different environmental compartments (Annex 4). This assessment has shown that the use of IPA in HERA applications results in risk characterisation ratio (RCR) less than 1 for all relevant environmental compartments (Table 3) and therefore the use of IPA in HERA applications has been classed of low environmental concern.

Table 3 RCRs in the relevant environmental compartments for IPA

	Local Water	WWTP	Local Sediment	Local Soil
PEC	0.016 mg/L	0.13 mg/L	0.013 mg/kg WW	2.9 E-05 mg/kg WW
PNEC	0.3 mg/L	10.4 mg/L	0.3 mg/kg WW	0.04 mg/kg WW
RCR[1]	**0.05**	**0.01**	**0.04**	**7 E-03**

1 Please note that differences in the RCRs reported in this table and those calculated in the EUSES output file are related to differences in the rounding of numbers.

4. Human Health Assessment

Consumers are exposed to IPA through their presence in household cleaning products, mainly via the dermal, but to some extend also via the oral and the inhalatory route. Skin exposure occurs mainly through hand-washed laundry, laundry pre-treatment and hand dishwashing, hand dishwashing and during hard surface cleaning. Orally, consumers are exposed to IPA through residues deposited on eating utensil and dishes after washing with IPA containing detergents. Since IPA has also been used in spray cleaners, the consumer can also be exposed to IPA containing aerosols generated by the sprayer.

Annex 6 provides a detailed consumer exposure assessment according to HERA exposure assessment guidelines. These exposure estimates take into account maximum finished product concentrations of IPA in household cleaners and habits and practice data, reflecting consumers' use of detergents in terms of gram per task, tasks per week and duration of task. The underlying data were collated by the HERA IPA substance team and the European Soap and Detergent Industry Association (AISE). The aggregate exposure to IPA via its use in household cleaning products has been estimated to be at maximum 104.5 µg/kg bw/d.

A thorough review of the toxicological data has been presented for the OECD HPV programme (OECD, 2000 and ECB, 2000). A summary of those toxicological endpoints and considerations relevant for the assessment of IPA in context of its use in household cleaning products has been attached in Annex 5.

A substantial amount of toxicological data and information *in vivo* and *in vitro* demonstrates that IPA has a low order of acute toxicity. There has been no evidence for IPA being genotoxic, mutagenic or carcinogenic. The systemic (non-cancer) toxicity of repeated exposure to IPA has been evaluated in rats and mice by the oral and inhalation routes. Rats exhibited an accumulation of hyaline (protein) droplets in kidney proximal tubule cells and an exacerbation of chronic progressive nephropathy, a spontaneous disease of unknown aetiology common in aged rats. In the mouse, minimal to mild effects to the kidney including renal tubular proteinosis and tubular dilation have been observed following chronic exposure. On the basis of a 12-week oral drinking water study, the no observed effect level (NOEL) has been assessed to be 870 mg/kg bw/d. Effects such as increased weights of kidneys, liver and adrenals as well as increase in formation of hyaline droplets in the proximal tubules of the kidney mentioned above have been observed at the lowest observed effect level (LOEL) at 1280 mg/kg/d. The NOEL determined in the oral exposure study fits well with NOAELs estimated from subchronic and chronic inhalation studies. In a 13 week GLP compliant rat study, a NOEL of 500ppm and a LOEL of 1500ppm was established. Assuming an average body weight of the rat of 350g and a respiratory minute volume of 240mL (Kennedy, 1989), this NOEL reflects an exposure of about 300 mg/kg bw/d and the LOEL an exposure of about 1500 mg/kg bw/d. In an 18

months mouse inhalation study, the NOEL was established to be 500ppm. This reflects, assuming an average body weight of the mouse of 30g and a respiratory minute volume of 45mL (Kennedy, 1989), an exposure of about 650 mg/kg bw/d.

A recent two-generation reproductive toxicity study characterized the reproductive hazard for IPA associated with oral gavage exposure. This study revealed that the only reproductive parameter affected has been a statistically significant decrease in male mating index of F_1 males. The SIDS review, however, concluded that is unclear as to whether these findings are biologically meaningful. Exposure to 1000 mg/kg bw/d and to a lesser extent 500 mg/kg bw/d resulted in a reduction in postnatal survival in both F1 and F2 litters. A derivation of an appropriate NOAEL for offspring effects was made difficult because of conflicting interpretations of the reductions in postnatal survival for the 500 mg/kg/d treatment group. To clarify the issue, a benchmark dose (BMD) assessment was conducted for the study's findings. For the offspring developmental effects BMD dosages ($BMDL_5$) of 449 and 418 mg/kg bw/d were estimated for F1 and F2 respectively and a $BMDL_{10}$ of 407 mg/kg bw/d was estimated for reproductive effects. The developmental toxicity of IPA was further characterized in rat and rabbit developmental toxicity studies and in a rat developmental neurotoxicity study. These studies indicate that IPA is not a selective development hazard. It produced developmental toxicity in rats, but not in rabbits. In the rat, the developmental toxicity, consisting of reduced foetal body weights per litter, occurred only at higher, maternally toxic doses. No evidence of teratogenicity was observed at any dose level. The study information suggested the developmental NOAEL as well as the NOAEL for maternal toxicity to be 400 mg/kg bw/d for rats and 480 mg/kg bw/d for rabbits.

Under the OECD review, NOAELs for IPA have been established and discussed for chronic, reproductive and developmental toxicity. The lowest NOAEL has been set at 400 mg/kg bw/d. This level has been considered relatively close to the $BMDL_{10}$ of 407 mg/kg bw/d which has been estimated for reproductive effects. The comparison of the aggregate exposure of 104.5 µg/kg bw/d to the lowest NOAEL of 400 mg/kg bw/d resulted in a MOE of 3827 (Annex 6). Taking into account the conservatism in the exposure calculations and the assigned NOAEL for IPA, this margin of exposure has been considered to be large enough to account for the inherent uncertainty and inter- and intra species variability.

In summary, this human health risk assessment demonstrates that the use of IPA in household laundry and cleaning detergents has been considered safe and does not cause concern with regard to consumer use.

5. Conclusion

IPA has been widely used as an industrial solvent, a component of industrial and consumer products and as a disinfectant. Uses of IPA in household cleaning products, the scope of HERA, includes laundry detergents, hand dishwashing liquids and various hard surface cleaners.

This HERA environmental and human health risk assessment demonstrates that the use of IPA in these applications can be considered as safe for the consumer and the environment. An extensive internationally agreed environmental and human health data set has been available. By using the HERA risk assessment methodology as described in the HERA Guidance Document, it has been shown that the use of IPA in HERA applications results in environmental risk characterization ratios less than one, indicating no concern, for all environmental compartments. For human health, a margin of exposure of about 3800 has

been calculated for the total aggregate consumer exposure. This MOE has been considered very large, large enough to account for the inherent uncertainty and variability of the database and inter and intra-species extrapolations, which have been considered by an assessment factor of 100 or greater.

The outcome of this HERA risk assessment focussing on the specific uses of IPA in household cleaning detergents has been fully consistent with that of the OECD HPV review which looked at all global uses of IPA. Considering IPA's wide use, the database available on human/mammalian and environmental effects and its 'considerable potential for both occupational and consumer exposure', the SIDS initial assessment profile (SIAP) concluded that IPA has been considered of low priority for further work.

6. Contributions to the Report

This risk assessment was developed by Sasol Germany GmbH, Shell Chemicals Ltd. and Exxon-Mobil Petroleum Chemicals. Additional input was given by the HERA Environmental and Human Health task force and the Oxygenated Solvents Petroleum Association (OSPA) as well as by THE WEINBERG GROUP.

Annex 1. Physical/Chemical Properties of IPA for EUSES

Property	Results	Protocol/Method
EINECS name	Propan-2-ol	
CAS number	67-63-0	
EINECS number	200-661-7	
Smiles code	CC(OH)C	
Molecular weight	60 g/Mol	
Melting point	90 ºC	ASTM D97
Boiling point	82 ºC (at 1012 hPa)	ASTM D1078
Vapour pressure	42 hPa at 20 ºC	Calculated
Log Octanol-Water partition coefficient (Log Kow)	0.05 at 25 ºC	Shake-flask method
Water solubility	Miscible (100 vol% at 20 ºC)	Not known
Henry's law constant	7.52×10^{-6} atm·m^3 / mole	Calculated
Transport and distribution	In air 22.3% In water 77.7% In sediment 0% In soil 0%	Calculated (fugacity level 1 type)

Annex 2. EUSES 2.03 output report

DEFAULTS

DEFAULT IDENTIFICATION

General name	Standard Euses 2.0		D
Description	According to TGDs		D

CHARACTERISTICS OF COMPARTMENTS

GENERAL

Density of solid phase	2.5	[kg.l-1]	D
Density of water phase	1	[kg.l-1]	D
Density of air phase	1.3E-03	[kg.l-1]	D
Environmental temperature	12	[oC]	D
Standard temperature for Vp and Sol	25	[oC]	D
Constant of Junge equation	0.01	[Pa.m]	D
Surface area of aerosol particles	0.01	[m2.m-3]	D
Gas constant (8.314)	8.314	[Pa.m3.mol-1.K-1]	D

SURFACE WATER

Volume fraction solids in suspended matter	0.1	[m3.m-3]	D
Volume fraction water in suspended matter	0.9	[m3.m-3]	D
Weight fraction of organic carbon in suspended matter	0.1	[kg.kg-1]	D
Wet bulk density of suspended matter	1.15E+03	[kg.m-3]	O

SEDIMENT

Volume fraction solids in sediment	0.2	[m3.m-3]	D
Volume fraction water in sediment	0.8	[m3.m-3]	D
Weight fraction of organic carbon in sediment	0.05	[kg.kg-1]	D
Bulk density of sediment	1.3E+03	[kgwwt.m-3]	O
Conversion factor wet-dry sediment	2.6	[kgwwt.kgdwt-1]	O

SOIL

Volume fraction solids in soil	0.6	[m3.m-3]	D
Volume fraction water in soil	0.2	[m3.m-3]	D
Volume fraction air in soil	0.2	[m3.m-3]	D
Weight fraction of organic carbon in soil	0.02	[kg.kg-1]	D
Weight fraction of organic matter in soil	0.034	[kg.kg-1]	O
Bulk density of soil	1.7E+03	[kgwwt.m-3]	O
Conversion factor wet-dry soil	1.13	[kgwwt.kgdwt-1]	O

