HERA

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

Polycarboxylates used in detergents (Part II)

Polyacrylic/maleic acid copolymers and their sodium salts (CAS 52255-49-9)

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Version 3.0

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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 copolymers in detergent applications covered by HERA was updated to 33,000 tons/year in 2011. The mean molecular weight (MW) of the copolymers P-AA/MA ranges from approximately 12,000 to 100,000. Most investigations have been performed on the most commonly used commercial copolymers with MW of 70,000. 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/MA homopolymers from waste water has been investigated in multiple laboratory studies. The results indicate that P-AA/MA 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 copolymers 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. Polycarboxylates are of low acute toxicity to the rat (LD_{50} > 5 g/kg bw/d). The copolymers (P-AA/MA) show no irritating potential on either target tissue (skin/eye) based on the given data. Further P-AA/MA 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 1.0 mg/m^3 for P-AA/MA 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 no evidence for a genotoxic potential of P-AA/MA using a variety neither 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/MA as 26 µg/kg bw/day. The exposure by oral uptake was estimated for P-AA/MA as 2.36 µg/ kg bw/day.

For P-AA/MA, an MOE of 7.2 x 10^4 is calculated from the NOEL of a 28 d dermal study in rabbits.

The exposure resulting from oral uptake via substance residues on machine washed eating utensils and via drinking water is estimated to amount to approx. 4.21 µg/ kg bw/ day for P-AA/MA. For P-AA/MA based on a NOAEL of 1,871 mg/kg bw/d from a subchronic drinking water study in rats an MOE of 7.9 x 10^5 is established for this scenario.

For inhalative exposure of P-AA/MA, a worst case MOE of 1.7 x 10^5 was calculated 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 copolymers of acrylic acid and maleic acid which are generally used as sodium salts. The various polycarboxylates are distinguished by the monomers used for their preparation, acrylic acid (AA) and maleic anhydride (MA) and their molecular weight (MW).

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

P-AA/MA: copolymers of acrylic/maleic acid and their sodium salts

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

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

CAS No.	CAS Name
29132-58-9	2-Butenedioic acid (Z), polymer with 2-propenoic acid
51025-75-3	2-Butenedioic acid (Z), monosodium salt, polymer with sodium 2-propenoate
51344-35-5	2-Butenedioic acid (Z), sodium salt, polymer with sodium 2-propenoate
60449-78-7	2-Butenedioic acid, disodium salt, polymer with sodium 2-propenoate
60472-42-6	2-Butenedioic acid (Z), polymer with 2-propenoic acid, sodium salt
61842-61-3	2-Butenedioic acid (Z), disodium salt, polymer with 2-propenoic acid
61842-65-7	2-Butenedioic acid (Z), monosodium salt, polymer with 2-propenoic acid
63519-67-5	2-Butenedioic acid (Z), sodium salt, polymer with 2-propenoic acid
112909-09-8	2-Butenedioic acid (Z), disodium salt, polymer with sodium 2-propenoate
126595-54-8	2-Butenedioic acid (Z), polymer with sodium 2-propenoate
52255-49-9	2-Propenoic acid, polymer with 2,5-furandione, sodium salt

The family of linear copolymers P-AA/MA cover different products with a molecular broad range of 12,000 to 100,000. The copolymer mostly used in detergents has a typical molecular weight (MW) of approximately 70,000, which has been taken into account in this HERA risk assessment. The structural formula is shown in figure 1:

