HERA

Human & Environmental Risk Assessment on ingredients of European household cleaning products

Polycarboxylates used in detergents (Part I)

Polyacrylic acid homopolymers and their sodium salts (CAS 9003-04-7)

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Version 3.0

The content of this document has been prepared and reviewed by experts on behalf of HERA with all possible care and from the available scientific information. It is provided for information only**.** Much of the original underlying data which has helped to develop the risk assessment is in the ownership of individual companies.

1. EXECUTIVE SUMMARY

1.1 General

Water-soluble linear polycarboxylates are used in household cleaning products, e.g. in laundry detergents, automatic dishwashing detergents and various hard surface-cleaning formulations, and also in institutional and industrial cleaning processes and a variety of technical applications. Polycarboxylates are used in low-phosphate and phosphate-free detergents for avoiding incrustation and soil redeposition. Their effect is not based on complexing properties and therefore not comparable with typical chelating agents. The mechanism is the dispersion of calcium carbonate or calcium phosphate and the suspended solids during washing processes.

Major polycarboxylates used in detergents products comprise two different types of polymer families which distinguish in their technical applications and physical chemical properties: homopolymers of acrylic acid (P-AA) which is described in part I and copolymers of acrylic/maleic acid (P-AA/MA) which is described in part II of the HERA report. For this updated version 3.0 the European total consumption of homopolymers in detergent applications covered by HERA was updated to 21,000 tons/year in 2011. The mean molecular weight (MW) of the homopolymers P-AA ranges from approximately 1,000 to 78,000. Most investigations have been performed on the most commonly used commercial homopolymers with MW of 4,500. They generally are used in neutralised form (pH 6-8) as their sodium salts.

A comprehensive overview on their ecological and toxicological properties has been published by ECETOC (1993). The present HERA Targeted Risk Assessment updates this information and provides a focused risk assessment under the scope of HERA.

1.2 Environment

The main pathway of polycarboxylates into the environment is via domestic waste water and sewage treatment to surface waters. Thus, the removal of polycarboxylates from waste water before and during waste water treatment is the crucial factor that governs the distribution of polycarboxylates into the environment.

Over the past 25 years, the elimination of P-AA homopolymers from waste water has been investigated in multiple laboratory studies. The results indicate that P-AA differ to some extent in their eliminability although they are alike in many other physical and ecological attributes. While adsorption onto solids and precipitation are the principal mechanisms of abiotic elimination for this type of polymer, the degree of elimination differs and is strongly influenced by test concentration and water hardness. To refine the Predicted Environmental Concentrations (PEC), all available elimination data with good quality were used for the calculation of a geometric mean of removal rate in the current risk assessment. In addition, to better understand the distribution of the polymer between water phase and solid phase, partition coefficients (Kd) of the activated sludge, soil and sediment were determined with radiolabelled material.

Predicted No Effect Concentrations (PNECs) were calculated based on multiple acute as well as chronic data for different environmental compartments including water, sediment, soil, and sewage treatment plants (STP). This updated version 3.0 incorporates new toxicity data on the terrestrial compartment. In particular, recently generated data on soil microorganism have been used to derive a refined PNEC in soil. As the result, revised Risk Characterisation Ratio (RCR, expressed as the PEC/PNEC ratio) was established, which were below one for all relevant environmental compartments including water, soil, sediment, and STP. The outcome of this current environmental assessment provides a sound basis for the conclusion that the

use of polycarboxylates homopolymers in detergent products does not pose risk to the environment.

1.3 Human Health

Scenarios relevant to the consumer exposure to polycarboxylates have been identified and assessed using a Margin of Safety approach.

Polycarboxylates are of low toxicity by all exposure routes examined. Homopolymers (P-AA) are of low acute toxicity to the rat (LD_{50} > 5 g/kg bw/d) and are not irritating to the rabbit's skin and, at the most, slightly irritating to the eye. Further P-AA has no sensitising potential. The adverse effect after repeated inhalation dosing (91-d/rat) was a mild, reversible pulmonary irritation. This effect is considered as not substance-related owing to the physical property of the respirable dust, which caused local and not systemic lung effects. Nevertheless, in a worst case scenario, the NOEC of 0.2 mg/m^3 for P-AA was taken forward into a Margin of Exposure calculation under the worst case assumption of a ten percent deposition into the lung and 100% absorption of the deposited material. There was neither evidence for a genotoxic potential of P-AA using a variety of genetic endpoints *in-vitro* and *in-vivo*, nor for developmental toxicity or reprotoxicity in the rat. Based upon the available data, it is considered that exposure to polycarboxylates does not imply any particular hazard to humans.

Owing to the presence of polycarboxylates in many commonly used household detergents, consumers are exposed to polycarboxylates mainly via the dermal route, but also to a minor extent via the oral and inhalation route. The exposure resulting from dermal contact was estimated for P-AA as 4.4 µg/kg bw/day. The exposure by oral uptake was estimated for P-AA as 2.48 µg/kg bw/day.

Based on a NOAEL of 1,136 mg/kg bw/day from an oral study in rats, as a worst case scenario in the absence of a dermal NOAEL, a Margin of Exposure (MOE) of 2.5 x 10^5 can be assessed for P-AA for dermal contact.

The exposure resulting from oral uptake via substance residues on machine washed eating utensils and via drinking water is estimated to amount to 10.62 µg/ kg bw/ day for P-AA. From the NOEL of the 28 d rat study an MOE of 4.6 x 10^5 is assessed for this scenario.

For inhalative exposure a separate MOE of 2 x 10^5 was calculated for P-AA assuming 100% bioavailability of a hypothetical inhalable dust burden. All MOEs indicate no risk for human health.

In summary, based on the available data, the human risk assessment considers the use of polycarboxylates in household laundry products and automatic dishwashing detergents as safe and of no concern with regard to consumer use.

2. CONTENTS

3. SUBSTANCE CHARACTERISATION

3.1 Chemical Structure and Composition

Important polycarboxylates in detergents are homopolymers of acrylic acid which are generally used as sodium salts. The various polycarboxylates are distinguished by the monomers used for their preparation, acrylic acid (AA) and their molecular weight (MW).

In this HERA report part I the homopolymers are designated by codes consisting of the corresponding abbreviations (ECETOC, 1993):

P-AA: homopolymers of acrylic acid and their sodium salts

Table 1 shows the most important CAS Registry Numbers for this type of P-AA used as (co-) builders in household cleaning products:

Table 1: CAS Numbers for P-AA of acrylic acid and their sodium salts

CAS No.	CAS Name
9003-01-4	2-Propenoic acid, homopolymer
9003-04-7	2-Propenoic acid, homopolymer, sodium salt
25549-84-2	2-Propenoic acid, sodium salt, homopolymer
28603-11-4	2-Propenoic acid, homopolymer, sodium salt, isotactic
68479-09-4	2-Propenoic acid, telomere with sodium hydrogen sulphite, sodium salt

The family of linear P-AA homopolymers covers different products with a broad molecular weight (MW) ranging from 1,000 to 78,000. The polymer mostly used in detergents has a typical molecular weight (MW) of approximately 4,500, which has been taken into account in this HERA risk assessment. The structural formula is shown in figure 1:

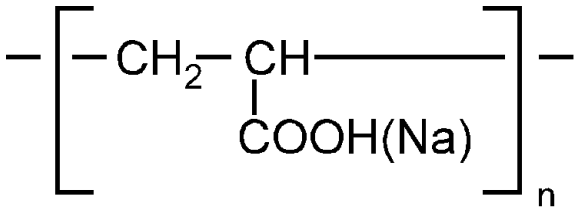

Figure 1: Structure of P-AA

Table 2: Physical-chemical data of P-AA

Parameter	Data	Reliability	Reference
Typical molecular weight (g/mol)	4,500	2	BASF AG, 2002
Molecular weight distribution M_w/M_n *)	app. 2	2	BASF SE, internal data
Melting Point	> 150°C (decomp.)	2	BASF SE, internal data
Boiling Point	not applicable		
Vapour Pressure	not applicable		
Water Solubility	> 40% (>400g/L)	2	BASF SE, internal data
Viscosity	not applicable		
pKa	not applicable		
pH (10 % in water at 20°C)	app. 8	2	BASF AG, 2002

*) Mw/Mn = equation of weight-average molar mass (Mw) and number-average molar mass (Mn); polymer dispersity
Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

3.2 Manufacturing route and production/volume Statistics

Polycarboxylates used in detergents are generally prepared by free-radical polymerisation of acrylic acid in aqueous solution. The molecular weight is influenced by the reaction conditions such as temperature and concentration, but the most important factors are the proportion and nature of initiators and chain-transfer agents used. For initiation, peroxides, azo compounds and redox systems such as iron (II) and hydrogen peroxide or sulphite and peroxidisulphate are employed. The most important chain-transfer agents include alcohols, amines, mercaptans (Jung et al, 1980), sodium bisulphite and sodium phosphinate. Depending on the reaction process, the residual content of acrylic acid and their sodium salts in P-AA can be as high as 0.5%; however, in most cases it is generally lower than 0.1%.

This updated risk assessment is based on the most recent and realistic market survey by A.I.S.E., which estimated a total consumption tonnage of homopolymers for the year 2011 for household and industrial and institutional uses (A.I.S.E., 2013). The following amount of P-AA was used for the risk assessment for Europe:

P-AA 21,000 tons per annum

It has to be noted that the overall homo- and copolymer volume has decreased in comparison to the HERA report version 2 (80,000 tons/year versus 54,000 tons/year for the present version). This trend can be explained by the shift from powder to liquid detergents over the past years (Euromonitor, 2012).

3.3 Use Applications Summary

Homopolymers are used in low-phosphate and phosphate-free detergents for household and industrial and institutional uses for avoiding incrustation and soil redeposition. P-AA is mainly used in automatic dishwashing detergents with a typical average concentration of approximately 0.5% in finished products, whereas their usage in laundry detergents is minimum.

4. ENVIRONMENTAL ASSESSMENT

An environmental report on polycarboxylates as used in detergents was prepared by ECETOC (1993) and has been used as the basis of this HERA Environmental Risk Assessment part I. Some recent studies were performed and used to refine this current environmental assessment, which mainly focused on the use scenario of the polymer as ingredient in low-phosphate and phosphate-free detergents for household (wide dispersive use).

4.1 Environmental Exposure Assessment

4.1.1 Environmental Fate and Removal of P-AA

In Chapter 4, the available environmental fate including biodegradation and removal data of P-AA (table 3-4) are listed and evaluated in terms of their reliability according to the criteria by Klimisch et al. (1997).

Aerobic Biodegradation and Elimination

Aerobic biodegradation data based on measurement of CO_2 evolution are available for a number of P-AA types with different MW and are summarised and evaluated in table 3. In addition, data on elimination based on measurements of dissolved organic carbon (DOC) or removal of radioactivity ^{14}C labelled material in simulated wastewater treatment process for a number of P-AA types with different MW are available and summarised in table 4. Although the homopolymer with MW of 4,500 is most representative commercial product for P-AA used in detergents, the test results for the other homopolymers with slightly lower and higher MW are considered helpful for a better understanding of the mechanisms responsible for the removal of these polymers in the environment.