STP SLUDGE			
Fraction of organic carbon in raw sewage sludge	0.3	[kg.kg-1]	D
Fraction of organic carbon in settled sewage sludge	0.3	[kg.kg-1]	D
Fraction of organic carbon in activated sewage sludge	0.37	[kg.kg-1]	D
Fraction of organic carbon in effluent sewage sludge	0.37	[kg.kg-1]	D
DEGRADATION AND TRANSFORMATION RATES			
Rate constant for abiotic degradation in STP	0	[d-1]	D
Rate constant for abiotic degradation in bulk sediment	0	[d-1] (12[oC])	D
Rate constant for anaerobic biodegradation in sediment	0	[d-1] (12[oC])	D
Fraction of sediment compartment that is aerated	0.1	[m3.m-3]	D
Concentration of OH-radicals in atmosphere	5E+05	[molec.cm-3]	D
Rate constant for abiotic degradation in bulk soil	0	[d-1] (12[oC])	D
RELEASE ESTIMATION			
Fraction of EU production volume for region	100	[%]	D
Fraction of EU tonnage for region (private use)	10	[%]	D
Fraction connected to sewer systems	80	[%]	D
SEWAGE TREATMENT			
GENERAL			
Number of inhabitants feeding one STP	1E+04	[eq]	D
Sewage flow	200	[l.eq-1.d-1]	D
Effluent discharge rate of local STP	2E+06	[l.d-1]	O
Temperature dependency correction	No		D
Temperature of air above aeration tank	15	[oC]	D
Temperature of water in aeration tank	15	[oC]	D
Height of air column above STP	10	[m]	D
Number of inhabitants of region	2E+07	[eq]	D
Number of inhabitants of continental system	3.5E+08	[eq]	O
Windspeed in the system	3	[m.s-1]	D
RAW SEWAGE			
Mass of O2 binding material per person per day	54	[g.eq-1.d-1]	D
Dry weight solids produced per person per day	0.09	[kg.eq-1.d-1]	D
Density solids in raw sewage	1.5	[kg.l-1]	D
Fraction of organic carbon in raw sewage sludge	0.3	[kg.kg-1]	D
PRIMARY SETTLER			
Depth of primary settler	4	[m]	D
Hydraulic retention time of primary settler	2	[hr]	D
Density suspended and settled solids in primary settler	1.5	[kg.l-1]	D
Fraction of organic carbon in settled sewage sludge	0.3	[kg.kg-1]	D

ACTIVATED SLUDGE TANK			
Depth of aeration tank	3	[m]	D
Density solids of activated sludge	1.3	[kg.l-1]	D
Concentration solids of activated sludge	4	[kg.m-3]	D
Steady state O2 concentration in activated sludge	2E-03	[kg.m-3]	D
Mode of aeration	Surface		D
Aeration rate of bubble aeration	1.31E-05	[m3.s-1.eq-1]	D
Fraction of organic carbon in activated sewage sludge	0.37	[kg.kg-1]	D
Sludge loading rate	0.15	[kg.kg-1.d-1]	D
Hydraulic retention time in aerator (9-box STP)	6.9	[hr]	O
Hydraulic retention time in aerator (6-box STP)	10.8	[hr]	O
Sludge retention time of aeration tank	9.2	[d]	O
SOLIDS-LIQUIDS SEPARATOR			
Depth of solids-liquid separator	3	[m]	D
Density suspended and settled solids in solids-liquid separator	1.3	[kg.l-1]	D
Concentration solids in effluent	30	[mg.l-1]	D
Hydraulic retention time of solids-liquid separator	6	[hr]	D
Fraction of organic carbon in effluent sewage sludge	0.37	[kg.kg-1]	D
LOCAL DISTRIBUTION			
AIR AND SURFACE WATER			
Concentration in air at source strength 1 [kg.d-1]	2.78E-04	[mg.m-3]	D
Standard deposition flux of aerosol-bound compounds	0.01	[mg.m-2.d-1]	D
Standard deposition flux of gaseous compounds	4E-04	[mg.m-2.d-1]	O
Suspended solids concentration in STP effluent water	15	[mg.l-1]	D
Dilution factor (rivers)	10	[-]	D
Flow rate of the river	1.8E+04	[m3.d-1]	D
Calculate dilution from river flow rate	No		D
Dilution factor (coastal areas)	100	[-]	D
SOIL			
Mixing depth of grassland soil	0.1	[m]	D
Dry sludge application rate on agricultural soil	5E+03	[kg.ha-1.yr-1]	D
Dry sludge application rate on grassland	1000	[kg.ha-1.yr-1]	D
Averaging time soil (for terrestrial ecosystem)	30	[d]	D
Averaging time agricultural soil	180	[d]	D
Averaging time grassland	180	[d]	D
PMTC, air side of air-soil interface	1.05E-03	[m.s-1]	O
Soil-air PMTC (air-soil interface)	5.56E-06	[m.s-1]	D
Soil-water film PMTC (air-soil interface)	5.56E-10	[m.s-1]	D
Mixing depth agricultural soil	0.2	[m]	D
Fraction of rain water infiltrating soil	0.25	[-]	D
Average annual precipitation	700	[mm.yr-1]	D

REGIONAL AND CONTINENTAL DISTRIBUTION

CONFIGURATION

Fraction of direct regional emissions to sea water	1	[%]	D
Fraction of direct continental emissions to sea water	0	[%]	D
Fraction of regional STP effluent to sea water	0	[%]	D
Fraction of continental STP effluent to sea water	0	[%]	D
Fraction of flow from continental rivers to regional rivers	0.034	[-]	D
Fraction of flow from continental rivers to regional sea	0	[-]	D
Fraction of flow from continental rivers to continental sea	0.966	[-]	O
Number of inhabitants of region	2E+07	[eq]	D
Number of inhabitants in the EU	3.7E+08	[eq]	D
Number of inhabitants of continental system	3.5E+08	[eq]	O

AREAS

REGIONAL

Area (land+rivers) of regional system	4E+04	[km2]	D
Area fraction of fresh water, region (excl. sea)	0.03	[-]	D
Area fraction of natural soil, region (excl. sea)	0.27	[-]	D
Area fraction of agricultural soil, region (excl. sea)	0.6	[-]	D
Area fraction of industrial/urban soil, region (excl. sea)	0.1	[-]	D
Length of regional sea water	40	[km]	D
Width of regional sea water	10	[km]	D
Area of regional sea water	400	[km2]	O
Area (land+rivers+sea) of regional system	4.04E+04	[km2]	O
Area fraction of fresh water, region (total)	0.0297	[-]	O
Area fraction of sea water, region (total)	9.9E-03	[-]	O
Area fraction of natural soil, region (total)	0.267	[-]	O
Area fraction of agricultural soil, region (total)	0.594	[-]	O
Area fraction of industrial/urban soil, region (total)	0.099	[-]	O

CONTINENTAL

Total area of EU (continent+region, incl. sea)	7.04E+06	[km2]	D
Area (land+rivers+sea) of continental system	7E+06	[km2]	O
Area (land+rivers) of continental system	3.5E+06	[km2]	O
Area fraction of fresh water, continent (excl. sea)	0.03	[-]	D
Area fraction of natural soil, continent (excl. sea)	0.27	[-]	D
Area fraction of agricultural soil, continent (excl. sea)	0.6	[-]	D
Area fraction of industrial/urban soil, continent (excl. sea)	0.1	[-]	D
Area fraction of fresh water, continent (total)	0.015	[-]	O
Area fraction of sea water, continent (total)	0.5	[-]	D
Area fraction of natural soil, continent (total)	0.135	[-]	O
Area fraction of agricultural soil, continent (total)	0.3	[-]	O
Area fraction of industrial/urban soil, continent (total)	0.05	[-]	O

MODERATE			
Area of moderate system (incl.continent,region)	8.5E+07	[km2]	D
Area of moderate system (excl.continent, region)	7.8E+07	[km2]	O
Area fraction of water, moderate system	0.5	[-]	D
TEMPERATURE			
Environmental temperature, regional scale	12	[oC]	D
Environmental temperature, continental scale	12	[oC]	D
Environmental temperature, moderate scale	12	[oC]	D
Environmental temperature, arctic scale	-10	[oC]	D
Environmental temperature, tropic scale	25	[oC]	D
Enthalpy of vaporisation	50	[kJ.mol-1]	D
Enthalpy of solution	10	[kJ.mol-1]	D
MASS TRANSFER			
Air-film PMTC (air-water interface)	6.01E-03	[m.s-1]	O
Water-film PMTC (air-water interface)	6.49E-06	[m.s-1]	O
PMTC, air side of air-soil interface	1.05E-03	[m.s-1]	O
PMTC, soil side of air-soil interface	4.72E-08	[m.s-1]	O
Soil-air PMTC (air-soil interface)	5.56E-06	[m.s-1]	D
Soil-water film PMTC (air-soil interface)	5.56E-10	[m.s-1]	D
Water-film PMTC (sediment-water interface)	2.78E-06	[m.s-1]	D
Pore water PMTC (sediment-water interface)	2.78E-08	[m.s-1]	D
AIR			
GENERAL			
Atmospheric mixing height	1000	[m]	D
Windspeed in the system	3	[m.s-1]	D
Aerosol deposition velocity	1E-03	[m.s-1]	D
Aerosol collection efficiency	2E+05	[-]	D
RAIN			
Average precipitation, regional system	700	[mm.yr-1]	D
Average precipitation, continental system	700	[mm.yr-1]	D
Average precipitation, moderate system	700	[mm.yr-1]	D
Average precipitation, arctic system	250	[mm.yr-1]	D
Average precipitation, tropic system	1.3E+03	[mm.yr-1]	D
RESIDENCE TIMES			
Residence time of air, regional	0.687	[d]	O
Residence time of air, continental	9.05	[d]	O
Residence time of air, moderate	30.2	[d]	O
Residence time of air, arctic	22.3	[d]	O
Residence time of air, tropic	38.6	[d]	O

WATER

DEPTH

Water depth of fresh water, regional system	3	[m]	D
Water depth of sea water, regional system	10	[m]	D
Water depth of fresh water, continental system	3	[m]	D
Water depth of sea water, continental system	200	[m]	D
Water depth, moderate system	1000	[m]	D
Water depth, arctic system	1000	[m]	D
Water depth, tropic system	1000	[m]	D

SUSPENDED SOLIDS

Suspended solids conc. fresh water, regional	15	[mg.l-1]	D
Suspended solids conc. sea water, regional	5	[mg.l-1]	D
Suspended solids conc. fresh water, continental	15	[mg.l-1]	D
Suspended solids conc. sea water, continental	5	[mg.l-1]	D
Suspended solids conc. sea water, moderate	5	[mg.l-1]	D
Suspended solids conc. sea water, arctic	5	[mg.l-1]	D
Suspended solids conc. sea water, tropic	5	[mg.l-1]	D
Concentration solids in effluent, regional	30	[mg.l-1]	D
Concentration solids in effluent, continental	30	[mg.l-1]	D
Concentration biota	1	[mgwwt.l-1]	D

RESIDENCE TIMES

Residence time of fresh water, regional	43.3	[d]	O
Residence time of sea water, regional	4.64	[d]	O
Residence time of fresh water, continental	172	[d]	O
Residence time of sea water, continental	2.1E+03	[d]	O
Residence time of water, moderate	3.03E+03	[d]	O
Residence time of water, arctic	5.84E+03	[d]	O
Residence time of water, tropic	1.09E+04	[d]	O