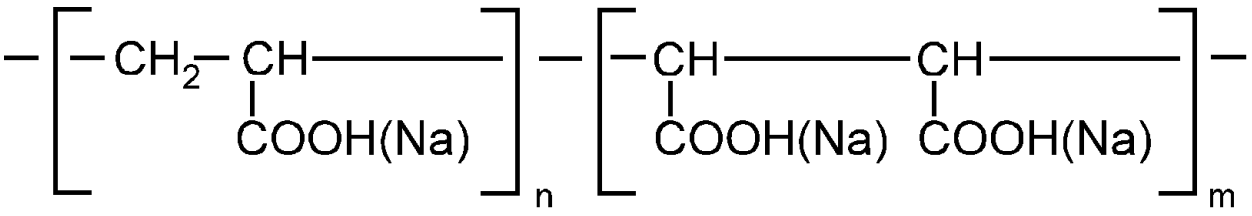

Figure 1: Structure of P-AA/MA

Table 2: Physical-chemical data of P-AA/MA

Parameter	Data	Reliability	Reference
Typical molecular weight (g/mol)	70,000	2	BASF AG, 2002
Molecular weight distribution M_w/M_n *)	app. 10	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, or acrylic acid and maleic anhydride in aqueous solution. The molecular weight is influenced by the reaction conditions such as temperature, concentrations and proportion and nature of initiators. For initiation, peroxides, azo compounds and redox systems such as iron (II) and hydrogen peroxide or sulphite and peroxidisulphate are employed. 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/MA was used for the risk assessment for Europe:

P-AA/MA 33,000 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

Copolymers are used in low-phosphate and phosphate-free detergents for household and industrial and institutional uses for avoiding incrustation and soil redeposition. P-AA/MA is mainly used in laundry detergent powders and tablets but to a low extent in automatic dishwashing detergents, too. A typical concentration of P-AA/MA in these products is approximately 3.0 %.

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 II. 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/MA

In Chapter 4, the available environmental fate including biodegradation and removal data of P-AA/MA (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/MA 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/MA types with different MW are available and summarised in table 4. Although the copolymer with MW of 70,000 is most representative commercial product for P-AA/MA used in detergents, the test results for the other copolymers 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/MA based on CO2 evolution

Mean MW (g/mol)	**Method/Remark**	**Result**	**Reliability**	**Reference**
Water				
12,000	CO_2 Evolution Test, river water, ^{14}C tagged	A: 21 % CO_2 after 100 days (chain labelled) B: 31 % CO_2 after 100 days (carboxyl labelled)	1	Procter & Gamble, 1985 f
12,000	CO_2 Evolution Test, domestic activated sludge, ^{14}C tagged	A: 39 % CO_2 after 90 days (chain labelled) B: 13 % CO_2 after 90 days (carboxyl labelled)	1	Procter & Gamble, 1985 h
70,000	CO_2 Evolution Test, river water, ^{14}C tagged	12 % CO_2 after 100 days (chain labelled)	1	Procter & Gamble, 1985 g

Mean MW (g/mol)	Method/Remark	Result	Reliability	Reference
70,000	CO_2 Evolution Test, domestic activated sludge, ^{14}C tagged	A: 13 % CO2 after 90 days (chain labelled) B: 18 % CO2 after 90 days (carboxyl labelled)	1	Procter & Gamble, 1985 h
Sediment				
12,000	CO_2 Evolution Test, river water and sediment, ^{14}C tagged	A: 41 % CO_2 after 100 days (chain labelled) B: 6 % CO_2 after 100 days (carboxyl labelled)	1	Procter & Gamble, 1985 g
70,000	CO_2 Evolution Test, river water and sediment, ^{14}C tagged	A: 11 % CO_2 after 100 days (chain labelled) B: 13 % CO_2 after 100 days (carboxyl labelled)	1	Procter & Gamble, 1985 g
Soil				
12,000	CO_2 Evolution Test, sludge treated soil, ^{14}C tagged	A: 32 % CO_2 after 165 days (chain labelled) B: 10 % CO_2 after 165 days (carboxyl labelled)	1	Procter & Gamble, 1985 i
70,000	CO_2 Evolution Test, sludge treated soil, ^{14}C tagged	A: 8 % CO_2 after 165 days (chain labelled) B: 11 % CO_2 after 165 days (carboxyl labelled)	1	Procter & Gamble, 1985 i

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/MA based on DOC or ^{14}C removal