Table 3: Summary of biodegradation data of P-AA based on CO_2 evolution

Mean MW (g/mol)	**Method/Remark**	**Result**	**Reliability**	**Reference**
Water				
1,000	CO_2 Evolution Test, river water, ^{14}C tagged	20 % CO_2 after 135 days	1	Procter & Gamble, 1985 b
1,000	CO_2 Evolution Test, domestic activated sludge, ^{14}C tagged	43 % CO_2 after 90 days	1	Procter & Gamble, 1985 c
2,000	CO_2 Evolution Test, river water, ^{14}C tagged	10 % CO_2 after 135 days	1	Procter & Gamble, 1985 b
2,000	CO_2 Evolution Test, domestic activated sludge, ^{14}C tagged	19 % CO_2 after 90 days	1	Procter & Gamble, 1985 c
4,500	CO_2 Evolution Test, domestic activated sludge, ^{14}C tagged	10 % CO_2 after 31 days	1	Procter & Gamble, 1985 d
10,000	CO_2 Evolution Test, river water, ^{14}C tagged	7 % CO_2 after 135 days	1	Procter & Gamble, 1985 b

Mean MW (g/mol)	Method/Remark	Result	Reliability	Reference
10,000	CO_2 Evolution Test, domestic activated sludge, ^{14}C tagged	17 % CO_2 after 90 days	1	Procter & Gamble, 1985 c
Sediment				
1,000	CO_2 Evolution Test, river water and sediment, ^{14}C tagged	58 % CO_2 after 135 days	1	Procter & Gamble, 1985 b
2,000	CO_2 Evolution Test, river water and sediment, ^{14}C tagged	37 % CO_2 after 135 days	1	Procter & Gamble, 1985 b
4,500	CO_2 Evolution Test, river water and sediment, ^{14}C tagged	6 % CO_2 after 106 days	1	Procter & Gamble, 1984 a
10,000	CO_2 Evolution Test, river water and sediment, ^{14}C tagged	12 % CO_2 after 135 days	1	Procter & Gamble, 1985 b
Soil				
1,000	CO_2 Evolution Test, sludge treated soil, ^{14}C tagged	35 % CO_2 after 165 days	1	Procter & Gamble, 1985 e
2,000	CO_2 Evolution Test, sludge treated soil, ^{14}C tagged	11 % CO_2 after 165 days	1	Procter & Gamble, 1985 e
4,500	CO_2 Evolution Test, sludge treated soil, ^{14}C tagged	6 % CO_2 after 81 days	1	Procter & Gamble, 1985 d
10,000	CO_2 Evolution Test, sludge treated soil, ^{14}C tagged	5 % CO_2 after 165 days	1	Procter & Gamble, 1985 e

Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

Table 4: Summary of elimination data of P-AA based on DOC or ^{14}C removal

Mean MW (g/mol)	Method/Remark	Result	Reliability	Reference
Water				
1,000	OECD 302 A (SCAS Test)	45 % DOC after 7 days	1	Procter & Gamble, 1983 a
2,000	OECD 302 A (SCAS Test)	21 % DOC after 7 days	1	Procter & Gamble, 1983 b
2,000	OECD 302 A (SCAS Test)	12 % DOC after 25 days	2	Procter & Gamble, 1985 f

Mean MW (g/mol)	**Method/Remark**	**Result**	**Reliability**	**Reference**
2,000	OECD 302 A (SCAS Test)	16 % DOC after 7 days	2	Procter & Gamble, 1985 g
3,400	OECD 302 A (SCAS Test)	22 % DOC after 7 days	2	Procter & Gamble, 1984 a
4,500	OECD 302 A (SCAS Test)	40 % DOC after 7 days	1	Procter & Gamble, 1984 b
4,500	OECD 302 A (SCAS Test)	29 % DOC after 7 days	2	Procter & Gamble, 1985 g
4,500	OECD 302 A (SCAS Test)	37.5 % ± 3.0 DOC removal	1	Hamilton et al, 1996
15,000	OECD 302 A (SCAS Test)	58 % DOC after 7 days	1	Procter & Gamble, 1985 a
15,000	OECD 302 B, industrial activated sludge	< 10 % DOC	2	BASF, 1989
Sewage treatment plant (STP)				
1,000	OECD 303 A (Activated sludge simulation test)	A: 9 % (DOC influent concentration 15 mg/l) B : 24 % (DOC influent concentration 10 mg/l)	1	Procter & Gamble, 1984
2,000	OECD 303 A (Activated sludge simulation test)	A : 13 % (DOC influent concentration 18 mg/l) B : 24 % (DOC influent concentration (10 mg/l)	1	Procter & Gamble, 1983 d
4,500	Waste water treatment simulation test, domestic	76 ± 8 % removal radiolabelled	1	Rohm & Haas, 1991 d
4,500	OECD 303 A (Activated sludge simulation test)	55 % removal radiolabelled	1	Hamilton et al, 1996

Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

The assessment of the distribution of the homopolymer in the water and solid phase is important for the quantification of the elimination of the polymers in different environmental compartments. The distribution coefficient (Kd) is defined as the concentration ratio at equilibrium of a dissolved substance in a two-phase system consisting of a solid (typically activated sludge, soil or sediment) and a water phase

Kd = homopolymer in solid phase / Homopolymer in water phase

The solid-water partition coefficient Kd was recently determined in a new study (BASF SE, 2013) for different environmental compartments including activated sludge, soil and sediment (table 5). Under mean water hardness conditions, very low polymer concentrations were expected, which was certainly a challenge for analysis. A limit of quantification (LOQ) was determined as 0.3 mg/L DOC (dissolved organic carbon) for P-AA using cold material and the application of DOC analytical method (Tomforde, master thesis, 2012). This high concentration was not suitable for the determination of Kd values under realistic environmental water hardness conditions. Therefore ^{14C}-labelled P-AA was synthesized and used in the experiments for Kd determination.

Based on the current available synthesis manual and laboratory process conditions, the ^{14}C synthesis resulted in a P-AA with an average MW of 16,100 g/mol, which is slightly higher than the typical MW of 4500 g/mol. However, this radio-labelled polymer was deemed to be representative for the broad range of the whole polymer group.

Realistic environmental conditions were used in the Kd measurements. The P-AA concentrations used for the experimental determination of Kd in activated sludge, soil and sediment were 1.3, 0.02 and 0.2 mg/L, respectively and were based on the calculated predicted environmental concentrations (PEC) from the HERA v2 report (2009). In addition, some test parameters were adjusted to mimic the real environment scenario. For example, the Kd sludge was determined after an aeration time of 3 h (Görner K. and Hübner K., 2001) and sedimentation time of 4 h according to OECD guideline 303A (OECD, 2001). The activated sludge concentration in the test system was adjusted to 6.3 g/L dry weight, which was identical to the original conditions in the clarifier of the municipal waste water treatment plant in Mannheim, Germany.

The determination of the Kd followed OECD guideline and are considered in good quality. For example, for the soil compartment was based on polymer concentration in the soil pore water. The P-AA concentration in the pore water was based on a soil to solution ratio of 1/25 (OECD 106 guideline, 2000). The water hardness concentrations used in Kd measurement can be referred to publication by Koppe and Stozek 1986, Dietrich et al 1975 and the OECD 106 guideline. The pH range in these tests was between 7.0 and 8.0, which was suggested by Imhoff et al 2009.

Table 5: Summary of Kd values for P-AA on activated sludge, soil and sediment

Solids	Activated sludge	Soil	Sediment
Concentration [mg/L] (pore water)	1.3	0.02	0.2
Water hardness [mg/L]	70	400	40
pH	7.5	7.0	8.0
Kd-value [L/kg]	1,825 (7 h)	27 (24 h)	54 (24 h)

For EUSES modelling purpose, a Koc value as input parameter of 4,932 L/kg was derived based on the Kd-value for activated sludge (BASF SE, 2013)

Conclusion for the evaluation of the biodegradation and elimination of homopolymers

The dominant fate pathway of homopolymers used in detergents into the environment is via domestic wastewater. Polymers with a lower molecular weight of MW < 2,000 g/mol can be partly biodegraded. However, high MW species used in detergents are considered poorly biodegradable. In contrast to biodegradation processes, insoluble salts will be formed in the

presence of calcium cations and will be eliminated either by adsorption or precipitation processes. Recent determined Kd of 1,825 L/kg clearly suggests a high adsorption potential of the soluble P-AA on activated sludge (BASF SE, 2013). Therefore, it can be concluded that independent of the soluble and insoluble state of P-AA elimination processes can occur in the presence of sufficient high amount of activated sludge, which is the major elimination process in waste water treatment plants.

All elimination data based on DOC or radiolabelled analytical measurements showed no clear relationship between elimination and molecular weight. Basically all studies in table 4 were performed with domestic activated sludge with one exemption P-AA 15,000, BASF 1989. Therefore, for all the studies in table 4 a geometric mean value of 25 % elimination rate was calculated.

Based on the available data it can be concluded that P-AA is not readily biodegradable but is partly accessible to ultimate biodegradation particularly under long incubation conditions (cf. mineralisation data). Lower molecular weight homopolymers (MW < 2,000) are partly biodegradable under the conditions of soil or sediment inoculation. Test results with activated sludge inoculum indicate different elimination degrees, apparently due to adsorption and precipitation processes. The removal degrees of different P-AA types show no clear relationship between elimination extent and molecular weight. To fully leverage all the available data, the geometric mean value of 25 % is used for the EUSES calculations of the P-AA exposure assessment.

Anaerobic Biodegradation and Elimination

No data on anaerobic biodegradation are available for P-AA. There is only one study performed with the copolymer P-AA/MA 70,000 g/mol in batch experiments. About 80 % of the radio-labelled carbon was adsorbed on the sludge phase and about 3 % was mineralised to CO_2. This result could be confirmed by studies simulating the digestion of sewage sludge (Schumann and Kunst, 1991). Therefore, no anaerobic degradation of P-AA was assumed in the context of the HERA risk assessment.

4.1.2 Abiotic degradability of P-AA

Photodegradation

Due to the high water solubility and low volatility of P-AA in general and the fact that the emissions are directed to sewage, the compartment air is not a relevant fate pathway and therefore is not considered in this assessment.

Hydrolytic stability

Polycarboxylates are very stable compounds as the carboxyl part of the molecule is the only functional group. The presence of the multiple neighbouring carboxyl groups along the polymer chain adds further to the stability. Therefore, the hydrolytic stability of these compounds is very high.

Conclusion

Abiotic degradation mechanisms like photolytic and hydrolytic processes do not significantly influence the environmental fate of polycarboxylates.

4.1.3 Bioconcentration and Bioaccumulation of P-AA

Experimental data on the bioaccumulation potential of polycarboxylates are not available. Estimated bioconcentration factors based on the octanol-water partition coefficient are not appropriate since P-AA is beyond the molecular weight range for which the estimation approaches have been developed. However, based on several considerations bioaccumulation is regarded as insubstantial for P-AA. The molecular weight of approximately 4,500 g/mol is far above the molecular weight limit of 700 g/mol which is suggested in the EU Technical

Guidance Document. In addition, the high water solubility of the parent compound together with its property to form insoluble calcium salts in natural waters suggests that bioaccumulation is unlikely. Hence, it is highly unlikely that P-AA is taken up via the mechanism which has been established for hydrophobic chemicals.

Mechanisms for uptake of charged molecules are ion pumps or ion channels. These are effective for small charged cations but have not been described for polymers carrying multiple negative charges. Likewise there is no evidence of transmembrane transport modes involving carriers or endocytosis playing a significant role in xenobiotic bioaccumulation. Based on the above discussion of uptake paths, bioaccumulation is regarded as insubstantial.