SEDIMENT

DEPTH

Sediment mixing depth	0.03	[m]	D

PHYSICO-CHEMICAL PROPERTIES

Molecular weight	60	[g.mol-1]	S
Melting point	90	[oC]	S
Boiling point	82	[oC]	S
Vapour pressure at test temperature	42	[hPa]	S
Temperature at which vapour pressure was measured	20	[oC]	S
Vapour pressure at 25 [oC]	5.93E+03	[Pa]	O
Octanol-water partition coefficient	0.05	[log10]	S
Water solubility at test temperature	1E+05	[mg.l-1]	S
Temperature at which solubility was measured	25	[oC]	D
Water solubility at 25 [oC]	1E+05	[mg.l-1]	O

PARTITION COEFFICIENTS AND BIOCONCENTRATION FACTORS

SOLIDS-WATER

Chemical class for Koc-QSAR	Predominantly hydrophobics (default QSAR)	D	
Organic carbon-water partition coefficient	1.38	[l.kg-1]	O
Solids-water partition coefficient in soil	0.0277	[l.kg-1]	O
Solids-water partition coefficient in sediment	0.0692	[l.kg-1]	O
Solids-water partition coefficient suspended matter	0.138	[l.kg-1]	O
Solids-water partition coefficient in raw sewage sludge	0.415	[l.kg-1]	O
Solids-water partition coefficient in settled sewage sludge	0.415	[l.kg-1]	O
Solids-water partition coefficient in activated sewage sludge	0.512	[l.kg-1]	O
Solids-water partition coefficient in effluent sewage sludge	0.512	[l.kg-1]	O
Soil-water partition coefficient	0.242	[m3.m-3]	O
Suspended matter-water partition coefficient	0.935	[m3.m-3]	O
Sediment-water partition coefficient	0.835	[m3.m-3]	O

AIR-WATER

Sub-cooled liquid vapour pressure	3.8E+04	[Pa]	O
Fraction of chemical associated with aerosol particles	2.63E-09	[-]	O
Henry's law constant	3.56	[Pa.m3.mol-1]	O
Air-water partitioning coefficient	1.5E-03	[m3.m-3]	O

BIOCONCENTRATION FACTORS

PREDATOR EXPOSURE

Bioconcentration factor for earthworms	0.853	[l.kgwwt-1]	O

HUMAN AND PREDATOR EXPOSURE

Bioconcentration factor for fish	1.41	[l.kgwwt-1]	O
QSAR valid for calculation of BCF-Fish	Yes		O
Biomagnification factor in fish	1	[-]	O
Biomagnification factor in predator	1	[-]	O

BIOTA-WATER

FOR REGIONAL/CONTINENTAL DISTRIBUTION

Bioconcentration factor for aquatic biota	1.41	[l.kgwwt-1]	O

DEGRADATION AND TRANSFORMATION RATES

CHARACTARIZATION

Characterization of biodegradability	Readily biodegradable		S

STP

Degradation calculation method in STP	First order, standard OECD/EU tests	D	
Rate constant for biodegradation in STP	24	[d-1]	O
Total rate constant for degradation in STP	24	[d-1]	O
Maximum growth rate of specific microorganisms	2	[d-1]	D
Half saturation concentration	0.5	[g.m-3]	D

WATER/SEDIMENT

WATER

Rate constant for hydrolysis in surface water	6.93E-07	[d-1] (12[oC])	O
Rate constant for photolysis in surface water	6.93E-07	[d-1]	O
Rate constant for biodegradation in surface water	0.0462	[d-1] (12[oC])	O
Total rate constant for degradation in bulk surface water	0.0462	[d-1] (12[oC])	O

SEDIMENT

Rate constant for biodegradation in aerated sediment	0.0231	[d-1] (12[oC])	O
Total rate constant for degradation in bulk sediment	2.31E-03	[d-1] (12[oC])	O

AIR

Specific degradation rate constant with OH-radicals	0	[cm3.molec-1.s-1]	D
Rate constant for degradation in air	0	[d-1]	O

SOIL

Rate constant for biodegradation in bulk soil	0.0231	[d-1] (12[oC])	O
Total rate constant for degradation in bulk soil	0.0231	[d-1] (12[oC])	O

REMOVAL RATE CONSTANTS SOIL

Total rate constant for degradation in bulk soil	0.0231	[d-1] (12[oC])	O
Rate constant for volatilisation from agricultural soil	0.0158	[d-1]	O
Rate constant for volatilisation from grassland soil	0.0316	[d-1]	O
Rate constant for leaching from agricultural soil	9.91E-03	[d-1]	O
Rate constant for leaching from grassland soil	0.0198	[d-1]	O
Total rate constant for removal from agricultural top soil	0.0488	[d-1]	O
Total rate constant for removal from grassland top soil	0.0746	[d-1]	O

RELEASE ESTIMATION

CHARACTERIZATION AND TONNAGE

High Production Volume Chemical	No		S
Production volume of chemical in EU	1.57E+04	[tonnes.yr-1]	S
Fraction of EU production volume for region	100	[%]	D
Regional production volume of substance	1.57E+04	[tonnes.yr-1]	O
Continental production volume of substance	0	[tonnes.yr-1]	O
Volume of chemical imported to EU	0	[tonnes.yr-1]	D
Volume of chemical exported from EU	0	[tonnes.yr-1]	D
Tonnage of substance in Europe	1.57E+04	[tonnes.yr-1]	O

OTHER LIFE CYCLE STEPS

USE PATTERN

Industry category	5 Personal / domestic use		S
Use category	9 Cleaning/washing agents and additives	S	
Extra details on use category	Unknown type		D
Extra details on use category	No extra details necessary		D

PRIVATE USE

Use specific emission scenario	No		D
Emission scenario	Emission fractions, fraction-main-source	S	

TONNAGE

Fraction of tonnage for application	1	[-]	O
Fraction of chemical in formulation	1	[-]	D
Tonnage of formulated product	1.57E+04	[tonnes.yr-1]	O
Relevant tonnage for application	1.57E+04	[tonnes.yr-1]	O
Regional tonnage of substance	1.57E+04	[tonnes.yr-1]	O
Tonnage of formulated product	1.57E+04	[tonnes.yr-1]	O
Regional tonnage of substance (private use step)	1.57E+03	[tonnes.yr-1]	O
Continental tonnage of substance (private use step)	1.41E+04	[tonnes.yr-1]	O
Total of fractions for all applications	1	[-]	O

USE PATTERN 2

RELEASE FRACTIONS AND EMISSION DAYS [2 ""]

PRIVATE USE

Emission tables	A4.1 (specific uses), B4.# (specific uses)	S	

RELEASE FRACTIONS

Fraction of tonnage released to air	0	[-]	O
Fraction of tonnage released to waste water	0.99	[-]	O
Fraction of tonnage released to surfacewater	0	[-]	O
Fraction of tonnage released to industrial soil	1E-02	[-]	O
Fraction of tonnage released to agricultural soil	0	[-]	O
Emission fractions determined by special scenario	No		O

EMISSION DAYS			
Fraction of the main local source	5E-04	[-]	O
Number of emission days per year	365	[-]	O
Emission day determined by special scenario	No		O
REGIONAL AND CONTINENTAL RELEASES [2 ""]			
PRIVATE USE			
REGIONAL			
Regional release to air	0	[kg.d-1]	O
Regional release to waste water	4.26E+03	[kg.d-1]	O
Regional release to surface water	0	[kg.d-1]	O
Regional release to industrial soil	43	[kg.d-1]	O
Regional release to agricultural soil	0	[kg.d-1]	O
CONTINENTAL			
Continental release to air	0	[kg.d-1]	O
Continental release to waste water	3.83E+04	[kg.d-1]	O
Continental release to surface water	0	[kg.d-1]	O
Continental release to industrial soil	387	[kg.d-1]	O
Continental release to agricultural soil	0	[kg.d-1]	O
REGIONAL AND CONTINENTAL TOTAL EMISSIONS			
Total regional emission to air	2.15E+03	[kg.d-1]	O
Total regional emission to wastewater	3.51E+03	[kg.d-1]	O
Total regional emission to surface water	877	[kg.d-1]	O
Total regional emission to industrial soil	47.3	[kg.d-1]	O
Total regional emission to agricultural soil	0	[kg.d-1]	O
Total continental emission to air	0	[kg.d-1]	O
Total continental emission to wastewater	3.07E+04	[kg.d-1]	O
Total continental emission to surface water	7.67E+03	[kg.d-1]	O
Total continental emission to industrial soil	387	[kg.d-1]	O
Total continental emission to agricultural soil	0	[kg.d-1]	O
[2 ""] [PRIVATE USE]			
Local emission to air during episode	0	[kg.d-1]	O
Emission to air calculated by special scenario	No		O
Local emission to wastewater during episode	2.13	[kg.d-1]	O
Emission to water calculated by special scenario	No		O
Show this step in further calculations	Yes		O
Intermittent release	No		D

DISTRIBUTION

SEWAGE TREATMENT

CONTINENTAL

Fraction of emission directed to air	1.08	[%]	O
Fraction of emission directed to water	12.3	[%]	O
Fraction of emission directed to sludge	0.013	[%]	O
Fraction of the emission degraded	86.6	[%]	O
Total of fractions	100	[%]	O
Indirect emission to air	330	[kg.d-1]	O
Indirect emission to surface water	3.79E+03	[kg.d-1]	O
Indirect emission to agricultural soil	4	[kg.d-1]	O

REGIONAL

Fraction of emission directed to air	1.3	[%]	O
Fraction of emission directed to water	12.2	[%]	O
Fraction of emission directed to sludge	0.013	[%]	O
Fraction of the emission degraded	86.4	[%]	O
Total of fractions	100	[%]	O
Indirect emission to air	45.5	[kg.d-1]	O
Indirect emission to surface water	430	[kg.d-1]	O
Indirect emission to agricultural soil	0.457	[kg.d-1]	O

LOCAL

[2 ""] [PRIVATE USE]

INPUT AND CONFIGURATION [2 ""] [PRIVATE USE]

INPUT

Use or bypass STP	Use STP		D
Local emission to wastewater during episode	2.13	[kg.d-1]	O
Concentration in untreated wastewater	1.06	[mg.l-1]	O
Local emission entering the STP	2.13	[kg.d-1]	O

CONFIGURATION

Type of local STP	With primary settler (9-box)		D
Number of inhabitants feeding this STP	1E+04	[eq]	O
Effluent discharge rate of this STP	2E+06	[l.d-1]	O
Calculate dilution from river flow rate	No		O
Flow rate of the river	1.8E+04	[m3.d-1]	O
Dilution factor (rivers)	10	[-]	O
Dilution factor (coastal areas)	100	[-]	O

OUTPUT [2 ""] [PRIVATE USE]

Fraction of emission directed to air by STP	1.38	[%]	O
Fraction of emission directed to water by STP	12.2	[%]	O
Fraction of emission directed to sludge by STP	0.013	[%]	O
Fraction of the emission degraded in STP	86.4	[%]	O
Total of fractions	100	[%]	O
Local indirect emission to air from STP during episode	0.0294	[kg.d-1]	O
Concentration in untreated wastewater	1.06	[mg.l-1]	O
Concentration of chemical (total) in the STP-effluent	0.13	[mg.l-1]	O
Concentration in effluent exceeds solubility	No		O
Concentration in dry sewage sludge	0.351	[mg.kg-1]	O
PEC for micro-organisms in the STP	0.13	[mg.l-1]	O