Mean MW (g/mol)	Method/Remark	Result	Reliability	Reference
Water				
12,000-14,000	OECD 302 A (SCAS Test)	83 % DOC after 7 days	1	Procter & Gamble, 1983 e
50,000-60,000	OECD 302 A (SCAS Test)	95 % DOC after 7 days	1	Procter & Gamble, 1983 f
60,000	OECD 302 A (SCAS Test)	93 % DOC after 7 days	1	Procter & Gamble, 1983 e
60,000	OECD 302 A (SCAS Test)	85 % DOC after 8 days	1	Procter & Gamble, 1985 j

Mean MW (g/mol)	Method/Remark	Result	Reliability	Reference
70,000	OECD 302 B (Zahn - Wellens Test)	97-99 % DOC after 2 days	2	BASF AG, 1990
70,000	ISO 18749 (Adsorption Test modified to Zahn – Wellens)	90-100 % DOC after 1 day	2	BASF AG, 2001
Sewage treatment plant (STP)				
12,000	OECD 303 A (Simulation test)	A: 71 % DOC removal (15 mg/l DOC influent concentration) B: 80 % DOC removal (30 mg/l DOC influent concentration)	1	Procter & Gamble, 1983 d
50,000-60,000	OECD 303 A (Simulation test)	93 % 15 mg/l DOC influent	1	Procter & Gamble, 1983 d
70,000	OECD 303 A (Simulation test)	> 94 % DOC removal	2	Opgenorth, 1987
70,000	OECD 303 A (Simulation test)	97-98 % DOC removal	2	Schumann, 1990

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 copolymer 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

$$Kd = C_{polymer\ in\ solid\ phase} / C_{polymer\ in\ water\ phase}$$

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/MA 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/MA with an average MW of 66,500 g/mol, which is slightly lower than the typical MW of 70,000 g/mol. 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/MA concentrations used for the experimental determination of Kd in activated sludge, soil and sediment were 0.7, 0.8 and 0.4 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/MA 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/MA on activated sludge, soil and sediment

Solids	Activated sludge	Soil	Sediment
Concentration [mg/L] (pore water)	0.7	0.8	0.4
Water hardness [mg/L]	70	400	40
pH	7.5	7.0	8.0
Kd-value [L/kg]	15,714 (7 h)	407 (24 h)	90 (24 h)

For EUSES modelling purpose, a Koc value as input parameter of 42,470 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 copolymers

The dominant fate pathway of copolymers used in detergents into the environment is via domestic wastewater. Copolymers can be partly biodegraded under long exposure periods in the range of 90 to 165 days in water, sediment and soil. All these investigations were performed with radio labelled material of P-AA/MA in a broad molecular range. However, independent of the molecular weight of P-AA/MA used in detergents, copolymers basically tends to be poorly biodegradable as measured by carbon dioxide evolution. In contrast to biodegradation processes, in the presence of calcium cations, insoluble salts will be formed and will be eliminated by adsorption and precipitation processes. Recent determined Kd of 15,714 L/kg clearly suggests a high adsorption potential of the soluble P-AA/MA on activated sludge (BASF SE, 2013). Therefore, it can be concluded that independent of the soluble and insoluble state of P-AA/MA 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 show high degree of elimination in STP. Basically all studies in table 4 were performed with domestic activated sludge. Based on the available data it can be concluded that P-AA/MA is not readily biodegradable but is partly accessible to ultimate biodegradation particularly under long incubation conditions (cf. mineralisation data). In summary, the results from screening and simulation tests suggest that copolymers in biological waste water treatment plants are predominantly eliminated by adsorption/precipitation in the presence of activated sludge.

Therefore, a geometric mean value of 89 % elimination rate was calculated and used for the EUSES calculations of the P-AA/MA exposure assessment.

Anaerobic Biodegradation and Elimination

The anaerobic biodegradability of P-AA/MA (70,000 g/mol) was investigated by incubation of radiolabelled P-AA/MA in a mixture of digester sludge and nutrient solution over 258 days at 35 °C. The results indicated a biodegradability extent between 11 and 16 % (Opgenorth, 1990). As a result, no anaerobic degradation of P-AA/MA was assumed in the context of the HERA risk assessment.