4.1.4 Secondary Poisoning / Exposure of Humans via the Environment

In addition to effects resulting from direct exposure, there is the general concern that bioaccumulation in food chains may lead to secondary effects for predating organisms. In the specific case of P-AA such indirect exposure can be considered negligible based on the arguments provided above on minimum potential on bioconcentration and bioaccumulation of P-AA.

In addition, it is unlikely that humans will be exposed to P-AA directly by contact with air or through indirect exposure via the food chain. This is because P-AA does not bioaccumulate (see 4.1.3). Due to the water solubility, the high molecular weight and the tendency of adsorption on solids (high Kd value for activated sludge) volatilization is not expected.

4.1.5 Monitoring Data

Monitoring data are not available.

4.1.6 PEC Calculations

Polycarboxylates represent a group of high production volume detergent ingredients predominantly used in phosphate-reduced or phosphate-free detergents in the Western European market (*EU15 + 3). Therefore, PEC calculations were performed by using the EUSES scenario according to EU TGD (EU, 2003; Industry category **5**: Personal & domestic use, Use category **9**: Cleaning/ washing agents and additives).

The tonnage data reported in Chapter 3.2 will be used for the following PEC calculations according to the A.I.S.E. SPERC, HERA and default values of EU TGD methodology (EUSES). A.I.S.E. SPERCs are release estimates for the detergent and cleaning product industry. They define the environmental releases from formulation of such products and from their use. The EU TGD defaults and expert knowledge available in the sector have been employed to derive the SPERCs for formulation (Price et. al, 2010). Price et al. (2010) did an in-depth analysis coupled market insight data with population density data and concluded that a value 4 % for laundry care is an appropriate worst case assumption reflecting more than 99.9th percentile of product usage distribution. This fraction of EU tonnage used in the region is implemented in the A.I.S.E. SPERC, 2012.

In consideration of this specific consumption scenario, the exposure calculations are based on the following general assumption:

- Fraction of production tonnage to region 5.5 % in EUSES
- Fraction of continental tonnage to region (private use) 4 %
- Fraction connected to sewer systems: 80 %
- Fraction of the main local source: 0.00075

For the refined PEC calculations the Kd values for sludge, soil and sediment (table 3) and the geometric mean value of 25 % elimination (table 4) were used as input data for the EUSES calculations.

The relevant input data for the partition among different environmental compartments in exposure calculations are as follows:

- European tonnages release into waste water: 100 %
- Fraction of emission directed to air 0
- Fraction of emission directed to water 0.75
- Fraction of emission directed to sludge 0.25

The standard default sludge application rate of 5 t/ha per year, the default value in EUSES model is much higher compared to reported sludge application rate in EU. Although the maximum quantities of sludge application have been set between 1 to 10 metric tons per hectare per year, sludge quantities used on agricultural land have been reported to range from 2 to 3 t/ha per year (Schowanek et al., 2004, European Commission, 2010) and often not to exceeding 2 t/ha per year (Andersen, 2001) in actual practice. Moreover, the application of sludge to land is not necessarily done on an annual basis (Schowanek et al., 2004). For example, Germany has the highest sludge production in EU (Laturnus et al, 2007; Milieu Ltd, WRc and RPA for European Commission, 2010) laid down the limit for maximum quantity of sludge application of 5 metric tons over a period of 3 years, which corresponds to < 2 t/ha per year (Andersen, 2001). This issue was discussed in detail in the Technical Report N°92 (ECETOC, 2004) with the proposal to change the current default parameter of 5 t/ha per year in the TGD making them compatible with the proposed revisions of Sludge in Agriculture Directive, to use e.g. 3 t/ha per year reflecting the current practice throughout the EU. Moreover, the value of 3 t/ha per year was already assumed as an average mass of sludge application on land (INERIS, 2008). The INERIS study indicated that the current European agriculture practice is closer to 2 t/ha per year.

The EUSES estimate for the concentration in agricultural soil is based on the assumption that sludge application occurs in 10 consecutive years. As a consequence, EUSES predicts an unrealistic accumulation in soil which results in an overestimation of PECsoil. Given this degree of overestimation, it can be expected that the combination of annual sludge application (following EUSES default) with a sludge application rate of 3 tons per year is sufficiently conservative.

Based on reasons discussed above, the PEC and RCR were calculated with a more realistic but still conservative sludge application rate of 3 t/ha per year.

The results of the PEC calculations for P-AA are presented in table 6:

Table 6: PEC calculations for P-AA in water, sediment, soil and STP effluent

Compartment	**Predicted environmental concentrations (PEC)**
Water	
$PEC_{regional,\ water}$ [mg/l]	0.043
$PEC_{local,\ water}$ [mg/l]	0.11
Sediment	
$PEC_{regional,sediment}$ [mg/kgwwt]	4.88
$PEC_{local,\ sediment}$ [mg/kgwwt]	11.6
Soil	
$PEC_{regional,\ soil}$ [mg/kgwwt]	0.47
$PEC_{local,\ soil}$ [mg/kgwwt]	4.37
STP Effluent	
$PEC_{local,\ stp}$ [mg/l]	0.65

4.2. Environmental Effects Assessment

In the following chapter, the available ecotoxicity data of P-AA (table 7-10) are listed and evaluated in terms of their reliability according to the criteria by Klimisch et al. (1997).

4.2.1 Ecotoxicity of P-AA

P-AA has a low acute ecotoxicity profile (table 7). All ecotoxicity studies showed the L(E)C50 beyond the highest tested concentration (> 200 mg/l) with the exception of algae. Toxicity to aerobic bacteria is low as well. Several chronic studies on fish, daphnia and algae are also available (table 8). The chronic NOEC data with Daphnia magna of P-AA with the same molecular weight of 4,500 had a broad range between 12 and 450 mg/L. Several studies on sediment or soil ecotoxicity are available confirming again the low ecotoxicity of P-AA (table 10).

Table 7: Acute Aquatic Ecotoxicity of P-AA

Mean MW (g/mol)	**Test species**	**Method**	**LC/EC_{50} [mg/l] Exposure time**	**Reliability**	**Reference**
Acute Toxicity to Fish					
1,000	*Brachydanio rerio*	OECD 203 (range finding)	> 200 (96 h)	1	Procter & Gamble, 1983 g
1,000	*Salmo gairdneri*	Standard method for acute toxicity tests	> 1,000 (96 h)	1	Rohm & Haas, 1983 a
1,200	*Leuciscus idus*	DIN 38412 part 15	> 500 (96 h)	1	BASF AG, 1987 a
2,000	*Brachydanio rerio*	OECD 203 (range finding)	> 200 (96 h)	1	Procter & Gamble, 1983 g
2,500	*Leuciscus idus*	DIN 38412 part 15	> 500 (96 h)	1	BASF AG, 1987 b
4,500	*Brachydanio rerio*	US and European guidelines	> 200 (96 h)	4	Freeman et al., 1993
4,500	*Lepomis macrochirus*	OECD 203	> 1,000 (96 h)	1	Procter & Gamble, 1984 d
4,500	*Lepomis macrochirus*	Standard method for acute toxicity tests	> 1,000 (96 h)	1	Rohm & Haas, 1983 b
4,500	*Salmo gairdneri*	US and European guidelines	700 (96 h)	4	Freeman et al., 1993
8,000	*Leuciscus idus*	DIN 38412 part 15	> 500 (96 h)	1	BASF AG, 1987 c
10,000	*Lepomis macrochirus*	US EPA, 1975	> 1,000 (96 h)	1	Procter & Gamble, 1983 h
15,000	*Leuciscus idus*	DIN 38412 part 15	> 10,000 (96 h)	1	BASF AG, 1987 d

Mean MW (g/mol)	**Test species**	**Method**	**LC/EC_{50} [mg/l] Exposure time**	**Reliability**	**Reference**
78,000	*Brachydanio rerio*	ISO 7346/3	> 400 (96 h)	2	Henkel KGaA, 1987
Acute Toxicity to Aquatic Invertebrates					
1,000	*Daphnia magna*	OECD 202	> 200 (48 h)	1	Procter & Gamble, 1983 i
1,000	*Daphnia magna*	Standard method for acute toxicity tests	> 1,000 (48 h)	1	Rohm & Haas, 1983 c
2,000	*Daphnia magna*	OECD 202	> 200 (48 h)	1	Procter & Gamble, 1983 i
4,500	*Daphnia magna*	OECD 202	> 200 (48 h)	1	Procter & Gamble, 1984 e
4,500	*Daphnia magna*	Standard method for acute toxicity tests	> 1,000 (48 h)	1	Rohm & Haas, 1983 d
78,000	*Daphnia magna*	OECD 202	276 (24 h)	2	Henkel KGaA, 1987
Acute Toxicity to Algae					
8,000	*Selenastrum capricor-nutum*	US EPA TSCA 797.1050	40 (72 h)	1	BASF Corp., 1989
78,000	*Scenedesmus subspicatus*	OECD 201	44 (96 h)	2	Henkel KGaA, 1987

Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

Table 8: Chronic Aquatic Ecotoxicity of P-AA

Mean MW (g/mol)	**Test species**	**Method**	**NOEC [mg/l] Exposure time**	**Reliability**	**Reference**
Chronic Toxicity to Fish					
4,500	*Pimephales promelas*	TSCA 797.1600, Early life stage	56 (32 days)	2	Rohm & Haas, 1991 a
4,500	*Brachydanio rerio*	OECD 204	> 450 (28 days)	1	Procter & Gamble, 1986 a
78,000	*Brachydanio rerio*	OECD 204	> 400 (14 days)	2	Henkel KGaA, 1987
Chronic Toxicity to Aquatic Invertebrates					
4,500	*Daphnia magna*	US and European guidelines	5.6 (21 days)	4	Freeman et al, 1993
4,500	*Daphnia magna*	OECD 202	450 (21 days)	1	Procter & Gamble, 1989 a
4,500	*Daphnia magna*	TSCA 797.1330	58 (21 days)	1	Rohm & Haas, 1991 e
4,500	*Daphnia*	OECD 202	12 (21 days)	2	Rohm & Haas,

Mean MW (g/mol)	Test species	Method	NOEC [mg/l] Exposure time	Reliability	Reference
	magna				1991 b
78.000	*Daphnia magna*	OECD 202 (Life-Cycle)	100 (21 days)	2	Henkel KGaA, 1987
Chronic Toxicity to Algae					
4,500	*Scenedesmus subspicatus*	OECD 201	180 (96 h)	2	Hennes, 1991
78,000	*Scenedesmus subspicatus*	OECD 201	32.8 (96 h)	2	Henkel KGaA, 1987

Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

Conclusion for the $PNEC_{water}$ derivation based on aquatic toxicity data

The acute aquatic toxicity of P-AA is generally low and was not considered for the $PNEC_{water}$ derivation. Instead, available chronic toxicity data (table 8) are more sensitive and have been used for the $PNEC_{water}$ derivation.