REGIONAL, CONTINENTAL AND GLOBAL DISTRIBUTION

PECS

REGIONAL

Regional PEC in surface water (total)	2.6E-03	[mg.l-1]	O
Regional PEC in sea water (total)	2.04E-04	[mg.l-1]	O
Regional PEC in surface water (dissolved)	2.6E-03	[mg.l-1]	O
Qualitative assessment might be needed (TGD Part II, 5.6)	No		O
Regional PEC in sea water (dissolved)	2.04E-04	[mg.l-1]	O
Qualitative assessment might be needed (TGD Part II, 5.6)	No		O
Regional PEC in air (total)	5.49E-05	[mg.m-3]	O
Regional PEC in agricultural soil (total)	1.12E-05	[mg.kgwwt-1]	O
Regional PEC in pore water of agricultural soils	7.88E-05	[mg.l-1]	O
Regional PEC in natural soil (total)	1.42E-05	[mg.kgwwt-1]	O
Regional PEC in industrial soil (total)	7.75E-04	[mg.kgwwt-1]	O
Regional PEC in sediment (total)	1.8E-03	[mg.kgwwt-1]	O
Regional PEC in sea water sediment (total)	1.44E-04	[mg.kgwwt-1]	O

GLOBAL: MODERATE

Moderate PEC in water (total)	1.7E-09	[mg.l-1]	O
Moderate PEC in water (dissolved)	1.7E-09	[mg.l-1]	O
Moderate PEC in air (total)	2.46E-07	[mg.m-3]	O
Moderate PEC in soil (total)	6.35E-08	[mg.kgwwt-1]	O
Moderate PEC in sediment (total)	1.19E-09	[mg.kgwwt-1]	O

STEADY-STATE FRACTIONS

REGIONAL

Steady-state mass fraction in regional fresh water	2.18	[%]	O
Steady-state mass fraction in regional sea water	0.191	[%]	O
Steady-state mass fraction in regional air	0.518	[%]	O
Steady-state mass fraction in regional agricultural soil	0.0213	[%]	O
Steady-state mass fraction in regional natural soil	3.04E-03	[%]	O
Steady-state mass fraction in regional industrial soil	0.0615	[%]	O
Steady-state mass fraction in regional fresh water sediment	0.0174	[%]	O
Steady-state mass fraction in regional sea water sediment	4.62E-04	[%]	O

CONTINENTAL

Steady-state mass fraction in continental fresh water	21.6	[%]	O
Steady-state mass fraction in continental sea water	33.3	[%]	O
Steady-state mass fraction in continental air	9.09	[%]	O
Steady-state mass fraction in continental agricultural soil	0.189	[%]	O
Steady-state mass fraction in continental natural soil	0.027	[%]	O
Steady-state mass fraction in continental industrial soil	0.504	[%]	O
Steady-state mass fraction in continental fresh water sediment	0.172	[%]	O
Steady-state mass fraction in continental sea water sediment	4.04E-03	[%]	O

GLOBAL: MODERATE

Steady-state mass fraction in moderate water	15.4	[%]	O
Steady-state mass fraction in moderate air	4.47	[%]	O
Steady-state mass fraction in moderate soil	0.0491	[%]	O
Steady-state mass fraction in moderate sediment	3.75E-04	[%]	O

STEADY-STATE MASSES

REGIONAL

Steady-state mass in regional fresh water	9.37E+03	[kg]	O
Steady-state mass in regional sea water	817	[kg]	O
Steady-state mass in regional air	2.22E+03	[kg]	O
Steady-state mass in regional agricultural soil	91.3	[kg]	O
Steady-state mass in regional natural soil	13	[kg]	O
Steady-state mass in regional industrial soil	264	[kg]	O
Steady-state mass in regional fresh water sediment	74.6	[kg]	O
Steady-state mass in regional sea water sediment	1.98	[kg]	O

CONTINENTAL

Steady-state mass in continental fresh water	9.26E+04	[kg]	O
Steady-state mass in continental sea water	1.43E+05	[kg]	O
Steady-state mass in continental air	3.9E+04	[kg]	O
Steady-state mass in continental agricultural soil	809	[kg]	O
Steady-state mass in continental natural soil	116	[kg]	O
Steady-state mass in continental industrial soil	2.16E+03	[kg]	O
Steady-state mass in continental fresh water sediment	737	[kg]	O
Steady-state mass in continental sea water sediment	17.3	[kg]	O

GLOBAL: MODERATE

Steady-state mass in moderate water	6.62E+04	[kg]	O
Steady-state mass in moderate air	1.92E+04	[kg]	O
Steady-state mass in moderate soil	211	[kg]	O
Steady-state mass in moderate sediment	1.61	[kg]	O

[2 ""] [PRIVATE USE]

LOCAL CONCENTRATIONS AND DEPOSITIONS [PRIVATE USE]

Concentration in air during emission episode	8.17E-06	[mg.m-3]	O
Annual average concentration in air, 100 m from point source	8.17E-06	[mg.m-3]	O
Total deposition flux during emission episode	1.18E-05	[mg.m-2.d-1]	O
Annual average total deposition flux	1.18E-05	[mg.m-2.d-1]	O
Concentration in surface water during emission episode (dissolved)	0.013	[mg.l-1]	O
Annual average concentration in surface water (dissolved)	0.013	[mg.l-1]	O
Concentration in sea water during emission episode (dissolved)	0.0106	[mg.l-1]	O
Annual average concentration in sea water (dissolved)	0.0106	[mg.l-1]	O
Concentration in agric. soil averaged over 30 days	2.72E-04	[mg.kgwwt-1]	O
Concentration in agric. soil averaged over 180 days	5.95E-05	[mg.kgwwt-1]	O
Concentration in grassland averaged over 180 days	1.63E-05	[mg.kgwwt-1]	O
Fraction of steady-state (agricultural soil)	1	[-]	O
Fraction of steady-state (grassland soil)	1	[-]	O

LOCAL PECS [PRIVATE USE]

Annual average local PEC in air (total)	6.31E-05	[mg.m-3]	O
Local PEC in surface water during emission episode (dissolved)	0.0156	[mg.l-1]	O
Qualitative assessment might be needed (TGD Part II, 5.6)	No		O
Annual average local PEC in surface water (dissolved)	0.0156	[mg.l-1]	O
Local PEC in fresh-water sediment during emission episode	0.0127	[mg.kgwwt-1]	O
Local PEC in sea water during emission episode (dissolved)	0.0109	[mg.l-1]	O
Qualitative assessment might be needed (TGD Part II, 5.6)	No		O
Annual average local PEC in sea water (dissolved)	0.0109	[mg.l-1]	O
Local PEC in marine sediment during emission episode	8.82E-03	[mg.kgwwt-1]	O
Local PEC in agric. soil (total) averaged over 30 days	2.86E-04	[mg.kgwwt-1]	O
Local PEC in agric. soil (total) averaged over 180 days	7.37E-05	[mg.kgwwt-1]	O
Local PEC in grassland (total) averaged over 180 days	3.05E-05	[mg.kgwwt-1]	O
Local PEC in pore water of agricultural soil	5.18E-04	[mg.l-1]	O
Local PEC in pore water of grassland	2.15E-04	[mg.l-1]	O
Local PEC in groundwater under agricultural soil	5.18E-04	[mg.l-1]	O

[2 ""] [PRIVATE USE]

CONCENTRATIONS IN FISH, PLANTS AND DRINKING WATER [2 ""] [PRIVATE USE]

Local concentration in wet fish	0.022	[mg.kg-1]	O
Local concentration in root tissue of plant	4.89E-04	[mg.kg-1]	O
Local concentration in leaves of plant	3.99E-05	[mg.kg-1]	O
Local concentration in grass (wet weight)	3.98E-05	[mg.kg-1]	O
Fraction of total uptake by crops from pore water	4.35E-03	[-]	O
Fraction of total uptake by crops from air	0.996	[-]	O
Fraction of total uptake by grass from pore water	1.81E-03	[-]	O
Fraction of total uptake by grass from air	0.998	[-]	O
Local concentration in drinking water	0.0156	[mg.l-1]	O
Annual average local PEC in air (total)	6.31E-05	[mg.m-3]	O

EFFECTS

INPUT OF EFFECTS DATA

MICRO-ORGANISMS

Test system	Respiration inhibition, EU Annex V C.11, OECD 209	D	
EC50 for micro-organisms in a STP	??	[mg.l-1]	D
EC10 for micro-organisms in a STP	??	[mg.l-1]	D
NOEC for micro-organisms in a STP	104	[mg.l-1]	S

AQUATIC ORGANISMS

FRESH WATER

L(E)C50 SHORT-TERM TESTS

LC50 for fish	4.2E+03	[mg.l-1]	S
L(E)C50 for Daphnia	9.714E+03	[mg.l-1]	S
EC50 for algae	1.8E+03	[mg.l-1]	S
LC50 for additional taxonomic group	??	[mg.l-1]	D
Aquatic species	other		D

NOEC LONG-TERM TESTS

NOEC for fish	??	[mg.l-1]	D
NOEC for Daphnia	30	[mg.l-1]	S
NOEC for algae	??	[mg.l-1]	D
NOEC for additional taxonomic group	??	[mg.l-1]	D
NOEC for additional taxonomic group	??	[mg.l-1]	D
NOEC for additional taxonomic group	??	[mg.l-1]	D
NOEC for additional taxonomic group	??	[mg.l-1]	D

MARINE

ND

NOEC LONG-TERM TESTS

ND

FRESH WATER SEDIMENT

ND

MARINE SEDIMENT

ND

EC10/NOEC LONG-TERM TESTS

ND

TERRESTRIAL ORGANISMS

ND

ENVIRONMENTAL EFFECTS ASSESSMENT

ENVIRONMENTAL PNECS

FRESH WATER

Toxicological data used for extrapolation to PNEC Aqua	30	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC Aqua	100	[-]	O
PNEC for aquatic organisms	0.3	[mg.l-1]	O

INTERMITTENT RELEASES

Toxicological data used for extrapolation to PNEC Aqua	1.8E+03	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC Aqua	100	[-]	O
PNEC for aquatic organisms, intermittent releases	18	[mg.l-1]	O

STATISTICAL

PNEC for aquatic organisms with statistical method	??	[mg.l-1]	D

MARINE

Toxicological data used for extrapolation to PNEC Marine	30	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC Marine	1000	[-]	O
PNEC for marine organisms	0.03	[mg.l-1]	O

STATISTICAL

PNEC for marine organisms with statistical method	??	[mg.l-1]	D

FRESH WATER SEDIMENT

Toxicological data used for extrapolation to PNEC sediment (fresh)		?? [mg.kgwwt-1]	O	
Assessment factor applied in extrapolation to PNEC sediment (fresh)		??	[-]	O
PNEC for fresh-water sediment organisms (from toxicological data)		?? [mg.kgwwt-1]	O	
PNEC for fresh-water sediment organisms (equilibrium partitioning)		0.244 [mg.kgwwt-1]	O	
Equilibrium partitioning used for PNEC in fresh-water sediment?	Yes		O	
PNEC for fresh-water sediment-dwelling organisms	0.244	[mg.kgwwt-1]	O	