4.1.2 Abiotic degradability of P-AA/MA

Photodegradation

Due to the high water solubility and low volatility of P-AA/MA 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/MA

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/MA 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/MA. The molecular weight of approximately 70,000 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/MA 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/MA such indirect exposure can be considered negligible based on the

arguments provided above on minimum potential on bioconcentration and bioaccumulation of P-AA/MA.

In addition, it is unlikely that humans will be exposed to P-AA/MA directly by contact with air or through indirect exposure via the food chain. This is because P-AA/MA 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 AISE 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 89 % 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 0.11
- Fraction of emission directed to sludge 0.89

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/MA are presented in table 6:

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

Compartment	Predicted environmental concentrations (PEC)
Water	
$PEC_{regional,\ water}$ [mg/l]	0.035
$PEC_{local,\ water}$ [mg/l]	0.049
Sediment	
$PEC_{regional,sediment}$ [mg/kgwwt]	38.8
$PEC_{local,\ sediment}$ [mg/kgwwt]	45.4
Soil	
$PEC_{regional,\ soil}$ [mg/kgwwt]	35.2
$PEC_{local,\ soil}$ [mg/kgwwt]	26.8
STP effluent	
$PEC_{local,\ stp}$ [mg/l]	0.15

4.2. Environmental Effects Assessment

In the following chapter, the available ecotoxicity data of P-AA/MA (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/MA

P-AA/MA has a low acute ecotoxicity profile (table 7). All ecotoxicity studies showed the L(E)C50 beyond the highest tested concentration ($\geq$100 mg/l). 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/MA with the same molecular weight of 70,000 reside in a broad range between 3.75 and 350 mg/L. Several chronic studies on soil ecotoxicity are available confirming again the low ecotoxicity of P-AA/MA (table 10).

Table 7: Acute Aquatic Ecotoxicity of P-AA/MA

Mean MW (g/mol)	**Test species**	**Method**	**LC/EC_{50} [mg/l] Exposure time**	**Reliability**	**Reference**
Acute Toxicity to Fish					
12,000	*Brachydanio rerio*	OECD 203 (range finding)	> 200 (96 h)	1	Procter & Gamble, 1982 a
50,000	*Leuciscus idus*	DIN 38412 part L15	> 500 (96 h)	2	BASF AG, 1987 e
70,000	*Brachydanio rerio*	OECD 203 (range finding)	> 100 (96 h)	1	Procter & Gamble, 1982 b
100,000	*Brachydanio rerio*	OECD 203	> 100 (96 h)	1	BASF AG, 2002 a
Acute Toxicity to Aquatic Invertebrates					
12,000	*Daphnia magna*	OECD 202 (range finding)	> 200 (48 h)	1	Procter & Gamble, 1984 f
70,000	*Daphnia magna*	OECD 202 (range finding)	> 100 (48 h)	1	Procter & Gamble, 1982 b
70,000	*Daphnia magna*	OECD 202	> 500 (48 h)	1	BASF AG, 1985
100,000	*Daphnia magna*	OECD 202	> 100 (48 h)	1	BASF AG, 2002 b
Acute Toxicity to Algae					
70,000	*Scenedesmus subspicatus*	OECD 201	> 500 (96 h)	1	BASF AG, 1985 c
70,000	*Chlorella vulgaris*	OECD 201	> 500 (96 h)	1	BASF AG, 1987 g
100,000	*Scenedesmus subspicatus*	OECD 201	> 100 (72 h)	1	BASF AG, 2002 c

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/MA

Mean MW (g/mol)	**Test species**	**Method**	**NOEC [mg/l] Exposure time**	**Reliability**	**Reference**
Chronic Toxicity to Fish					
70,000	*Brachydanio rerio*	OECD 204	100 (14 days)	2	BASF AG, 1986 a
70,000	*Brachydanio rerio*	OECD 210	100 (42 days)	1	BASF AG, 1986 b
Chronic Toxicity to Aquatic Invertebrates					
70,000	*Daphnia magna*	OECD 202	350 (21 days)	1	Procter & Gamble, 1986 b
70,000	*Daphnia magna*	OECD 202	6.2 (21 days)	1	BASF AG, 1986 n
70,000	*Daphnia*	OECD 202	7.5 (21 days)	1	BASF AG, 1985 e