It has been noted that the rather large variability of chronic aquatic toxicity results for *Daphnia magna* in the range between 12 and 450 mg/L with the same molecular weight of 4,500. The solubility behaviour of P-AA in water presumably explains these observations since the aquatic toxicity directly linked to its solubility behaviour in water. The water solubility of P-AA in distilled water is over 40 % (>400 g/L). However, under test conditions in ecotoxicity studies, water solubility decreased considerably with different water hardness. In the presence of Ca^{++} or Mg^{++} cations this solubility decreased considerably. In excess of 2^{+}-ions, homopolymers form insoluble precipitates because the carboxylic groups are saturated. With increasing concentrations of homopolymers in water, e.g. in excess of polymers compared to 2^{+}-ions, this phenomenon declines in the way that less to no precipitation occurs at high polymer concentrations in water. This correlation was confirmed in a recent study by BASF SE (BASF SE, 2012). In this study, the water solubility of P-AA was determined with radio labelled compound with Ca-concentration of 70 mg/L, which corresponds to the mean water hardness similar to the Daphnia media M4 in the OECD guideline 202. Under these water hardness conditions the solubility of P-AA was 1.3 mg/L after 24 h. This study demonstrates that P-AA is predominantly present in form of insoluble precipitation products which causes the adverse effects of *Daphnia magna* at low concentrations.

Two different NOECs of 450 mg/L (soluble state of P-AA) and 12 mg/L (insoluble state of P-AA) were determined depending on the test design. The chronic daphnia study by Rohm & Haas (1991b) with a NOEC of 12 mg/L represents the most critical study for aquatic invertebrates. Although these effects were caused indirectly from precipitation products and not from the soluble P-AA itself, this NOEC value is used for the derivation of the $PNEC_{water}$ as a worst case approach. With acute and chronic data from all three trophic levels, an application factor of 10 was used according to EU TGD (EU, 2003).

Table 9: Acute Toxicity to Bacteria of P-AA

Mean MW (g/mol)	Test species	Method	EC [mg/l] Exposure time	Reliability	Reference
1,000	Activated sludge	OECD 209 (range finding)	EC_{50} > 100	2	Procter & Gamble, 1985 a

Mean MW (g/mol)	Test species	Method	EC [mg/l] Exposure time	Reliability	Reference
2,000	Activated sludge	OECD 209 (range finding)	EC_{50} > 100	2	Procter & Gamble, 1985 a
4,500	Activated sludge	ESD standard method VIII-D-1, 1982	EC_{50} > 1,000	1	Procter & Gamble, 1985 j
15,000	Activated sludge	OECD 209	EC_{20} > 1,000 (30 min)	2	BASF AG, 1989
78,000	*Pseudomonas putida*	DIN 38412 part 8	EC_{10} (16 h)	2	Henkel KGaA, 1987

Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

Conclusion for the $PNEC_{STP}$ derivation based on bacteria toxicity data

The most valid study on bacteria toxicity is the acute oxygen consumption inhibitory test with activated sludge, which was used for derivation of the $PNEC_{STP}$. Although the EC_{50} value for P-AA (4,500) was > 1,000 mg/l, an EC_{50} = 1,000 mg/l was conservatively assumed and an application factor of 100 was used.

Table 10: Ecotoxicity of P-AA to Terrestrial and Sediment Organisms

Mean MW (g/mol)	Test species	Method	Effect [mg/kg] Exposure time	Reliability	Reference
Toxicity to Soil Dwelling Organisms					
4,500	*Eisenia foetida*	US and European guidelines	EC_0 = 1,000 (96 h)	4	Freeman et al, 1993
4,500	*Eisenia foetida foetida*	OECD 207	EC_0 = 1,000 (14 days)	1	Rohm & Haas, 1991 c
78,000	*Eisenia foetida andrei*	Earthworm tox. Test (UBA, 1984)	EC_0 = 1,000 (14 days)	2	Henkel KGaA, 1987
Toxicity to Terrestrial Plants					
4,500	Corn, soybean, wheat and grass seeds	No data available	EC_0 = 225	4	Hennes, 1991
78,000	*Brassica rapa*	EEC Directive 79/831, Annex V	NOEC = 1,000 (21 days)	2	Henkel KG aA, 1987
Toxicity to soil Microorganisms					
4,500	Nitrogen transformation	OECD 216	EC_{10} > 2,500 mg/kgdw (28 days)	1	BASF SE, 2012 d

Mean MW (g/mol)	Test species	Method	Effect [mg/kg] Exposure time	Reliability	Reference
4,500	Carbon transformation	OECD 217	EC_{10} > 2,500 mg/kgdw (28 days)	1	BASF SE, 2012 b
Toxicity to Sediment Dwelling Organisms					
4,500	*Chironomus riparius* (larvae)	Sediment batch system	EC_0 > 4,500 mg/kgdw (96 h)	1	Procter & Gamble, 1989 b

Reliability criteria of IUCLD according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

Conclusion for $PNEC_{soil}$ derivation based on terrestrial toxicity data

The $PNEC_{soil}$ calculation is based on the most reliable data from chronic nitrogen and carbon transformation studies (EC_{10} > 2,500 mg/kgdw) (Table 10). The EC_{10} value was recalculated to > 2,212 mg/kgwwt related to wet weight using a conversion factor of 1.13 (EU TGD, 2003) and was used together with an assessment factor of 100 according to EU TGD (EU, 2003) for the $PNEC_{soil}$ derivation.

Conclusion for $PNEC_{sediment}$ derivation based on sediment equilibrium partitioning method

Experimental data on sediment-dwelling organisms are available for P-AA with *Chironomus riparius* (Procter & Gamble, 1989 b). The chironomids did not show any visual sign of harm during 96 h exposure at the highest test concentration of 4,500 mg/kg. Therefore, the EC_0 is considered above 4,500 mg/kg and an assessment factor cannot apply. Due to the limited test data, equilibrium partitioning method with the newly generated Kd on sediment were used to derive $PNEC_{sediment}$.

4.2.2 Derivation of PNEC

Acute and Chronic toxicity data exist for all three aquatic trophic levels fish, daphnia and algae. In addition, in this updated HERA risk assessment version 3.0 supplementary recent data on terrestrial toxicity are used for a refinement of the $PNEC_{soil}$ derivation. Key studies and assessment factors used for the PNEC derivation are summarised in table 11:

Table 11: Summary of the PNEC calculations of P-AA

Key study for compartment	Reference (No)Effect concentration	Application Factor	PNEC
$PNEC_{water}$ [mg/l]	NOEC = 12 mg/l	10	1.2
$PNEC_{sediment}$ [mg/kgwwt]	EUSES calculation acc. to equilibrium partitioning method	Not applicable*	130
$PNEC_{soil}$ [mg/kgwwt]	EC_{10} > 2,212 mg/kgwwt	100	22.1
$PNEC_{stp}$ [mg/l]	EC_{50} > 1000 mg/l	100	10

*The equilibrium partitioning method used the default value of 0.05 as the weight fraction of organic carbon in sediment according to EU TGD (EU, 2003).

4.3. Environmental Risk Characterisation

In the following table 12 the Risk Characterisation Ratios (RCR) for the environmental compartments water, sediment, soil and, STP were calculated from the PECs summarised in table 6 and the PNECs derived from table 11:

Table 12: Environmental Risk Characterisation Ratio RCR of P-AA

Risk Characterisation Water compartment	**RCR**
$PEC_{regional,\ water.}/PNEC_{water}$	0.04
$PEC_{local,\ water.}/PNEC_{water}$	0.09
Risk Characterisation Sediment compartment	
$PEC_{regional,\ sed.}/PNEC_{sed.}$	0.04
$PEC_{local,\ sed.}/PNEC_{sed.}$	0.09
Risk Characterisation Soil compartment	
$PEC_{regional,\ soil}/PNEC_{soil}$	0.02
$PEC_{local,\ soil}/PNEC_{soil}$	0.2
Risk Characterisation Sewage Treatment Plant	
$PEC_{local,\ stp}/PNEC_{stp}$	0.07

4.4 Discussion and Conclusions

The environmental risk assessments of P-AA were conducted according to the EU TGD (2005) with calculation model of EUSES under A.I.S.E. SPERC, HERA exposure senario. For exposure assessment, sorption coefficients Kd generated from recent studies with radio labelled PAA homopolymer in activated sludge, soil and sediment are used. Another key parameter is the elimination rate in STP. For this assessment, a geometric mean removal rate of 25 % was derived from several degradation and simulated STP studies.

Acute and chronic aquatic toxicity data are available for all three aquatic trophic levels fish, daphnia and algae. Recent studies confirm earlier observations that the water solubility of P-AA is heaviliy dependend on the water hardness and the test concentrations. More specifically, the water solubility, determined with radio labelled compound, resulted in 1.3 mg/L under conditions similar to the mean water hardness in Daphnia media. The solubility and precipitation behaviour of P-AA in the presence of 2^{+}-ions like ubiquitous calcium and magnesium ions has a an important impact on the interpretation of the available chronic aquatic toxicity test results of P-AA. It also explains the observed large variability with *Daphnia magna* of NOECs in the range between 12 to 450 mg/L. P-AA forms insoluble precipitation products at low concentrations. These insoluble products may potentially cause secondary adverse effects which results in a NOEC value of 12 mg/L. This value was used in the risk assessment as a worst case scenario.

The PNEC derivation for sediment using the equilibrium partitioning method indicates low toxicity on sediment organisms. This outcome was confirmed by experimental data with the sediment-dwelling organisms *Chironomus riparius.* The chironomids did not show any adverse effects even at the highest test concentration of 4,500 mg/kg. Therefore, the EC_0 is considered above 4,500 mg/kg and an assessment factor cannot apply. For this reason the derivation of the $PNEC_{sediment}$ was based on the application of the equilibrium partitioning method.

New long-term soil toxicity data were supplemented and current studies on microbial activity of nitrogen and carbon transformation allowed a refinement of the evaluation of the terrestrial

compartment.The EC_{10} values indicate very low toxicity effects above 2,500 mg/kgdw. The EC_{10} value was recalculated to > 2,212 mg/kg on wet weigt base based on using a conversion factor of 1.13 (EU TGD, 2003).

The updated version 3 of the HERA risk assessment report does not indicate environmental risks for all relevant compartments including water, sediment, soil and sewage treatment plant (STP) with all risk characterisation ratios (RCR) below 1. The outcome of this present environmental risk assessment provides a sound basis for the conclusion that the use of homopolymers in detergent products does not pose a risk to the environment.

5. HUMAN HEALTH ASSESSMENT

5.1 Consumer Exposure

Polycarboxylates are used in low-phosphate and phosphate-free detergents for avoiding incrustation and soil redeposition. Homopolymers are used mainly in automatic dishwashing detergents whereas their use in laundry detergents is of minor importance. Polycarboxylates are usually not contained in manual dishwashing detergents. A typical mean concentration of polycarboxylates is 0.5 % for P-AA in laundry detergents.
See also 3.3.

5.1.2 Consumer Contact Scenarios

As relevant consumer contact scenarios, the following consumer exposure routes were identified and assessed:

- Direct skin contact from hand-washed laundry, direct skin contact via laundry/dishwashing tablets or powder
- Indirect skin contact via release from cloth fibres to skin
- Oral ingestion of residual amounts on dishes and eating utensils
- Oral ingestion of residues in drinking water
- Inhalation of detergent dust during washing processes
- Accidental or intentional overexposure

5.1.3 Consumer Exposure Estimates

There is a consolidated overview concerning habits and uses of detergents and surface cleaners in Western Europe issued by A.I.S.E., 2002. This list reflects the consumers' use of detergents in g/cup, tasks/week, duration of task and other uses of products and is relevant data for the calculation and reflection about consumer exposure in the following.