MARINE SEDIMENT

Toxicological data used for extrapolation to PNEC sediment (marine)		?? [mg.kgwwt-1]	O	
Assessment factor applied in extrapolation to PNEC sediment (marine)		??	[-]	O
PNEC for marine sediment organisms (from toxicological data)	??	[mg.kgwwt-1]	O	
PNEC for marine sediment organisms (equilibrium partitioning)	0.0244	[mg.kgwwt-1]	O	
Equilibrium partitioning used for PNEC in marine sediment?	Yes		O	
PNEC for marine sediment organisms	0.0244	[mg.kgwwt-1]	O	

TERRESTRIAL

Toxicological data used for extrapolation to PNEC Terr	??	[mg.kgwwt-1]	O
Assessment factor applied in extrapolation to PNEC Terr	??	[-]	O
PNEC for terrestrial organisms (from toxicological data)	??	[mg.kgwwt-1]	O
PNEC for terrestrial organisms (equilibrium partitioning)	0.0427	[mg.kgwwt-1]	O
Equilibrium partitioning used for PNEC in soil?	Yes		O
PNEC for terrestrial organisms	0.0427	[mg.kgwwt-1]	O

STATISTICAL

PNEC for terrestrial organisms with statistical method	??	[mg.kgwwt-1]	D

STP

Toxicological data used for extrapolation to PNEC micro	104	[mg.l-1]	O
Assessment factor applied in extrapolation to PNEC micro	10	[-]	O
PNEC for micro-organisms in a STP	10.4	[mg.l-1]	O

ENVIRONMENTAL EXPOSURE

LOCAL

RISK CHARACTERIZATION OF [2 ""] [PRIVATE USE]

WATER

RCR for the local fresh-water compartment	0.052	[-]	O
Intermittent release	No		D
RCR for the local marine compartment	0.362	[-]	O
RCR for the local fresh-water compartment, statistical method	??	[-]	O
RCR for the local marine compartment, statistical method	??	[-]	O

SEDIMENT

RCR for the local fresh-water sediment compartment	0.052	[-]	O
Extra factor 10 applied to PEC/PNEC	No		O
RCR for the local marine sediment compartment	0.362	[-]	O
Extra factor 10 applied to PEC/PNEC	No		O

SOIL

RCR for the local soil compartment	6.7E-03	[-]	O
Extra factor 10 applied to PEC/PNEC	No		O
RCR for the local soil compartment, statistical method	??	[-]	O

STP

RCR for the sewage treatment plant	0.0114	[-]	O

PREDATORS

RCR for fish-eating birds and mammals (fresh-water)	??	[-]	O
RCR for fish-eating birds and mammals (marine)	??	[-]	O
RCR for top predators (marine)	??	[-]	O
RCR for worm-eating birds and mammals	??	[-]	O

REGIONAL

WATER

RCR for the regional fresh-water compartment	8.67E-03	[-]	O
RCR for the regional marine compartment	6.81E-03	[-]	O
RCR for the regional fresh-water compartment, statistical method	??	[-]	O
RCR for the regional marine compartment, statistical method	??	[-]	O

SEDIMENT

RCR for the regional fresh-water sediment compartment	7.39E-03	[-]	O
Extra factor 10 applied to PEC/PNEC	No		O
RCR for the regional marine sediment compartment	5.89E-03	[-]	O
Extra factor 10 applied to PEC/PNEC	No		O

SOIL

RCR for the regional soil compartment	2.62E-04	[-]	O
Extra factor 10 applied to PEC/PNEC	No		O
RCR for the regional soil compartment, statistical method	??	[-]	O

Annex 3. Summary of Toxicological Data of Relevance in the HERA Assessment

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
ECOTOXICOLOGY						
Acute toxicity to fish	*Pimephales promelas* (freshwater)	LC50 (flow through)	96 hours	9640 mg/L The test result is based on analytical data taken during the study period	No	SIDS Dossier Veith et al, 1983
	Rasbora heteromorpha (marine)	LC50 LC10 (flow-through)	96 hours 96 hours	4200 mg/L 1500 mg/L	No	IUCLID Dossier
	Leuciscus idus melanotus (freshwater)	LC50 (static)	48 hours	8970 mg/L	No	IUCLID Dossier
Acute toxicity to aquatic invertebrates	*Daphnia magna* (freshwater)	EC50 (static)	24 hours	9714 mg/L	No	IUCLID Dossier
	Daphnia magna (freshwater)	EC50 (static)	24 hours	>10 000 mg/L	No	SIDS Dossier (Bringmann & Kuehn, 1980)
	Daphnia magna (freshwater)	EC50 (static)	48 hours	13299 mg/L	No	IUCLID Dossier
	Crangon crangon (marine)	LC50 (semi-static)	96 hours	903 mg/L	No	IUCLID Dossier
	Crangon crangon (marine)	LC50 (semi-static)	48 hours	1400 mg/L	No	SIDS Dossier

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
Toxicity to aquatic plants	*Scenedesmus quadricuada* (freshwater)	Toxicity Threshold (LOEC) (growth rate)	7 days	1800 mg/L	No	SIDS Dossier (Bringmann & Kuehn, 1980)
	Scenedesmus subspicatus (freshwater)	EC50 (growth rate)	72 hours	>1000 mg/L	No	IUCLID Dossier
Toxicity to micro-organisms	*Chilomonas paramaecium* (ciliated protozoa)	Toxicity Threshold (Growth inhibition test)	48 hour	104 mg/L The $PNEC_{microorganism}$ was derived from this study and an assessment factor of 1 was applied as the toxicity threshold was determined to be equivalent to an EC3 value.	No	IUCLID Dossier
	Pseudomonas putida	Toxicity Threshold (Growth inhibition test)	16 hours	1050 mg/L In this experiment the toxicity threshold is defined as the concentration at which the inhibitory action of IPA at the end of the test period is greater or equal to 3% below the mean value for extinction for the control cultures.	No	SIDS Dossier (Bringmann&Kuehn, 1980)
	Entosiphon sulcatum	Toxicity Threshold (Growth inhibition test)	72 hours	4930 mg/L In this experiment the toxicity threshold is defined as the concentration at which the inhibitory action of IPA at the end of the test period is greater or equal to 3% below the mean value for extinction for the control cultures.	No	SIDS Dossier (Bringmann&Kuehn, 1980)
	OECD synthetic sewage	EC50 Respiration inhibition test (ISO 8192)	30 days	39540 mg/L EC50 is the test substance concentration which reduces the oxygen consumption by 50%	No	IUCLID Dossier

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
Chronic toxicity to aquatic invertebrates	*Daphnia magna* (freshwater)	NOEC	21 days	30 mg/L The PNECaquatic was derived from this chronic value in the absence of any other chronic toxicity data for fish and algae representing other trophic levels an assessment factor of 100 was applied to this value.	No	IUCLID Dossier
	Daphnia Magna (freshwater)	NOEC (growth reduction)	16 days	141 mg/L	No	SIDS Dossier
Toxicity to terrestrial plants	*Lactuva sativa* (Dicotyledon)	EC50	3 days	2100 mg/L The reported effect parameter is inhibition of seed germination.	No	SIDS Dossier (Reynolds, 1977)
	Hordeum vulgare	EC100	4 days	39426 mg/L Concentration at which total inhibition of the germination of barley grains was reached after incubation of 4 days.	No	IUCLID Dossier
Toxicity to other non-mammalian terrestrial species	*Drospholia*	LC50	48 hours	10200 – 13340 mg/L The insects were exposed to the propan-2-ol nutrient medium.	No	SIDS Dossier (David & Bocquet, 1976)
HUMAN TOXICOLOGY						
Acute Oral Toxicity	Rat	LD50	n/a	4710 – 5840 mg/kg	No	SIDS Dossier
	Mouse	LD50	n/a	4475 mg/kg	No	SIDS Dossier, (Guseinov, V.G., 1985)
	Rabbit	LD50	n/a	5030 – 7990 mg/kg	No	SIDS Dossier
	Dog	LD50	n/a	4830 mg/kg	No	IUCLID Dossier

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
Acute Dermal Toxicity	Rat	LD50	n/a	12800 mg/kg	No	IUCLID Dossier
	Rabbit	LD50	n/a	12870 mg/kg	No	SIDS Dossier, (Smyth, H.F, 1948)
Acute Inhalation Toxicity	Rat	LC50	4 hour	72.6 mg/L	No	SIDS Dossier (Guseinov, V.G., 1985)
	Mouse	LC50	8 hour	29 – 55.1 mg/L	No	IUCLID Dossier
	Mouse	LC50	2 hour	53 mg/L	No	SIDS Dossier (Guseinov, V.G., 1985)
	Mouse	LC50	4 hour	27.2 mg/L	No	IUCLID Dossier
Skin Irritation	Rabbit	N/a	N/a	Not Irritating	No	SIDS Dossier (Smyth, H.F, 1948)
	Rabbit	FHSA procedure 'Primary skin irritants'	4 hour contact period	Sum of mean oedema and erythema scores at 4, 24, 48 h (6 animals): 0.0; for intact & abraded skin	No	IUCLID Dossier
	Guinea Pig	FHSA procedure 'Primary skin irritants'	4 hour contact period	Sum of mean oedema and erythema scores at 4, 24, 48 h (6 animals): 0.0; for intact & abraded skin	No	IUCLID Dossier
Eye Irritation	Rabbit	Draize Test	No rinsing	Maximum Draize score of 37; rated to be moderately irritating to irritating Further studies report IPA to be irritating to the eyes	No data Generally no; one GLP compliant	SIDS Dossier (Morgan, R. L., 1987) SIDS Dossier; IUCLID Dossier
Sensitisation	Guinea Pig	Buehler Test	N/a	Not sensitizing (0/20)	No	SIDS Dossier

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
Repeated Dose Toxicity Oral	Rat	General toxicity	12 weeks to 0, 1, 2, 3, or 5% in drinking water	NOEL: 870 mg/kg/d LOEL:1280 mg/kg/d Effects: increase in weights of liver kidneys and adrenals; increase in formation of hyaline casts and droplets in proximal tubules of the kidneys	No data	SIDS Dossier (Pilegaard, K. 1993)
			27 weeks to 0, 600 & 2300 mg/kg/d (males) and 0, 1000 & 3900 mg/kg/d (females) in drinking water	NOEL: 600 mg/kg/d (males) 1000 mg/kg/d (females) LOEL: 2300 mg/kg/d (males) 3900 mg/kg/d (females) Effects: decreased body weight gains during first 13 weeks of study, then increased body weight gain for the remainder of the study; female rats showed decreased BW gain throughout the whole study	No	SIDS Dossier (Lehmann, A.J., 1944)
Inhalation	Rat (Fisher 344)	General toxicity; US EPA TSCA test guidelines	13 weeks (6 hours/day; 5 days/week) to 0, 100, 500, 1500, and 5000ppm.	NOEL: 500ppm LOEL: 1500ppm Effects: Narcotic effects observed at 1500 and 5000ppm. Ataxia and decreased body weights observed following exposure to 5000ppm. Only microscopic change observed was hyaline droplets within the kidneys of all male rats. Size and frequency of these droplets were increased in the exposed groups.	Yes	SIDS Dossier (Burleigh-Flayer, H.D., 1994a)
	Rat (Wistar)	General Toxicity	12 weeks (6 hours/day; 5 days/week) to 0, 400, 1000, 4000, or 8000 ppm; 20 weeks to 1000 or 8000ppm	NOEL: 400ppm LOEL: 1000ppm Effects: reduced body weight gain and marked local irritation in groups given > 1000ppm; decrease in erythrocyte and hemoglobin values in groups exposed to >4000ppm; and increases in serum GOT and GPT and total cholesterol in groups exposed 20 weeks to 8000ppm	No data	SIDS Dossier (Nakaseko, H., 1991)