Mean MW (g/mol)	Test species	Method	NOEC [mg/l] Exposure time	Reliability	Reference
	magna				
70,000	*Daphnia magna*	OECD 202	3.75 (21 days)	1	BASF AG, 1985 f
Chronic Toxicity to Algae					
70,000	*Scenedesmus subspicatus*	OECD 201	EC_{10} = 32 (96 h)	4	Schumann, 1990
100,000	*Scenedesmus subspicatus*	OECD 201	37.2 (72 h)	1	BASF AG, 2002 c

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/MA 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 3.75 and 350 mg/L with the same molecular weight of 70,000. The solubility behaviour of P-AA/MA in water presumably explains these observations since the aquatic toxicity directly linked to its solubility behaviour in water. The water solubility of P-AA/MA 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, water solubility of P-AA/MA was determined in dependence of water hardness and P-AA/MA concentration. In this study the solubility behaviour of P-AA/MA in concentration between 11 to 1000 mg/L was measured in distilled water and compared with OECD 202 medium of Daphnia magna (medium M4 with a water hardness of 13.8 °dH, which is equivalent to 2.46 mmol/L CaO). The solubility was determined analytically via the ratio of dissolved organic carbon (DOC) and total organic carbon (TOC). In distilled water (without 2+ ions) P-AA/MA was 100 % soluble in all concentrations. In M4 medium P-AA/MA was completely soluble at concentrations higher than 500 mg/L. At concentrations below 500 mg/L the precipitation process starts and under 25 mg/L almost all P-AA/MA exists in an insoluble Ca-form. This study demonstrates that P-AA/MA is predominantly present in form of insoluble precipitation products which causes the adverse effects of *Daphnia magna* at low concentrations.

Two different NOECs of 350 mg/L (soluble state of P-AA/MA) and 3.75 to 6.2 mg/L (insoluble state of P-AA/MA) were determined depending on the test design. Furthermore, the precipitation of P-AA/MA at concentrations below 10 mg/L were further investigated by microscope, showing that the observed chronic effects on Daphnia *magna* of P-AA/MA at low concentrations are likely due to precipitated copolymer products. Under conditions with low exposure concentration of P-AA/MA, the colour of the gastro-enteric tract of *Daphnia magna* changed from green (i.e. the typical colour resulting from the algae feed) to grey (i.e. the colour of the precipitated copolymers BASF AG, 1990 a). Thus, the observed effects at low concentrations may not be caused by intrinsic toxic properties of the polymer, but rather by secondary effect namely uptake of precipitates via ingestion of the algae food.

This observed secondary effect is probably not occurring under realistic environmental conditions. Compared to the 50 ml incubation beaker in the OECD 202 test design, the surface water dilution in natural compartments is unlimited. It has been considered that copolymers are preferentially associated with solids. Furthermore due to the high removal rate (i.e. 89%) of P-AA/MA in STP, precipitation in surface waters is unlikely. For these reasons a direct uptake of precipitates products or an indirectly uptake via algae food by aquatic filter feeding invertebrates will not be expected in surface water.

Three chronic daphnia studies by BASF presented a NOEC ranging from 3.75 to 7.5 mg/L for aquatic invertebrates. Although these effects were probably caused indirectly from precipitation products and not from the soluble P-AA/MA itself, the geometric mean of NOEC value from these three studies of 5.6 mg/L 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/MA

Mean MW (g/mol)	**Test species**	**Method**	**EC [mg/l] Exposure time**	**Reliability**	**Reference**
12,000	Activated sludge, domestic	OECD 209	EC_{50} > 100	1	Procter & Gamble, 1985 a
70,000	Activated sludge, domestic	OECD 209	EC_{50} > 200	1	Procter & Gamble, 1985 a
70,000	*Pseudomonas putida*	DIN 38412	> 500 mg/l	2	BASF AG, 1987 h
70,000	*Photobakterium phosphoreum*	DIN 38412	> 500 mg/l	2	BASF AG, 1985 d
80,000	*Pseudomonas pudita*	DIN EN ISO 10712	463 (16 h)	1	BASF AG, 1997

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 $PNEC_{STP}$. The EC_{50} > 200 mg/l (Procter & Gamble, 1985 a) for P-AA/MA (70,000) together with an application factor of 100 was used for a conservative $PNEC_{STP}$ calculation.