5.1.3.1 Direct skin contact via hand-washed laundry

P-AA under alkaline conditions are soluble depending on the molecular weight. The contact time with the polycarboxylates in the course of handwashing is, according to A.I.S.E., very short (approx. 10 min) and the percutaneous absorption of high molecular weight polymers will be very low to non existant. Likewise uptake via the intact skin of ionic, low molecular weight substances has also been reported to be very low (Schaefer and Redelmeier, 1996). Thus, it can be assumed that the amount of polycarboxylates systemically available via percutaneous absorption, if any, is very low. In the following calculations the worst case assumption has been made that 1% of the polycarboxylates are available for percutaneous absorption.

Additionally, the following worst case assumptions should adequately address this scenario:

- Concentration of laundry detergent in handwashing is approx. 1 % corresponding to 10 mg/ml (cm^3).
- Highest concentration of P-AA in laundry detergents in handwashing amounts to 0.5%
- Contact of hands and forearms with laundry detergent solution would expose about 1980 cm^2 of skin (EU EU TGD 1996)
- Assuming a fluid film thickness of 100 µm (0.1 mm or 0.01 cm) (Vermeire, 1993) on the skin and, as a worst case assumption, a percutaneous absorption of 1% for polycarboxylates in 24 h exposure time, the following amount of polycarboxylates absorbed via skin can be calculated:

For **P-AA:**
1980 cm^2 x 0.01 cm/day x 0.01 (fraction absorbed) x 10 mg/ml (ml = cm^3; 1% of detergent in washing fluid) x 0.005 (fraction of P-AA in detergent; 0.5%) = 0.0099 mg/day

0.0099 mg P-AA absorbed in 24 hours

In 15 min contact time a smaller amount of substance will be absorbed; for the sake of simplicity and as it can be assumed that the rate of percutaneous absorption is not linear in 24 hours and is possibly at its maximum in the first hour, 0.0099 mg is used in the assessment resulting in an estimated dose of (60 kg bw assumed):

$Exp_{sys(direct\ skin\ contact)}$ = 0.165 µg/kg bw/day

5.1.3.2 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 concentrated laundry liquid which is applied directly to the garment. In this exposure scenario, at most the skin surface of both hands is exposed and the time for this task is typically shorter than ten minutes. The following parameters are considered to represent a worst case scenario for this application:

- Concentration of laundry detergent in hand washing is approx. 60 %.
- The potentially affected skin surface is 840 cm^2
- Film thickness and absorption rate over one day with one task per day are the same as above

For P-AA:
840 cm^2 x 0.01 cm/day x 0.01 (fraction absorbed) x 600 mg/ml (ml = cm^3; 60% of detergent in washing fluid) x 0.005 (fraction of P-AA in detergent; 0.5%) = 0.25 mg/day

0.25 mg P-AA absorbed in 24 hours

In 10 min contact time a smaller amount of substance will be absorbed; for the sake of simplicity and as it can be assumed that the rate of percutaneous absorption is not linear in 24 hours and is possibly at its maximum in the first hour, 0.25 mg is used in the assessment resulting in an estimated dose of (60 kg bw assumed):

$Exp_{sys(direct\ skin\ contact)}$ = 4.2 µg/kg bw/day

5.1.3.3 Direct skin contact via laundry / dishwashing tablets or powder

Contact with laundry and dishwashing tablets occurs frequently when the tablets are unwrapped and placed into the washing or dishwashing machine. However, the contact time is very low (<1 min) and the area of contact with skin is so small (only the tips of thumb and index finger of one hand are exposed (approx. 2 cm^2 skin) that the amount taken up percutaneously is considered insignificant.

Some parts of the body, mainly the hand, might also come in contact with washing or dishwashing powder when transferring the product from the container into the machine or accidentally spilling some powder. Contact time during these scenarios is very low (<1 min), the skin area affected is small (usually much less than the area of one hand) and exposure

occurs only occasionally and not regularly with product use. Thus, the systemic exposure of polycarboxylates resulting from this scenario is also considered to be negligible.

5.1.3.4 Indirect skin contact wearing clothes

Residues of components of laundry detergents may remain on textiles after washing and could come in contact with the skin via transfer from textile to skin. Polycarboxylates, despite their solubility in water, are deposited in solid form and thus as a first rough estimation, the small amount of polycarboxylates absorbed via this route should be insignificant.

The fact that only minor amounts of polycarboxylates could be percutaneously absorbed is demonstrated by the following calculation, assuming the worst case scenario:

$$\mathbf{Exp_{sys} = F_1 \times C' \times S_{der} \times n \times F_2 \times F_3 \times F_4 / bw \ [mg/kg\ bw/\ day]}$$

F_1 = percentage (%) weight fraction of substance in product
C' = product load in [mg/cm^2]
S_{der} = surface area of exposed skin in [cm^2]
n = product use frequency in number [events/day]
F_2 = percentage (%) weight fraction transferred from medium to skin
F_3 = percentage (%) weight fraction remaining on skin
F_4 = percentage (%) weight fraction absorbed via skin
bw = body weight in [kg]

Determination of **C'** ("product applied to skin via fabric wash (hand, machine) and wear")

$$\mathbf{C' = M \times F' \times FD/w_l \ [mg/cm^2]}$$

M = amount of undiluted product used in [mg]
F' = percentage (%) weight fraction of substances deposited on fabric
FD = fabric density in [mg/cm^2]
w_l = total weight (of fabric per wash; 1 kg) in [mg]

According to these algorithms cited above, the following calculations were done:

Determination of **C'**

M = 200,000 [mg] product/cup maximum
F' = 5 (%) = 0.05 (worst case assumption!) (Matthies et al. 1990)
FD = 10 [mg/cm^2] Procter & Gamble, 1996
w_l = 1 000,000 [mg] (estimated)

$$\mathbf{C' (P\text{-}AA) = 0.1\ mg/cm^2}$$

Calculation for the systemic exposure:

F_1 = 0.5 % (P(AA))
C' = 0.1 [mg/cm^2]
S_{der} = 17,600 [cm^2] 2003)
n = 1 [event/day]
F_2 = 1 [%] = 0.01
F_3 = 100 [%] = 1 (worst case assumption)
F_4 = 1 [% bioavailability] = 0.01 (Schaefer et al. 1966; Worst Case for High Molecular Weight carboxylates; see section 5.1.3.1)

bw = 60 [kg]

Exp_{sys} (P-AA) = 0.0147 µg/kg bw/day

5.1.3.5 Oral ingestion of substance residues on dishes and eating utensils

Machine dishwashing powder and tablets contain up to 0.5 % of polyacrylates. Thus, residual P-AA may remain on dishes and eating utensils after cleaning and may be ingested upon migration into food and drink. According to A.I.S.E. (2002) the maximum amount of detergent used per wash is 50 g. A typical dishwashing programme consists of three to four wash-cycles using approximately 4.3 l water each. After each wash-cycle the washing liquor is pumped off and only 0.2-0.3 l remain (Bauknecht GmbH, 2002).

Based on the given data, the P-AA concentration is 58 mg/l during the first cycle. In the remaining washing liquor after the pumping-off process, 17.4 mg P-AA remain in the dishwashing machine. The P-AA concentration is decreased to 0.25 mg/l assuming three wash-cycles during which 0.3 l is left after pumping-off of the washing liquor and 4.3 l of fresh water are added.

0.55 µl of liquor remain on a surface of 1 cm^2 at the end of the wash process (O. J. France, 1990). Thus, a P-AA load of 0.14 x 10^{-6} mg/cm^2 can be calculated. The systemic oral exposure can then be determined according to the following algorithm (HERA Guidance Document 2002):

Exp_{sys} (P-AA)= F_1 x $C'_{P\text{-}AA}$ x S x F'' x F_9/bw= **1.2 * 10^{-2} µg/kg bw /day**

The terms are defined with the following values:

F1 = (weight fraction of substance in product; not used, already included in $C'_{P\text{-}AA}$)
$C'_{P\text{-}AA}$ = 0.14 x 10^{-6} mg/cm^2 (substance load)
S = 5,400 cm^2 (surface area of dishes/eating utensils used per day, (O. J. France, 1990)
F'' = 1 (weight fraction of substance transferred from article and ingested; it is assumed that all of the substance present on the article is transferred to food or drink and ingested)
F9 = 1 (weight fraction absorbed)
bw = 60 kg

5.1.3.6 Inhalation of detergent dust during washing processes

Fabric washing powders are manufactured to rigorous specifications of particle size, enhanced by the exclusion of particles small enough to be inhaled into the lungs. Tests on fabric washing powders over many years have shown a very low level of dust in these products and, within the dust, the level of respirable particles is extremely low and therefore negligible. According to van de Plassche et al. (1999), studies indicate an average exposure of about 0.27 µg of dust per cup of product used for machine laundering, of which up to **0.5% eq. 0.0014 µg/use** is P-AA.

For the estimated systemic dose (60 kg bw) can be calculated:

Exp/use = 0.000023 µg/kg bw P-AA

On average one use per day is estimated, therefore the values for the daily exposure apply.

5.1.3.7 Oral route via drinking water containing polycarboxylates

As detailed in Chapter 4.1.1 in Tables 5, an elimination of up to 25 % of P-AA during the process of waste water treatment was estimated. Additional potential elimination during drinking water preparation was not accounted for. Therefore the values presented below are worst case assumptions based on the $C_{groundwater}$ values according to TGD Part I, appendix III, Table 3. In the course of the HERA environmental risk assessment of polycarboxylates, a $C_{groundater}$ of 0.318 mg/l for P-AA was calculated in drinking water under the (worst case) assumption that only surface water is used for processing. In this calculation the HERA and EUSES scenarios are identical.

Taking into account the uptake of 2 l drinking water per day (WHO, 1996) the following doses can be calculated:

$Exp_{sys\ (oral\ route)}$ (P-AA) = 318 µg/l x 2 l/day/60 kg bw
= 10.6 µg/kg bw/day

This is a worst case scenario with the assumption that only surface water contributes to drinking water.

5.1.3.8 Accidental or intentional overexposure

Accidental or intentional overexposure to polycarboxylates may occur via laundry detergents. As this product may contain up to 0.5% of P-AA, this source of exposure is marginal.

We know no fatal cases arising from oral uptake of polycarboxylates. The accidental or intentional overexposure to polycarboxylates directly is not considered a likely occurrence for consumers, but it may occur via laundry detergents. The German Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV, 1999) recently published a report on products involved in poisoning cases. No fatal case of poisoning with detergents was reported in this publication. Detergent products were not mentioned as dangerous products with a high incidence of poisoning.

Equally, in the UK, the Department of Trade and Industry (DTI) produces an annual report of the home accident surveillance system (HASS). The data in this report summarizes 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 there being 43 and 50 cases, respectively, no fatalities were reported either.

5.1.3.9 Total Exposure

In the unlikely event of maximum worst case exposure from all sources the total exposure to P-AA from their use in household cleaning products would be 7 µg/kg bw/day.

The individual sources of exposure leading to the overall exposure are summarized in Table 13:

Table 13: Worst case exposure estimates from different consumer contact scenarios

Task	Worst case exposure estimate [µg/kg bw/day]
	P-AA
Direct skin contact via hand-washed laundry	0.165
Direct skin contact from pre-treatment of laundry	4.2
Indirect skin contact from wearing laundered clothes	0.0147
Inhalation of laundry powder dust	2.3×10^{-5}
Indirect oral exposure from dish washing	1.2×10^{-2}
Oral exposure from drinking water	10.6
Total exposure	**6.9 µg/kg bw/day**

5.2 Hazard Assessment

5.2.1 Summary of the available toxicological data

In the following data, reliability has been assigned according to the criteria defined by Klimisch et al. (1997), as outlined in the HERA Guidance Document (2002).