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
	Mouse (CD-1)	General Toxicity	13 weeks (6 hours/day; 5 days/week) to 0, 100, 500, 1500, and 5000ppm;	NOEL: 500ppm LOEL: 1500ppm Effects: Narcotic effects noted at 1500 and 5000ppm; increased body weight and body weight gain were observed for the 5000ppm female mice; no treatment-related effects were noted at gross necropsy or at histopathological examination	Yes	SIDS Dossier (Burleigh-Flayer, H.D., 1994b)
Genetic Toxicity In Vitro Bacterial	Salmonella Typhimurium TA98, 100, 1535, 1537	Reverse Mutation Assay	180 mmol/plate with and without metabolic activation	Negative with and without metabolic activation	No data	SIDS Dossier (Florin, I., 1980)
	Salmonella Typhimurium TA 97, 98, 100, 102, 104, 1535, 1537, 1538	Reverse Mutation Assay	100 mmol/plate with and without metabolic activation	Negative with and without metabolic activation	Yes	SIDS Dossier (Zeiger, E., 1992)
Non-bacterial	Chinese Hamster V79 Fibroblasts	Sister Chromatide Exchange	3.3, 10, 33.3, and 100 mmol/L with and without metabolic activation	Negative with and without metabolic activation	No	SIDS Dossier (Von der Hude, W., 1987)
	Chinese Hamster Ovary	Mutations in HPGRT (US EPA TSCA Test Guidelines)	0.5 – 5 mg/mL with and without metabolic activation	Negative with and without metabolic activation	Yes	SIDS Dossier (Kapp, R.W., 1993)

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
	Neurospora Crassa	Meiotic non-disjunction	No concentration data; without metabolic activation	Negative without metabolic activation	No	SIDS Dossier (Griffith, A.J.F; 1980)
	SA7 Syrian Hamster Embryo Cells	Cell transformation	62 – 1000 µg/mL without metabolic activation	Negative without metabolic activation	No	SIDS Dossier (Dipaolo, A.J., 1978)
Genetic Toxicity In Vivo	Mouse (ICR random bread)	Micronucleus Assay	Intraperitoneal injection of 350, 1173, 2500 mg/kg/bw (US EPA TSCA Guidelines)	Negative; Bone marrow examination after 24, 48 and 72 hours	Yes	SIDS Dossier (Kapp, R.W., 1993)
Carcinogenicity Inhalation	Mouse (C3H)	Lung tumours	5-8 months exposure (3-7 hours/day, 5 days/week) to 7700 mg/m3 (control group included)	No excess of lung tumours in treated mice versus control group	No	SIDS Dossier (Weil, C.S., 1952)
	Mouse (CD-1)	Carcinogenicity (US EPA TSCA Testing Guidelines)	18 months (6 hours/day; 5 days/week) to 0, 500, 2500, 5000ppm;	No increased frequency of neoplastic lesions in any of the IPA exposed groups, indicating a lack of carcinogenic activity of IPA; the uncertainty about kidney effects, in particular in male mice, lead to a NOEL of 500ppm and a LOEL of 2500ppm for non-cancer effects	Yes	SIDS Dossier (Burleigh-Flayer, H.D; 1994)

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
	Rat (Fisher 344)	Carcinogenicity (US EPA TSCA Testing Guidelines)	24 months (6 hours/day; 5 days/week) to 0, 500, 2500, 5000ppm;	An increased incidence of interstitial cell adenomas occurred in the testes of male rats. The frequency of interstitial (Leydig) cell tumours of the testis was also increased in a concentration-related patter for male rats in the study. The incidence of these tumours in IPA exposed groups was similar to that reported for unexposed rats in the NTP and previous studies at this laboratory, while the incidence of these tumours in unexposed rats in this study was well below historical levels. There were no increases in the incidence of other tumour types in the exposed animals compared to the controls.	Yes	SIDS Dossier (Garman, R., 1995)
Dermal	Mouse	Skin Tumours	52 weeks; treatment 3times a week (no information on exposure concentration)	There were no skin-related tumours reported.	No	SIDS Dossier
Reproductive Toxicity	Rat (Wistar)	One generation reproductive toxicity	Exposure to 0, 0.5, 1, 2% of IPA via drinking water prior to mating and to lactation and weaning of F1 Premating Exposure period: Male: 70 days Female: 21 days Duration of Test: To weaning (day 21 after birth)	NOEL Parental: 1% (825 and 625 mg/kg/d for males and females respectively) NOEL F1 Offspring: 1% Effects: Parental rats dosed with 2% had decreased body weight gain, corresponding reduced pup weight gain and decreased survival compared with controls; there was also a dose-related increase in relative liver weights in F1 (no histological changes). No effects on reproductive parameters.	Yes	SIDS Dossier

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
	Rat (Sprague Dawleyy)	Two generation study (US EPA TSCA Test Guidelines)	30 rats were exposed via gavage to 0, 100, 500 and 1000 mg/kg/day prior to mating and to lactation and weaning of F1 and F2 generations. Premating Exposure period: Male: 70 days Female: 70 days	NOEL Parental: < 500 mg/kg/d (BMDL10= 410 mg/kg/d) NOEL F1: < 500 mg/kg/d (BMDL5 = 449 mg/kg/d) NOEL F1: < 500 mg/kg/d (BMDL10= 449 mg/kg/d) Effects in parental animals included increased lactation body weight gain in the 500 and 1000 mg/kg groups of both sexes and centrilobular hypertrophy in some P2 males. Exposure to 1000 and a lesser extent 500 mg/kg/d resulted in a reduction in postnatal survival in both F1 and F2 litters. The study derived NOELS for the F1 and F2 offspring are contingent upon biological significance ascribed to the effects observed for the 500 mg/kg/d treatment group. A conservative perspective is that the reductions in postnatal survival are treatment and dose-related effects. Consequently the NOEL based on this interpretation would be set at 100 mg/kg/d. On the other hand, the NOEL may be set at 500 mg/kg/d if these observations are not deemed biologically significant. A benchmark dose assessment was conducted as a way of clarifying issues surrounding the derivation of effect levels for this study.	Yes	SIDS Dossier (Bevan, C., 1995)

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
Developmental Toxicity & Teratogenicit	Rat (Wistar)	Developmental toxicity	Female rats dosed continuously to 0, 0.5, 1.25, 2.5% of IPA in drinking water during day 6-16 of pregnancy; the study was terminated at day 20 of pregnancy	NOEL Maternal: 0.5% NOEL Developmental: 0.5% Effects: Maternal body weights were significantly decreased from gestational days 7-16. Animals exhibited reduced food and water consumption during the treatment period. In the 1.25% and 2.5% dose groups, foetal body weights were reduced on a per foetus basis, but a not on a per litter basis. No teratogenic effects were observed; but delayed ossification of the skeleton was noted in the 1.25% and 2.5% dose groups, consistent with retarded development as a result of maternal toxicity.	Yes	SIDS Dossier
	Rat (Sprague Dawley)	Developmental Toxicity (US EPA TSCA Test Guidelines)	Female rats dosed 0, 400, 800 and 1200 mg/kg/d IPA by gavage during day 6-15 of pregnancy; the study was terminated at day 20 of pregnancy	NOEL Maternal: 400 mg/kg/d NOEL Developmental: 400 mg/kg No dams aborted or delivered early. Reduced maternal gestational weight gain on gestational days 0 to 20 associated with significantly reduced gravid uterine weights were noted in the high dose animals. All gestational parameters were equivalent across the groups. Foetal body weights per litter were significantly reduced at the two highest doses. No evidence of teratogenicity was observed at any dose tested. Therefore IPA was not teratogenic to SD rats.	Yes	SIDS Dossier (Tyl, R.W., 1994)

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
	Rabbit (New Zealand)	Developmental Toxicity (US EPA TSCA Test Guidelines)	Female rabbits dosed 0, 120, 240 and 480 mg/kg/d IPA by gavage during day 6-18 of pregnancy; the study was terminated at day 28 of pregnancy	NOEL Maternal: 240 mg/kg/d NOEL Developmental: 480 mg/kg No dams aborted or delivered early. Maternal body weights were significantly reduced during treatment and clinical signs of toxicity were observed at 480 mg/kg. No adverse effects were noted at 120 or 240 mg/kg/d. All gestational parameters were equivalent across the groups. No evidence of increased teratogenicity was observed at any dose tested. Therefore, IPA was not teratogenic to NZW rabbits.	Yes	SIDS Dossier (Tyl, R.W, 1994)
Other relevant information		ADME		Numerous studies on the absorption, distribution, metabolism and excretion of IPA have been performed. These indicated that IPA is readily absorbed in animals and man through the lungs, skin and GI tract. There is evidence for a delay in absorption through the GI tract at high dose levels and an extension in half life suggesting limited metabolic capability. IPA is rapidly distributed throughout the body and has been shown to cross the blood/brain barrier. Elimination from the blood follows first order kinetics. Approximately 64-84% of an intravenous dose has been shown to be oxidised to acetone in rabbit. Elimination of IPA is retarded by ethanol and it has been shown that IPA is a poorer substrate for alcohol dehydrogenase than ethanol. Excretion occurs mainly through the expired air either as unchanged IPA or as acetone. Quantities of acetone and IPA are excreted in the urine together with the glucoronide conjugate of IPA. There is evidence in man that sulphonation may occur.		SIDS Dossier

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
				2-Propanol is absorbed easily from all segments of the GI tract, most rapidly from the small intestine & least rapidly from the stomach; 80% of an oral dose is absorbed within 30min & complete absorption occurs within 2 hours. Skin absorption is relatively slow. The kidney excretes about 20-50% of the ingested 2-propanol unchanged. 2-Propanol distributes in body water with an apparent volume of distribution of 0.6-0.7 L/kg		HSDB Ethyl Browning's Toxicity and Metabolism of Industrial Solvents, 1992
	Rats (Fisher 344)	In vivo dermal absorption	70% aqueous solution of IPA was applied under occluded conditions to shaved backs of the rats for 4 hours	Following the dermal exposure 84-86% of the dose was recovered from the application site. Dermal absorption rates were calculated by two independent methods: The values obtained were 0.78 ± 0.03 and 0.85 ± 0.04 mg/cm2/h for males and 0.77 ± 0.13 and 0.78 ± 0.16 mg/cm2/h for females. Calculated permeability coefficients of 1.37 to 1.5 x 10^{-3} cm/h for females indicate that in the rat, IPA is rapidly absorbed when applied dermally.	No data	Boatman, R.J. et al., 1996