Table 10: Toxicity to Terrestrial organisms of P-AA/MA

Mean MW (g/mol)	**Test species**	**Method**	**Effect [mg/kg] Exposure time**	**Reliability**	**Reference**
Toxicity to Soil Dwelling Organisms					
70,000	*Eisenia fetida*	EDWARDS, Commission of the European Community, 1983	EC_0 = 1,600 (14 days)	2	BASF AG, 1986 o

Mean MW (g/mol)	Test species	Method	Effect [mg/kg] Exposure time	Reliability	Reference
70.000	*Eisenia fetida*	OECD 222	NOEC = 500 mg/kg dw (56 days)	1	BASF SE, 2012 e
Toxicity to Terrestrial Plants					
70,000	Oats *Avena sativa*	German guideline according to UBA	NOEC > 1,000 (18 days)	2	BASF AG, 1985 g
70,000	Oats seed	No data available	NOEC = 400	4	Opgenorth, 1987
70,000	*Avena sativa*	OECD 208	EC_{10} = 625 (25 days)	1	BASF SE, 2009
70,000	*Brassica napus*	OECD 208	EC_{10} = 3,963 (25 days)	1	BASF SE, 2009
70,000	*Vicia sativa*	OECD 208	EC_{10} = 2,623 (25 days)	1	BASF SE, 2009
Toxicity to Bacteria					
70,000	Nitrogen transformation	OECD 216	EC_{10} > 10,000 (28 days)	2	BASF SE, 2012 c
70,000	Carbon transformation	OECD 217	EC_{10} > 10,000 (28 days)	2	BASF SE, 2012 a

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

Chronic soil toxicity data are available for earthworm, plants and microorganisms. Soil toxicity of higher plants was also determined for different endpoints such as the emergence rate of the seeds, the fresh and dry matter and the shoot length with *Avena sativa*, *Brassica napus* and *Vicia sativa*. For all three plant species the EC_{50} values were above 5000 mg/kg soil, which indicates the low toxicity of P-AA/MA on terrestrial organisms. The lowest test result showed an EC_{10} value of 625 mg/kg P-AA/MA for *Avena sativa*, based on the determination of the shoot length. The soil consistence appeared to be distinctly changed by visually inspection. The emergence rate of *Brassica napus* was affected at concentrations above 625 mg/kg soil. The possible impact by soil compaction and subsequent mechanical influences on the emergence rate were investigated in another study (BASF SE, 2008 b). The results demonstrated that the soil pressure was significantly increased even at the lowest test concentration of 313 mg P-AA/MA/kg soil, thus confirming the alteration of the soil consistence at P-AA/MA concentrations ≥ 300 mg P-AA/MA/kg soil. Consequently, this effect on the emergence rate of *Brassica napus* can be interpreted as a secondary effect strongly influenced by physical properties.

The $PNEC_{soil}$ is derived from the recent long-term study with *Eisenia fetida* with a NOEC of > 500 mg/kgdw (BASF SE, 2012). As described above soil compaction has a strong physical mechanical influence above 300 mg P-AA/MA/kg soil, which are unlikly to be found in

natural soil. It can be assumed that the observed long-term effects on the reproduction of *Eisenia fetida* at high concentrations are primarily based on secondary effects. For the risk assessment, the NOEC value was recalculated to >441 mg/kgwwt related to wet weight using a conversion factor of 1.13 (EU TGD, 2003) and was used for the $PNEC_{soil}$ derivation.