5.2.1.1 Acute Toxicity

5.2.1.1.1 Acute Oral Toxicity

Studies reporting the acute oral toxicity of the homopolymers at the highest doses tested are summarised in table 14. Throughout the studies, the acute oral toxicity of the homopolymers with MW 1,000- 78,000 is very low.

In rats the reported LD_{50} values range between 1000-10,000 mg/kg bw. The LD_{50} of >1000 mg/kg bw is due to the attainable limit dose of a 10% aq. solution in this study (Hicks, 1989). LD_{50} rat for P-AA1,200; P-AA2,500; P-AA8,000 is > 5,000 mg/kg bw. Animals of both sexes showed sedation, curved body position and ruffled fur during the first 5 h after oral administration. All rats recovered within 2 days after dosing and survived until necropsy. No macroscopic organ changes were observed in 8 rats, whereas 2 rats showed dark-red mottled lungs in the study with P-AA2,500 and P-AA8,000 (BASF, 1986).

Table 14: Summary table of the acute oral toxicity tests with homopolymers (P-AA)

Mean MW	Test species	Test Substance	LD_{50} [mg/kg bw]	Reliability	Reference
1,000	Rat	No data	LD_{50} > 5,000	2	Rohm & Haas, 1982
1,200	Rat	45% aq. solution	LD_{50} > 5,000	2	BASF, 1986 c
2,500	Rat	45% aq. solution	LD_{50} > 5,000	2	BASF, 1986 d
3,500	Rat	10% aq. solution	LD_{50} > 1,000	2	Hicks et al., 1989
4,500	Rat	No data	LD_{50} >5,000	4	Freeman et al., 1993

Mean MW	Test species	Test Substance	LD_{50} [mg/kg bw]	Reliability	Reference
8,000	Rat	45% aq. solution	LD_{50} > 5,000	2	BASF, 1986 e
15,000	Rat	undiluted	LD_{50} > 10,000	2	BASF 1978
70,000	Rat	40% aq. solution	LD_{50} > 10,000	2	BASF, 1976
78,000	Rat	No data	LD_{50} > 10,000	2	Degussa, 1983 a

MW Molecular Weight (g/mol)
Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

5.2.1.1.2 Acute Dermal Toxicity

The dermal LD_{50} in 2 rabbits using an occluded patch protocol was > 5,000 mg/kg body weight. Well defined erythema without oedema was noticed on day 1 with recovery by the second day. No mortality did occur (Rohm & Haas, 1982). No deaths were reported in the study with P-AA1, 000 (Rohm & Haas, 1982)

Table 15: Summary table of the acute dermal toxicity tests with homopolymers (P-AA)

Mean MW	Test species	Test Substance	LD_{50} [mg/kg bw]	Reliability	Reference
1,000	Rabbit	undiluted	LD_{50} > 5,000	2	Rohm & Haas, 1982
4,500	Rabbit	undiluted	LD_{50} > 5,000	4	Freeman et al., 1993
4,500	Rabbit	undiluted	LD_{50} > 5,000	2	Rohm & Haas, 1982

MW Molecular Weight (g/mol)
Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

Conclusion

Homopolymers with molecular weights ranging between 1,000 and 78,000 have a low acute oral toxicity. One study seemingly indicating a higher toxicity was tested as a 10% aqueous solution and therefore did not excede an effective concentration of 1000 mg/kg bw as limit dose. The data on acute dermal toxicity also indicate low acute dermal toxicity to rabbits.

5.2.1.1.3 Acute Inhalation Toxicity

Data on acute inhalation toxicity for P-AA are not available.

5.2.1.2 Skin Irritation

Several skin irritation studies on rabbits were investigated with P-AA of different molecular weights (1,000-78,000), concentrations between 15-45% or neat undiluted material (Table 16). Exposure was for 4 h -24 h with occlusive or semi-occlusive dressing. All studies show no skin irritation potential.

Table 16: Summary table of the skin irritation data of homopolymers (P-AA)

Mean MW	Test species	Test Substance	Result	Reliability	Reference
1,000	Rabbit	undiluted	Not classifiable as irritating	2	Rohm & Haas, 1982
1,200	Rabbit	45% aq. solution	Not classifiable as irritating	2	BASF, 1986 f
2,500	Rabbit	45% aq. solution	Not classifiable as irritating	2	BASF, 1986 g
No data	Rabbit	15% aq. solution	Not classifiable as irritating	4	Finnegan, 1953
4,500	Rabbit	undiluted	Not classifiable as irritating	4	Freeman et al., 1993
4,500	Rabbit	undiluted	Not classifiable as irritating	2	Rohm & Haas, 1982
8,000	Rabbit	45% aq. solution	Not classifiable as irritating	2	BASF, 1986 h
30,000	Rabbit	undiluted	Not classifiable as irritating	2	Rohm & Haas, 1988
70,000	Rabbit	40% aq. solution	Not classifiable as irritating	2	BASF, 1976
78,000	Rabbit	No data	Not classifiable as irritating	2	Degussa, 1983 b

MW Molecular Weight (g/mol)
Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

Three studies conducted in compliance with OECD Guideline 404 (4 h exposure, but occlusive dressing) with molecular weights of 1,200; 2,500; and 8,000, respectively, reflect the non- irritating potential. In all three studies the test substance was applied as a 45% solution to the intact skin (BASF, 1986 f; g; h).

Further studies with homopolymers of molecular weight 4,500; 70,000 and 78,000 were conducted neither in compliance with OECD Guideline 404 nor with GLP regulations, but they support indications of the non-irritating effect on skin.

Conclusion

None of the homopolymers tested either as undiluted neat substances or at very high concentrations have been reported to be irritating to the skin.

5.2.1.3 Eye Irritation

Three eye irritation studies with P-AA of molecular weight 1,200; 2,500 and 8,000, respectively, using a 45% aq. solution were conducted with rabbits according to OECD Guideline 405 (BASF 1986), but not according to GLP. The eyes were examined after 1, 24, 48 and 72 h after test substance administration (Table 17).

Table 17: Summary table of eye irritation data with homopolymers (P-AA)

Mean MW	Test species	Test Substance	Result	Reliability	Reference
No data	Rabbit	No data	irritating	4	Bottari, 1978
No data	Rabbit	No data	irritating	4	Finnegan, 1953
1,000	Rabbit	No data	Not classifiable as irritating	2	Rohm & Haas, 1982
2,500	Rabbit	45% aq. solution	Not classifiable as irritating	2	BASF, 1986 k
1,200	Rabbit	45% aq. solution	Not classifiable as irritating	2	BASF, 1986 j
4,500	Rabbit	undiluted	Not classifiable as irritating	2	Rohm & Haas, 1982
4,500	Rabbit	undiluted	Not classifiable as irritating	4	Freeman et al., 1993
8,000	Rabbit	45% aq. solution	Not classifiable as irritating	2	BASF, 1986 l
70,000	Rabbit	40% aq. solution	Not classifiable as irritating	2	BASF, 1976
70,000	Rabbit	No data	Not classifiable as irritating	2	ECETOC, 1993
78,000	Rabbit	No data	Not classifiable as irritating	2	Degussa, 1983 c

MW Molecular Weight (g/mol)
Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

In studies with P-AA1,200 and P-AA2,500 all animals showed moderate to severe discharge within 1 h, which was completely reversible after 24 h. With the exception of one female animal treated with P-AA1,200 that still showed slight discharge 24 h after application, however, the symptoms were reversible 48 h after treatment. The test substance is classified as not irritating to the eye (BASF, 1986 j, k). Similarly, evidence of slight eye irritation was observed for P-AA4,500, which is based on the conjunctiva effects at 24 h with recovery after 72 h. P-AA8,000 with slight discharge in the first hour after application and recovery after 24 h indicates a non-irritant potential (BASF, 1986 l).

Two non-OECD protocol studies with P-AA of high molecular weight of 70,000 and 78,000 were also slightly irritant to the rabbits' eyes with recovery after 72 h and 24 h, respectively (ECETOC, 1993; Degussa 1983).

Conclusion

Homopolymers tested either as undiluted neat substances or at very high concentrations show a non- to slight irritation potential to the rabbit.

5.2.1.4 Sensitisation

P-AA4,500 and P-AA78,000 have been demonstrated to be non-sensitisers in the Magnusson and Kligman Guinea Pig Maximisation test. A concentration of 5% P-AA4,500 has been used as induction and challenge dose (Rohm & Haas, 1988) (Table 18).

Table 18: Summary table of sensitisation data with homopolymers (P-AA)

Mean MW	Test species	Test Method	Result	Reliability	Reference
4,500	Guinea pig	Maximisation test	Not sensitising	2	Rohm & Haas, 1988
78,000	Guinea pig	Maximisation test	Not sensitising	4	Henkel, 1990

MW Molecular Weight (g/mol)
Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

P-AA78,000 has been tested as a 0.1% aqueous solution (0.1 ml intra-dermal) as one of the induction doses and as a 20% aqueous solution (0.2 ml) as the occluded patch induction dose. This was applied for 48 h. After the appropriate period, all animals received a challenge dose of 0.2 ml of a 2.5% solution of the test compound as a single occluded patch administration for 24 h. No skin reactions were observed in the test group or in the control group (Henkel, 1990). In both studies no reactions were observed.

Conclusion

P-AA showed no sensitising potential when tested in the GPMT as a low or high molecular weight polymer.

5.2.1.5 Repeated Dose Toxicity

Table 19: Summary table of the repeated dose toxicity tests with P-AA

Mole-cular Weight	Test species	Duration	Route	Estimated NO(A)EL	Doses	Reliability	Reference
2,500	Rat	4 weeks	Oral feed	NOAEL = 1136 mg/kg bw/d	1136 mg/kg bw/d	2	Unilever 1993
4,500	Rat	91 days	Inhalation	NOEC $_{lung}$ = 0.2 mg/m^3 NOEC $_{syst.}$ = 5 mg /m^3	0.2, 1.0, 5.0 mg /m^3	2	Procter & Gamble, 1991
No data	Rat	4 weeks	Inhalation	NOAEC = 4 mg/m^3 LOAEC= 21 mg/m^3	1.75, 4, 21 mg/m^3	4	Tansy, 1988
No data	Rat	4-13 weeks	Inhalation	NOAEC =14 mg/m^3 LOAEC = 56 mg/m^3	14, 56, 134,or 275 mg/m^3	4	Baldwin, 1986

MW Molecular Weight (g/mol)
Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

5.2.1.5.1 Inhalation route

P-AA4,500 has been tested in a 91 d inhalation study (Table 19). The study was conducted in compliance with the guidelines for the EPA's Toxic Substances Control Act and in

compliance with the EPA GLP Regulations (40CR, Part 792). 25 male and 25 female rats were exposed to 0.2, 1.0 and 5.0 mg /m^3 of the polymer for 6h/d, 5 d/wk for 13 weeks. The substance was administered as a dust aerosol. Ten animals/group were allowed to recover for a period of a further 91 days. Body and organ weights, food and water consumption, clinical observation and blood chemistry were all within the normal range. Histopathology of lung tissues from the animals necropsied after the last exposure revealed signs of mild pulmonary irritation based on at least one of the following local lung effects: increase in polymorphonuclear granulocytes or alveolar macrophages, pneumocyte hyperplasia, alveolar wall thickening and focal alveolitis in the animals exposed to 1 and 5 mg/m^3 of P-AA4,500. Histopathological examination of the animals in the recovery group showed no lasting or residual microscopic lesions, which could be considered treatment-related. From these studies it was concluded that the NOEC is 0.2 mg/m^3 for respirable dust of P-AA4,500 for local lung effects typical of insoluble respirable polymer dust (Procter & Gamble, 1991) whereas the NOEC for systemic effects was above 5 mg/m^3.