Study Type	Species	Endpoint/ Methodology	Exposure	Result	GLP	Reference
Human Experience		Accidental Exposures		Intoxications have been reported following ingestions, rectal administration and, in children, following inhalation and skin absorption. Signs of intoxications are CNS depression, leading to coma, respiratory arrest and death. GI effects and hypothermia may occur. Cardiac effects include severe hypotension, shock and cardiac arrest with tachycardia as a secondary effect. The lowest dose reported to be life threatening was 170 mL in an 18 month old child. Acetone can be detected in the blood, breath and urine after intoxication with IPA, but acidosis does not usually occur.		SIDS Dossier (World Health Organisation, 1990)
		Volunteer Studies		2.6 or 6.4 mg/kg/d IPA for 6 weeks was well tolerated by human male volunteers, there being no adverse effects on haematology, blood chemistry, urinalysis or ophtalmoscopy. Application of 0.5 mL undiluted IPA in an open arm patch test did not result in skin irritation. 10 minute covered patches produced transient erythema following immersion in water.		SIDS Dossier (World Health Organisation, 1990)

Annex 4. PEC_{HERA}/PNEC Ratios for the Different Environmental Compartments

Compartment	PEC_{HERA}	PNEC	Ratio (RCR)	Comment
Local freshwater water	0.016 mg/L	0.3 mg/L	0.05	To simulate a worst case scenario the local PEC_{HERA} for surface waters calculated using EUSES was divided by the $PNEC_{aquatic}$. The resulting ratio is well below 1 and therefore the use of IPA in household applications poses no concern in surface waters. However, it should be noted that it is possible that other sources of IPA could contribute to surface water load that where not considered here, however, the ratio is so small that this should not be of environmental concern.
WWTP	0.13 mg/L	10.4 mg/L	0.01	The PEC in the influent to the sewage treatment is much lower than the $PNEC_{microorganism}$ and therefore the risk for sewage treatment organisms from IPA is of no concern.
Sediment	0.013 mg/kg WW	0.3 mg/kg WW	0.04	The RCR for this compartment is very low and well below 1. Considering that IPA is very water soluble and readily biodegradable there is little concern that IPA could bioconcentrate in the sediment over time.
Soil	2.9 E-05 mg/kg WW	0.04 mg/kg WW	7.2 E-03	The soil compartment is adequately protected considering the very low RCR.

Annex 5. Consumer exposure assessment

Product types

In line with the objectives of the HERA initiative, this human exposure assessment will focus on the use of IPA in household cleaning products. Table 1 lists household cleaning applications and typical finished product concentration ranges of IPA used in household products.

Table 1: Household applications and finished product concentrations of Isopropanol (AISE, Unpublished data)

Product application	Range of IPA level in finished product	Typical content of IPA in finished product
Regular laundry detergents	0.0 – 0.3 %	0.0 – 0.3 %
Compact laundry detergents	0.0 – 2 %	0.0 – 2.0 %
Fabric conditioners	0.4 -2.56 %	0.4 - 2.56 %
Laundry additives	0.0 -10.0 %	0.0 -10.0 %
Hand dishwashing detergent	0.0 – 3.0 %	1.0 – 1.4 %
Machine dishwashing detergent	0.0 %	0.0 %
Surface cleaners	0.0 – 15.0 %	1.0 – 5.0 %
Toilet cleaner	0.0 %	0.0 %

Consumer contact scenarios

For the use of IPA the following consumer exposure scenarios have been identified and assessed:

1. Direct skin contact with neat (*e.g.*, laundry pre-treatment) or diluted consumer product (*e.g.*, hand-washed laundry, hand dishwashing, surface cleaning).
2. Inhalation of detergent dust during washing process or aerosols generated by spray cleaners.
3. Oral ingestion of residues deposited on dishes.
4. Accidental or intentional overexposure.

Consumer exposure estimates

There is a consolidated overview concerning habits and practices of use of detergents and surface cleaners in Western Europe which has been tabulated and issued by the European Soap and Detergent Industry Association, AISE (AISE, 2002). This table reflects consumers' use of detergents in g/task, tasks/week, duration of task and other uses of products and has been largely the basis for the exposure estimates in the following paragraphs. In some instances (*e.g.*, habits & practices (H&P) of pre-treatment of laundry), additional H&P information for a targeted exposure assessment has been directly provided by the member companies of AISE. The calculations of the estimated consumer exposures have been based on the highest relevant concentrations that consumers can be exposed to.

Direct skin contact from hand-washing laundry

Hand-washing laundry has been identified as a common consumer habit. In this task, the IPA containing laundry solution comes in direct contact with the skin of hands and forearms. A hand washing task can be expected to take 10 minutes (AISE, 2002). The dermal systemic exposure (Exp_{sys}) to IPA can be estimated according to the following algorithm from the HERA guidance document:

$$\mathbf{Exp_{sys} = F_1 \times C \times Kp \times t \times S_{der} \times n / BW} \quad \mathbf{(1)}$$

For this exposure estimate, the terms have been defined with following values for the calculation of a worst case scenario:

F_1	percentage weight fraction of substance in product	***2 %*** (Table 1; compact laundry gel; worst case)
C	product concentration	***10 mg/cm^3*** (AISE, 2002)
Kp	dermal penetration coefficient	***1.5 x 10^{-3} cm/h**** (Boatman, 1998)
t	duration of exposure or contact	***10 min*** (AISE, 2002)
S_{der}	surface area of exposed skin	***1980 cm^2*** (TGD, 2003)
n	product use frequency (tasks per day)	***1.4*** (AISE, 2002)
BW	body weight	***60 kg*** (TGD, 2003)

$$\mathbf{Exp_{sys}} = [0.02 \times (10\ mg/cm^3) \times (0.0015\ cm/h) \times (0.17\ h) \times 1.4 \times (1980\ cm^2)] / 60\ kg$$
$$\mathbf{= 13.86\ \mu g/kg\ bw/day}$$

* The dermal penetration rate for IPA has been determined in a rat in vivo study (Boatman 1998). This penetration rate has been assessed to be a conservative since it has been determined under fully occluded conditions. A further level of conservatism can be warranted by the fact that rat skin is typically more permeable to chemicals compared to human skin (Schaefer and Redelmeier, 1996; van Ravenzwaay and Leibold, 2004).

Direct skin contact from pre-treatment of laundry

Consumers typically spot-treat stains on the laundry by hand with the help of either a detergent paste (*i.e.*, water/laundry powder = 1:1) or a laundry liquid which can be applied directly on the garment. In this exposure scenario, at most the skin surface of both hands has been exposed and the time taken for the task can be typically less than 10 minutes. Algorithm (1) has been used to calculate the systemic exposure resulting from the pre-treatment of laundry. The following assumptions have been considered to represent a conservative reflection of this scenario:

F_1	percentage weight fraction of substance in product	***2 %*** (Table 1; compact laundry gel; worst case)
C	product concentration	***1000 mg/cm^3*** (AISE, 2002)
Kp	dermal penetration coefficient	***1.5 x 10^{-3} cm/h*** (Boatman, 1996)
t	duration of exposure or contact	***10 min*** (AISE, 2002)
S_{der}	surface area of exposed skin	***840 cm^2*** (TGD, 2003)
n	product use frequency (tasks per day)	***1*** (AISE, 2002)
BW	body weight	***60 kg*** (TGD, 2003)

Exp_{sys} = [0.02 x (1000 mg/cm^3) x (0.0015 cm/h) x (0.17 h) x (840 cm²)] / 60 kg
= **71.4 µg/kg bw/day**

The above exposure estimate can be regarded to be very conservative. Typically, consumers pre-wet the laundry before applying the detergent for pre-treatment or conduct the pre-treatment under running tap water. Both practices lead to a significant dilution which has not been reflected in this exposure estimate. The assumption that the consumer has been exposed to the concentrated laundry product can therefore be seen as a worst case assumption. It should also be considered that only a fraction of the hands' skin will actually be exposed to the product. The assumption that both hands will be fully immersed in the product is a likely overestimate of the true exposure.

Direct skin contact from hand dishwashing

To calculate the dermal systemic exposure from direct contact of the skin to dishwashing detergent algorithm (1) has been adapted. The determination of IPA exposure from hand dishwashing has been conducted in a manner very similar to that of hand-washed laundry. The following assumptions have been made to address a reasonable worst case scenario:

F_1	percentage weight fraction of substance in product	***3 %*** (Table 1; liquid concentrate; worst case)
C	product concentration	**2 *mg/cm^3*** (AISE, 2002)
Kp	dermal penetration coefficient	***1.5 x 10^{-3} cm/h*** (Boatman, 1998)
t	duration of exposure or contact	***45 min*** (AISE, 2002)
S_{der}	surface area of exposed skin	***1980 cm^2*** (TGD, 2003)
n	product use frequency (tasks per day)	***3*** (AISE, 2002)
BW	body weight	***60 kg*** (TGD, 2003)

Exp_{sys} = [0.03 x (2 mg/cm^3) x (0.0015 cm/h) x (0.75 h) x (1980 cm²) x 3] / 60 kg
= **6.68 µg/kg bw/day**

Direct skin contact from surface cleaners

During this task, the IPA containing hard surface cleaning solution comes into direct contact with the skin of the hands. A surface cleaning task takes at maximum 20 minutes (AISE, 2002). Algorithm (1) has been used to calculate the dermal systemic exposure to IPA via hard surface cleaner applications. This calculation can be seen as very conservative as the percentage of IPA in the product has been based on a concentrated formulation which has been diluted to the same extent as a regular liquid. It has been assumed that the concentrate is a liquid and all the assumptions where used from the AISE habits and practices table for liquids.