Supporting data on local lung effects with respirable dust of P-AA with unknown molecular weight are reported. The only evidence of toxicity in rats exposed to powdered P-AA at atmospheric concentrations of 1.75, 4 or 21 mg/m^3 for 6 h/d, 5 days/wk for 4 weeks, was a reversible effect on lung function in the top-dose females. Growth, organ weights and blood biochemistry were all normal, and microscopic examination of the tissues of the lungs, livers, kidneys, reproductive organs and blood system revealed no abnormalities (Tansy, 1988).

Rats exposed for 6 h/d, 5 days/wk, for 4 or 13 weeks to a test substance described as "non-ionic acrylic polymer dust" at concentrations of 14, 56, 134 or 275 mg/m^3 developed cellular changes in the lungs and increased lung weights at 56 mg/m^3 and at the higher concentrations. The investigators concluded that the responses were those expected from the inhalation of an excessive amount of an insoluble respirable dust (Baldwin, 1986).

5.2.1.5.2 Oral route

P-AA2,500 has been tested in a Non-Guideline study with substance application via oral feed for 28 days to examine the effect of the test substance on mineral homeostasis (Unilever, 1993) (Table 19). Six male rats were fed 2.5% of the test substance in the diet (about 1136 mg/kg bw/d). Growth, weight and appearance of the animals were normal throughout the study. In the last week, a small but significant decrease in the total weight of bone minerals was detected and confirmed by radiographic and histological examination. The concentration of magnesium in the bones and the plasma of the treated animals were significantly decreased. Calcium loss was slight and not statistically significant. Urinary excretion of sodium and phosphorus was markedly increased. Excretion of calcium was slightly increased. The result was interpreted by the authors to be due to a metabolic or nutritional imbalance rather than to a systemic toxicity. The excretion of sodium might have been increased by the high uptake of the sodium-neutralized test substance. The applied dose was therefore interpreted as a NOAEL.

5.2.1.5.3 Dermal route

For repeat dose dermal exposure no data are available for P-AA.

Conclusion

Table 20

Test Substance	Duration	Route of Exposure	Species	NOAE(L)C_{syst}	NOAE(L)C_{local}
P-AA2,500	4 wks	Oral feed	Rat	1,136 mg/kg bw/d	
P-AA4,500	13 wks	Inhalation	Rat	5 mg/m^3	0.2 mg/m^3

The similar acute oral and dermal toxicities of P-AA are suggestive that, for an approximate risk assessment, the repeat dose oral toxicity of P-AA can serve as a substitute – even as a worst case – for a potential dermal toxicity of P-AA upon repeated exposure.

5.2.1.6 Genotoxicity

5.2.1.6.1 In vitro

Table 21: Summary table of the genotoxicity in vitro of P-AA

Mean MW	Test system	Test Substance	Metabolic Activation	Result	Reliability	Reference
1,500-2,500	Cytogenetic Assay	No further data	No further data	positive[1]	4	Medvedev A. I., 1980
2,000	Ames	54% aq. solution	With and without	negative	2	Thompson, 1989
2,000	Mouse Lymphoma Assay	54% aq. solution	With and without	negative	2	Thompson, 1989
2,000	Unscheduled DNA synthesis	54% aq. solution	Without	negative	2	Thompson, 1989
4,500	Ames	48% aq. solution	With and without	negative	2	Thompson, 1989
4,500	Mouse Lymphoma Assay	48% aq. solution	With and without	negative	2	Thompson, 1989
4,500	Unscheduled DNA synthesis	48% aq. solution	Without	negative	2	Thompson, 1989
4,500	Cytogenetic assay (CHO)	48% aq. solution	With and without	negative	2	Thompson, 1989
4,500	Ames	No data	No data	negative[1]	4	Freeman et al., 1993
4,500	Mammalian cell gene mutation assay	No data	No data	negative[1]	4	Freeman et al., 1993
4,500	Unscheduled DNA synthesis	No data	No data	negative[1]	4	Freeman et al., 1993

MW Molecular Weight (g/mol)
Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

[1] Due to inadequate data reporting this result is not assignable with respect to its reliability

Ames Tests

The results obtained in studies with adequate validity do not suggest a genotoxic potential of the polymers tested.

Chromosome aberrations in cultured mammalian cells

Preliminary range finding cytotoxicity tests were performed to determine the effect of the test material on cell survival.

Neutralised test substances of aqueous solutions containing 48-54% P-AA2,000 have been tested for clastogenic activity using CHO cells. Cells were treated for 4 h in the presence and absence of S9 mix followed by 16 hrs in compound medium free of test substance. The test was conducted at concentrations up to 77 µl/ml in the presence and absence of S9 mix. Single cultures were used. No increases in chromosome aberrations were detected with either substance (Thompson et al., 1989).

Unscheduled DNA Synthesis

Neutralised test substances of aqueous solutions containing 45-54% P-AA2,000 and P-AA4,500 have been tested for induction of UDS (Unscheduled DNA Synthesis) in primary rat hepatocytes following the methods described by Williams et al. (1977). P-AA2,000 was tested to a maximum concentration of 5 µl/ml and P(AA)4500 to a maximum of 20 µl/ml. Both test substances showed appreciable toxicity at the highest concentrations tested. No evidence of UDS was observed (Thompson et al, 1989).

Conclusion in-vitro

Tests performed to determine the potential of these polymers to induce DNA damage in-vitro (Ames test and Induction of Unscheduled DNA Synthesis) were negative.
Similarly, a negative result was obtained when testing for the potential to induce chromosomal aberrations in-vitro.

5.2.1.6.2 In vivo

Micronucleus assay

P-AA2,000 has been tested in a mouse micronucleus assay using groups of 5 male and 5 female mice. The test substance or sterile distilled water (control vehicle) was administered by gavage at a volume of 20 ml/kg. Animals were dosed by gavage with the maximum tolerated dose (13,850 mg/kg bw) and observed over a 3-day period. Positive control animals were i.p. injected with mitomycin C that was prepared in sterile 0.9% saline at a concentration of 0.2 mg/ml. Animals were killed at 24, 48 and 72 h after dosing, bone marrow cells were harvested and 1,000 cells per animal were examined for micronuclei in polychromatic erythrocytes and also for the ratio for polychromatic to normochromatic erythrocytes. During the experiment 3 female mice died, 1 at each of the harvest times. Clinical signs of piloerection, hunched posture and lethargy were observed following dosing.

No increase in micronucleus induction was observed in the groups administered the test substance at any of the harvest times, when compared with the controls (Thompson et al., 1989).

Conclusion in-vivo

The negative test results obtained *in-vitro* for induction of DNA damage and chromosomal aberrations were corroborated with a test for chromosomal aberrations *in-vivo*. As no positive *in-vitro* evidence for a DNA damaging potential exists no further testing for induction of DNA damage *in-vivo* was performed.

5.2.1.7 Carcinogenicity

No studies on carcinogenicity are available for P-AA. P-AA is, however, devoid of any genotoxic potential in-vitro and in-vivo. P-AA did not show cellular hyperplasias in the available repeated dose toxicity studies. As acrylic homopolymers for detergent applications are manufactured to rigorous specification of particle size and exclusion of inhalable particles and as no long high dose inhalative exposure is anticipated from handling and use patterns in detergent application, especially in the absence of spray applications, a carcinogenic risk appears to be negligible.

Furthermore, the monomers are devoid of alerting groups for a genotoxic or carcinogenic potential.

5.2.1.8 Reproduction, Embryotoxicity, Developmental Toxicity

Table 22: Summary table of developmental toxicity data for P-AA

Mean MW	Test Species	Route	Test Substance	Doses [mg/kg]	NO(A)EL (mg/kg)	Reliability	Reference
4,500	Rat	Gavage	43.3 % aq. solution	500 ; 1,000 ; 3,000	M: >= 3,000 T: >= 3,000	2	Nolen, 1989
90,000	Rat	Gavage	77.5 % aq. solution	125; 375; 1,125	M: >= 375 T: >= 1,125	2	Nolen, 1989

M= Maternal toxicity, T= Teratogenicity
MW Molecular Weight (g/mol)
Reliability criteria of IUCLID according to Klimisch et al. (1997) are used:
1 valid without restriction 2 valid with restriction 3 not valid 4 validity is not assignable

P-AA4,500 was tested in a rat developmental toxicity study in which the compound was administered by gavage on day 6-15 of pregnancy at dose levels of 500; 1,000; and 3,000 mg/kg bw/day. No treatment related effects on foetal development or on pregnancy were noted. There were no significant differences in the body weight changes or feed intakes during pregnancy, the rats treated with 3,000 mg/kg of the test substance had soft or liquid stools during the treatment period. The NOEL was 3,000 mg/kg bw/day (Nolen, 1989).

P-AA90,000 was administered during the period of organogenesis. Groups of 28 or 29 rats were administered the test substance (77.5% aq. solution) at dose levels of 125; 375 and 1,125 mg/kg/d or vehicle (distilled water) by gavage. An additional group served as untreated control group. Conception was considered day 0 of pregnancy. 8 females/group were treated from day 6 to 13 of gestation and were killed on day 13 of gestation; the remaining animals in each group were sacrificed on day 19. Two-thirds of the foetuses were examined for visceral findings by the Wilson (1965) method and one-third was cleared and stained for skeletal examinations according to Dawson (1926). One mid-dose dam and 6 high dose dams died during the study, however four of these deaths were due to a technical error (malintubation), while 3 high-dose deaths were interpreted to be treatment-related. No data have been reported, however, as to significant pathological or clinical findings in these animals. No statistically significant differences were seen in maternal body weights, body weight gains or overall food intake. The only substance-related effect was a transient decrease in food consumption in high-dose dams during days 7-9 of gestation. The test substance administration had no effect on embryo or foetal viability. Examination of the foetuses revealed no significant embryotoxic effects or differences in the incidence of soft-tissue and/or skeletal abnormalities between treated and control groups. The NOEL for maternal toxicity was 375 mg/kg bw/d and that for developmental toxicity was 1,125 mg/kg bw (Nolen, 1989).

Conclusion

None of the P-AAs tested showed developmental toxicity or embryotoxic effects in rats.

In a ninety one days repeat dose study with substance application via inhalation no effects on the reproductive organs of the test animals were reported for P-AA.
From these observations a reprotoxic potential appears negligible.

5.2.1.9 Additional Endpoints

No data on toxicokinetics are available.

5.2.2 Critical Endpoints

5.2.2.1 Overview on hazard identification

Polyacrylates are of low acute oral toxicity. No mortalities were seen even when testing to the highest attainable doses. Typically the LD50 values in rats are above 5,000 to 10,000 mg/kg bw for molecular weights ranging from 1,000 to 78,000 g/mol.

The acute dermal toxicity determined for polyacrylates in the rabbit was likewise very low with an LD50 of > 5,000 mg/kg bw for substances with a molecular weight of 1,000 to 4,500.

Due to the typical high molecular weights of P-AA it can be safely assumed, however, that percutaneous penetration is very low to non-existent so that low dermal toxicity can be expected also for other species.

Data on acute inhalative toxicity are not available. In the absence of any spray application products with P-AA, inhalative exposure with these products is confined to the handling of fabric washing powders which have a very low level of respirable dust particles due to rigorous product specification (see chapter 5.1.3.6). Hence, no human health issues are to be expected.

Skin irritation studies in rabbits with P-AA in the molecular weight range from 1,000 to 78,000 at high concentrations have shown that these substances are essentially not irritating.

Eye irritation studies in rabbits have revealed, at most, slight irritation which, however, was reversible within the observation period. Therefore the effects were assessed as being not classifiable as irritating.

P-AA have been demonstrated to be not skin sensitising on the basis of independent studies performed with P-AA4,500 and P-AA78,000 in the guinea pig maximization test (GPMT).

Two P-AA with molecular weight of 2,500 and 4,500 have been tested in repeat dose studies via oral feed and inhalation as dust aerosols. Exposure times were from 4 – 13 weeks.

Oral exposure of rats via feed of P-AA2,500 in a non-guideline study led to a NOAEL of about 1136 mg/kg bw/day. In this study an increased excretion of bone minerals (Magnesium, phosphorus, some Calcium) was observed and interpreted as metabolic or nutritional imbalance. In view of the proven metal ion binding capacity of P-AA this result comes not unexpected. It can, however, be interpreted as an unrealistic high dose exposure scenario.

The study confirms a low repeat dose toxicity by the oral route.

P-AA tested by inhalative exposure for 4 to 13 weeks with dust aerosols have shown some local effects in the lung which can be attributed, however, to the typical nuisance dust effects observed which are also observed with other inert respirable dusts. Available data show that these effects have been reversible in the post exposure period.

Systemic toxicity in these studies was not observed up to the maximal concentration of 5 mg/m^3 tested in these studies.

P-AA are not considered to be mutagenic or genotoxic. P-AA does not possess structural elements alerting to genotoxicity and carcinogenicity. A number of studies have been

performed in-vitro in the Ames test and with mammalian cell cultures and in-vivo and have excluded the potential to induce DNA damage and chromosomal aberrations.
Though there are no carcinogenicity studies available there are no alerts which would lead to suspect a carcinogenic potential.

P-AA with molecular weights of 4,500 to 90,000 has been tested for developmental toxicity in rats. No significant embryotoxicity or developmental toxicity was detected in these studies. Furthermore, in a subchronic inhalation study in rats no substance related impairment of the reproductive organs was detected. Therefore, though results on guideline compliant reprotoxicity studies are not available, reprotoxic effects are not expected.

5.2.2.2 Rationale for identification of critical endpoints

Dermal exposure is the main exposure route for consumers and subsequently, dermal effects such as skin irritation and sensitisation as well as long term dermal toxicity must be considered for the human health risk assessment. Pertinent data are available addressing skin irritation and skin sensitisation potential of P-AA containing consumer product formulations. As high molecular weight polymers these substances are expected to have a low to non-existing potential to penetrate the intact skin to become systemically available. The available oral studies involving repeated exposures have shown a similar toxicity profile as compared to dermal exposure and therefore can be used to assess potential human exposure via the dermal route.

5.3 Risk Assessment

5.3.1 Margin of Exposure Calculation

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. For P-AA, a NOAEL of 1136 mg/kg bw/day from a 28-d oral feed study (Unilever 1993) was determined in rats.

NO(A)ELs for MOE Calculations:

— NOAEL rat, oral feed, 28 d study: **1,136 mg/kg bw/d for P-AA**

5.3.1.1 Exposure scenario: direct skin contact by hand-washed laundry

For calculation of the MOE for P-AA, the NOEL of **1,136** mg/ kg bw/d from the 28 day rat oral feed study was divided by the daily systemic dose of 4.4 µg/kg bw/d, taking into account an aggregate worst case scenario of skin contact with laundry detergent, including garment manual pretreatment (cf. section 5.1.3.1 & 5.1.3.2).

P-AA: $MOE_{\text{direct skin hand-washed laundry}}$ = 1136,000/4.4 = **2.5×10^5**

5.3.1.2 Exposure scenario: indirect skin contact wearing clothes

For calculation of the MOE for P-AA, the NOAEL of 1,136 mg/ kg bw/d from the 28 day rat oral feed study was taken as a worst case substitute and divided by the daily systemic dose of 0,0147 µg/kg bw/d.

P-AA: $MOE_{\text{indirect skin contact wearing clothes}}$ = 1136,000/0.0147 **= 7.7×10^7**

5.3.1.3 Exposure scenario: oral route from residues on dishes and eating utensils

For calculation of the MOE, the NOAEL of 1,136 mg/ kg bw/ day of P-AA were divided by the daily systemic dose of 1.2 x 10^{-2} and 7.3 x 10^{-2} µg/kg bw/ day, respectively (cf. section 5.1.3.5) .

P-AA: MOE $_{\text{oral route from residues on dishes and eating utensils}}$ = 1136,000/0.012 = **9.5×10^{7}**

5.3.1.4 Exposure scenario: oral route via drinking water containing P-AA

For calculation of the MOE, the NOEL of 1,136 mg/ kg bw/ day was divided by the daily systemic dose of 10.6 µg/kg bw/ day for the uptake of P-AA from drinking water.

P-AA: **MOE** $_{\text{oral route via drinking water}}$= 1136,000/10.6 = **$10.7 \times 10^{4}$**

5.3.1.5 Exposure scenario: inhalation of dust during washing process

The systemic dose of P-AA via inhalation of detergent dust during the washing process was estimated to amount to 2.3 x 10^{-5} µg/ kg bw/ day for P-AA.

In rats the adverse effect after repeated inhalation dosing (91-d/rat) was a mild, reversible pulmonary irritation. This effect was considered as not substance-related owing to the physical property of the respirable dust, which caused local and not systemic lung effects. Nevertheless, in a worst case scenario, the NOECs of 0.2 mg/m^3 for P-AA is taken forward into a Margin of Exposure calculation under the assumption of a ten percent deposition into the lung and a 100% absorption of the deposited material.

For **P-AA** a daily exposure to the NOEC of 0.2 mg/m^3 would lead to a hypothetical systemic dose of 0.2 [NOEC; mg/m^3] x 10^{-3} [Conversion m^3 to Litre] x 0.2 [Litre/min; Respiratory Minute Volume] x 60 [min] x 6 [hours/d; exposure duration per day] x 0.1 [10% deposition in the lung] / 0.3 [kg bw; rat] = 0.0048 mg / kg bw/ day (basic data according to Snipes et al, 1989). For the calculation of the MOE this value is divided by the estimated daily consumer exposure to laundry detergent dust (cf. section 5.1.3.6).

Under these assumptions the resulting MOE for inhalative exposure is calculated as follows:

P-AA: **MOE** $_{\text{dust inhalation}}$ = 0.0048 x 10^{3}/ 2.3 x 10^{-5} = **2×10^{5}**

5.3.1.6 Exposure scenario: oral ingestion via case of poisoning and accidental contact with the eyes

Accidental ingestion of milligrams of polycarboxylates as a consequence of accidental ingestion of laundry and cleaning products is not expected to result in any significant adverse health effects, given the low toxicity profile of laundry and cleaning products in general. Furthermore, the poison centres in Germany have not reported a case of lethal poisoning with detergents containing polycarboxylates.

Accidental contact of polycarboxylates with the eyes is not expected to cause more than a slight irritation on the basis of the experimental data.

5.3.1.7 Total Consumer Exposure

The consumer exposure via direct and indirect skin contact and via the oral route from residues on dishes and eating utensils and in drinking water are discussed separately:

Exposure by skin contact:

P-AA: (0.165 $_{\text{Hand washed laundry}}$ + 4.2 $_{\text{pretreatment laundry}}$ + 0.0147 $_{\text{wearing clothes}}$) [µg / kg bw/day]
= 4.4 µg/ kg bw/ day

P-AA: MOE $_{\text{skin contact}}$ = 1136,000/ 4.4 = **2.5×10^5**

Exposure by ingestion:

P-AA: (0.012 $_{\text{residues on dishes}}$ + 10.6 $_{\text{drinking water}}$) [µg / kg bw/day]
= 10.62 µg/ kg bw/ day

P-AA: MOE $_{\text{ingestion}}$ = 1136,000/ 10.62 = **10.69×10^4**

Inhalative dust exposure was not included in the calculation, as due to the specifications of particle size during manufacture no inhalable dusts are expected. Furthermore, due to the very low exposure to (non-inhalable) dust per application (see chapter 5.1.3.6) the change in the Total Consumer Exposure would not be numerically significant.

5.3.2 Risk Characterisation

Assessment of the contact scenarios revealed only remote consumer exposure to homopolymers via intended use of polycarboxylate-containing products. As a result, the MOEs for the total estimated systemic dose of homopolymers are very high

(P-AA: **$MOE_{\text{skin contact}} = 2.5 \times 10^5$**; **$MOE_{\text{ingestion}} = 10.69 \times 10^4$**; **$MOE_{\text{inhal}} = 2 \times 10^5$**)

and thus of no concern to human health. Furthermore, accidental exposure or intentional overexposure does not imply risk owing to the very low acute toxicity of both substances.

It can be concluded that P-AA in consumer washing and automatic dishwashing detergents are not considered to cause any risk to human health.

5.3.3 Summary and Conclusion

The polycarboxylate P-AA is widely used in laundry detergents (regular and compact powder) and dishwashing tablets. Thus, consumers are exposed to P-AA mainly via the dermal route by direct contact via hand-washed laundry and indirect contact via wearing clothes. Furthermore consumers are orally exposed to P-AA through residues remaining on eating utensils and dishes after running a typical dishwashing programme.

P-AA has a very low toxicity after oral or dermal application. In both routes of exposure, the LD_{50} is greater than 2,000 mg/kg bw/day in experimental animals. P-AA shows no skin-irritating potential on the one hand, but has a non- to slight eye-irritating potential on the other hand. Beyond that, there is no indication that P-AA is skin sensitising. Local dermal effects due to direct skin or indirect skin contact with P-AA-containing solutions in hand-washed laundry are not of concern because P-AA is not a contact sensitizer and is not expected to be irritating to the skin.

The adverse effect after repeated inhalation dosing (91d/rat) was a mild, reversible pulmonary irritation. This effect is considered as not substance-related owing to the physical property of the respirable dust created for this kind of study which caused local lung effects. Nevertheless, in a worst case scenario, the local NOEC of 0.2 mg/m^3 for P-AA was taken

forward into a Margin of Exposure calculation under the assumption of a ten percent deposition into the lung and a 100% absorption of the deposited material.

No studies are available on carcinogenicity. However, in the absence of genotoxicity, the lack of exposure to inhalable dust due to the manufacturing process and with no cellular hyperplasia being reported, no carcinogenic potential is expected for this substance group.

Data on developmental toxicity demonstrate that polycarboxylates are not developmentally toxic in rats.

Evidence from a subchronic study in rats where no effects on the reproductive organs and tissues were detected would further argue against a reprotoxic potential of these polymers.

In summary, based on the available data, the human risk assessment considers the use of polycarboxylates in household laundry products and automatic dishwashing detergents as safe and of no concern with regard to consumer use.

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7. CONTRIBUTORS

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