The terms have been defined with following values for the calculation of a worst case exposure estimate:

F_1	percentage weight fraction of substance in product	***8 %*** (Liquid)
C	product concentration	***22 mg/cm^3*** (AISE, 2002)
Kp	dermal penetration coefficient	***1.5 x 10^3 cm/h*** (Boatman 1998)
t	duration of exposure or contact	***20 min*** (AISE, 2002)
S_{der}	surface area of exposed skin	***840 cm^2*** (TGD, 2003)
n	product use frequency (tasks per day)	***1*** (AISE, 2002)
BW	body weight	***60 kg*** (TGD, 2003)

Exp_{sys} = [0.08 x (22 mg/cm^3) x (0.0015 cm/h) x (0.334 h) x 1 x (840 cm²)] / 60 kg
= **12.34 µg/kg bw/day**

Inhalation of detergent dust during washing processes

Filling powder into the washing machine dispenser can result in some detergent dust being generated. Studies have determined an average release of about 0.27 µg dust per cup of product (*i.e.*, laundry powder) used for machine laundering (van de Plassche *et al*., 1998). IPA has been present in laundry powder detergents at a maximum level of 0.5%. Exposure to detergent dust particles containing IPA can be calculated by algorithm (3) derived from the HERA guidance document. It should be pointed out that the assumptions made in this scenario, *i.e*., that all dust particles can be respirable and present in the breathing zone, are worst case and highly unrealistic.

$$\mathbf{Exp_{sys\ (inhalation)} = F_1 \times n \times F_5 \times F_6 / BW} \qquad \mathbf{(4)}$$

The variables are explained below with the relevant values which represent worst case exposure for this task:

F_1	percentage weight fraction of substance in product	***0.5 %*** (Table 1; Compact powder; worst case)
n	product use frequency (tasks per day)	***2.6*** (AISE, 2002)
F_5	amount of inhalable dust per task	***0.27 µg*** (van de Plassche *et al*., 1998)
F_6	percentage (%) weight fraction absorbed or inhaled	***100 %*** (worst case)
BW	body weight	***60 kg*** (TGD, 2003)

$$\mathbf{Exp_{sys\ (inhalation)}} = [0.005 \times 2.6 \times (0.27\ \mu g) \times 1] / 60\ kg$$
$$= \mathbf{0.00005\ \mu g\ /kg\ bw/\ day}$$

Inhalation of aerosols from cleaning sprays

IPA has also been present in surface cleaning sprays. The HERA guidance document specifies the algorithm to be used for calculation of consumers' worst-case exposure to IPA containing aerosols generated by the spray cleaner:

$$\mathbf{Exp_{sys} = F_1 \times C` \times Q_{inh} \times t \times n \times F_7 \times F_8 / BW}$$

The terms used in this algorithm are defined as follows:

F_1	percentage weight fraction of substance in product	***15 %*** (Table 1; Cleaning spray)
C`	product concentration in air:	***0.35 mg/m^3*** *(Procter and Gamble, 1996)
Q_{inh}	ventilation rate	***0.8 m^3/h*** (TGD, 2003)
t	duration of exposure	***10 min*** (AISE, 2002)
n	product use frequency (tasks per day)	***1*** (AISE, 2002)
F_7	weight fraction of respirable particles	***100 %*** (worst case)
F_8	weight fraction absorbed or bioavailable	***75 %*** (TGD, 2003)
BW	body weight	***60 kg*** (TGD, 2003)

* this value has been obtained by experimental measurements of the concentration of aerosol particles smaller than 6.4 microns in size which have been generated upon spraying with typical surface cleaning spray products.

$Exp_{(inhalation)}$ = [0.15 x (0.35 mg/m^3) x (0.8 m^3/h) x (0.17 h) x 1 x 1 x 0.75] / 60 kg
= **0.0893 µg/kg bw/day**

Oral exposures to IPA

Oral exposure to IPA can originate from residues on eating utensils and dishes as well as from exposure to residues found in water and food.

The daily exposure to IPA from eating with utensils and dishware that have been washed with IPA-containing dishwashing liquids can be estimated according to the following algorithm from the HERA guidance document:

$$\mathbf{Exp_{sys} = [F_1 \times C` \times T_{a'} \times S_a / BW] \times A}$$

For this exposure estimate, the terms have been defined with following values for the calculation considering a worst case scenario:

F_1	percentage weight fraction of substance in product	***3 %*** (Table 1; dishwashing liquid, worst case)
C`	concentration of product in dish wash solution:	***1 mg/cm^3*** (AISE, 2002)
$T_{a'}$	amount of water left on dishes after rinsing	***5.5 x 10^{-5} ml/cm^2*** (Schmitz, 1973)
S_a	area of dishes in daily contact with food	***5400 cm^2*** (TGD, 2003)
BW	body weight	***60 kg*** (TGD, 2003)
A	oral absorption	***100 %*** (worst case)

$Exp_{sys\ (oral\ dish\ deposition)}$ = [[0.03 x (1 mg/cm^3) x (5.5 x 10^{-5} ml/cm^2) x (5400 cm^2)] / 60 kg]
= **0.14 µg/kg bw/day**

Accidental or intentional overexposure

Accidental or intentional overexposure to IPA may occur via swallowing of solid detergents or drinking of liquid washing solutions. Typically, one would estimate that no more than 5 g of powder detergent (equals a maximum of 0.25 g of IPA) or 20 ml of dishwashing liquid (equals a maximum of 0.6 g of IPA) would be swallowed. Studies of acute oral toxicity demonstrate that the toxic dose of IPA has been many times higher than this, even for a toddler.

The Geman Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV, 1999) published a report on products involved in poisoning cases. No fatal case of poisoning with detergents have been reported. Detergent products are not mentioned as dangerous products with a high incidence of poisoning.

Accidental contact with the eyes can be possible by splashes of dilute washing solutions or to low amounts of the detergent powder from hands into the eyes. Also, spillage of undiluted detergents products may lead to inadvertent skin contact.

Therefore, the skin and eye irritation potential has to be considered when assessing the risks of accidental exposures.

Equally, in the UK, the Department of Trade and Industry (DTI) produced an annual report of the home accident surveillance system (HASS). The data in this report summarized the information recorded at accident and emergency (A&E) units at a sample of hospitals across the UK. It also includes death statistics produced by the Office for National Statistics for England and Wales. The figures for 1998 show that for the representative sample of hospitals surveyed, there were 33 reported accidents involving detergent washing powder (the national estimate being 644) with none of these resulting in fatalities (DTI, 1998). In 1996 and 1997, despite their being 43 and 50 reported cases, respectively, no fatalities have been reported either.

Total Consumer Exposure

In the unlikely event of maximum worst case exposure from all sources, the total exposure to IPA from its use in cleaning products would be 6.48 µg/kg bw/day. The individual sources of exposures leading to the overall exposure have been summarized in Table 2.

Table 2: Worst case exposure estimates for the different consumer contact scenarios

Task	Worst case exposure estimate (EXP_{sys}) [µg/kg bw/day]
Direct contact from hand washing laundry	13.86
Direct skin contact from pre-treatment of laundry	71.4
Direct skin contact from hand dishwashing	6.68
Direct skin contact from surface cleaners	12.34
Inhalation of laundry powder dust	0.00005
Inhalation of aerosol particles	0.089
Oral exposure to IPA	0.14
Total exposure	**104.5 µg/kg bw/day**

Annex 6. Calculation of the Margin of Exposure

The margin of exposure (MOE) is the ratio of the No Observed Adverse Effect Level (NOAEL) or an appropriate substitute (*e.g.*, NOEL) to the estimated or actual level of human exposure to a substance. In context of the OECD review of IPA, NOAELs have been discussed for chronic, reproductive and developmental toxicity. The lowest NOAEL has been that for developmental toxicity which has been set at 400 mg/kg bw/d (OECD, 2000). IPA has been shown to be readily absorbed following oral exposure. Complete absorption occurred within two hours following exposure. Thus, for the purpose of this risk assessment a systemic NOAEL of 400 mg/kg bw/d has been used to calculate the MOE values for the different exposure scenarios.

Exposure scenario: direct skin contact from hand-washed laundry

For calculation of the MOE, the NOAEL of 400 mg/kg bw/day has been divided by the daily systemic dose of 13.86 µg/kg bw/day which has been estimated for the dermal exposure to IPA from hand-washed laundry.

$$\mathbf{MOE_{direct\ skin\ hand\text{-}washed\ laundry}} = 400000/13.86\ [\mu g/kg\ bw/day] = \mathbf{28860}$$

Exposure scenario: direct skin contact from pre-treatment of clothes

The MOE has been calculated by dividing the NOAEL of 400 mg/kg bw/day by the estimated exposure from pre-treatment of clothes of 71.4 µg/kg bw/day.

$$\mathbf{MOE_{direct\ skin\ pre\text{-}treatment}} = 400000/71.4\ [\mu g/kg\ bw/day] = \mathbf{5602}$$

Exposure scenario: direct skin contact from hand dishwashing

The MOE has been calculated by dividing the NOAEL of 400 mg/kg bw/day by the estimated exposure from hand dishwashing of 6.68 µg/kg bw/day.

$$\mathbf{MOE_{direct\ skin\ \ hand\ dishwashing}} = 400000/6.68\ [\mu g/kg\ bw/day] = \mathbf{59880}$$

Exposure scenario: direct skin contact from hard surface cleaning

The MOE has been calculated by dividing the NOAEL of 400 mg/kg bw/day by the estimated exposure from hard surface cleaning of 12.34 µg/kg bw/day.

$$\mathbf{MOE_{direct\ skin\ hard\ surface\ cleaning}} = 400000/12.34\ [\mu g/kg\ bw/day] = \mathbf{32414}$$

Exposure scenario: inhalation of dust during washing process

The systemic dose of IPA via inhalation via detergent dust during the washing process has been estimated to amount **0.00005** µg/kg bw/day. The MOE that could be calculated from this low exposure has been much greater than 1000000. The

described exposure does not significantly add to the overall IPA exposure from using cleaning products and will therefore not be considered in the risk assessment.

Exposure scenario: inhalation of aerosols from cleaning sprays

For calculation of the MOE, the NOAEL of 400 mg/kg bw/day has been divided by the daily systemic dose of 0.089 µg/kg bw/d which has been estimated for the inhalation of IPA-containing aerosols in spray cleaning applications. This exposure results in a very large MOE (>> 100000) and does not significantly add to the overall exposure. It will therefore not be considered in the risk assessment

Exposure scenario: oral route from residues left on dinnerware

The MOE has been calculated by dividing the systemic NOAEL of 400 mg/kg bw/day by the estimated oral exposure from IPA residues left on eating utensils and dinnerware of 0.14 µg/kg bw/day. This exposure results in a very large MOE (>> 100000) and does not significantly add to the overall exposure. It will therefore not be considered in the risk assessment

Exposure scenario: oral route from accidental ingestion and eye contact

Accidental ingestion of a few milligrams of IPA as a consequence of accidental ingestion of laundry and cleaning products has not expected to result in any significant adverse health effects given the low toxicity profile of laundry and cleaning products in general, and IPA in particular. This view has been supported not only by available toxicological information from animal studies, but also by the fact that national poison control centres have not reported a case of lethal poisoning or severe health effects with detergents containing IPA.

Accidental eye contact with undiluted laundry or cleaning products have been expected to cause mild to moderate irritation which is fully reversible shortly after the accidental exposure. Considering the generally low levels of IPA in laundry and cleaning products, this response has, however, been only to a minor extent related to IPA. Nevertheless, in the case of accidental eye contact, immediate rinsing with plenty of water has been recommended. This immediate action has been shown in animal experiments to minimize irritation effects.

Total Consumer Exposure

In a worst case scenario, the consumer exposure from direct and indirect skin contact of neat or diluted IPA containing products, inhalation of IPA containing aerosols from spray cleaner applications and from the oral route via IPA residues on eating utensils and dinnerware, results in an estimated systemic IPA exposure of 104.5 µg/kg bw/day. The MOE can be calculated by dividing the NOAEL of 400000 µg/kg bw/day by the total exposure:

$$\mathbf{MOE_{total}} = 400000/104.5\ [\mu g/kg\ bw/day] = \mathbf{3827}$$

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