With the availability of chronic data cover three trophic levels of earthworm, plant species and microbial activity, an application factor of 10 was used for the $PNEC_{soil}$ derivation according to EU TGD, 2003. The value obtained for oats seed (Opgenorth, 1987) was discarded due to the low reliability of the study.

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

Experimental data on sediment-dwelling organisms is not available for P-AA/MA but for P-AA (see Part I). It can be assumed that the level of toxicity for P-AA/MA will be in the same range as for P-AA. In the absence of experimental sediment toxicity data, the $PNEC_{sediment}$ of P-AA/MA is derived by application of the equilibrium partitioning method as described in the EU TGD (EU, 2003). Generally, the equilibrium partitioning method has some limitation on calculation of $PNEC_{sediment}$ using data from aquatic species but is considered to be conservative enough to be comparable to experimental data. Therefore, in accordance with the conservative frame of this risk assessment, the $PNEC_{sediment}$ for P-AA/MA was calculated as 536 mg/kgwwt.

4.2.2 Derivation of PNEC

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/MA

Key study for compartment	Reference (No)Effect concentration	Application Factor	PNEC
$PNEC_{water}$ [mg/l]	NOEC = 5.6 mg/l	10	0.56
$PNEC_{sediment}$ [mg/kgwwt]	EUSES calculation acc. to equilibrium partitioning method	Not applicable*	517
$PNEC_{soil}$ [mg/kgwwt]	NOEC > 441 mg/kgwwt	10	44.1
$PNEC_{stp}$ [mg/l]	EC_{50} > 200 mg/l	100	2

*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/MA

Risk Characterisation Water compartment	RCR
$PEC_{regional, water.}/PNEC_{water}$	0.06
$PEC_{local, water.}/PNEC_{water}$	0.09
Risk Characterisation Sediment compartment	
$PEC_{regional, sed.}/PNEC_{sed.}$	0.08

$PEC_{local,\ sed.}/PNEC_{sed.}$	0.09
Risk Characterisation Soil compartment	
$PEC_{regional,\ soil}/PNEC_{soil}$	0.8
$PEC_{local,\ soil}/PNEC_{soil}$	0.61
Risk Characterisation Sewage Treatment Plant	
$PEC_{local,\ stp}/PNEC_{stp}$	0.08

4.4 Discussion and Conclusions

The environmental risk assessments of P-AA/MA were conducted according to the EU TGD (2005) with calculation model of EUSES under A.I.S.E. SPERC, HERA exposure scenario. For exposure assessment, sorption coefficients Kd generated from recent studies with radio labelled PAA/MA copolymer 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 89 % 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/MA is heaviliy dependend on the water hardness and the test concentrations. The solubility and precipitation behaviour of P-AA/MA in the presence of 2^{+}-ions like ubiquitous calcium and magnesium ions has an important impact on the interpretation of the available chronic aquatic toxicity test results of P-AA/MA. It also explains the observed large variability with *Daphnia magna* of NOECs in the range between 3.75 to 350 mg/L. P-AA/MA forms insoluble precipitation products at low concentrations. These insoluble products may potentially cause secondary adverse effects which results in a NOEC value of 5.6 mg/L. This value was used in the risk assessment as a worst case scenario.

In the absence of experimental sediment toxicity data, the $PNEC_{sediment}$ of P-AA/MA calculation was derived by application of the equilibrium partitioning method. Generally, the equilibrium partitioning method has some limitation on calculation of $PNEC_{sediment}$ using data from aquatic species. However, results by equilibrium partitioning method were considered conservative enough to be comparable to experimental data. Therefore, in accordance with the conservative frame of this risk assessment the $PNEC_{sediment}$ for P-AA/MA was calculated as 536 mg/kgwwt.

New chronic soil toxicity data on earthworm and microbial activity of nitrogen and carbon transformation allowed a refinement of the evaluation of the terrestrial compartment. The NOEC values indicates very low toxicity effects above 500 mg/kgdw. The NOEC value was recalculated to > 443 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 copolymers 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. Copolymers are used almost exclusively in laundry detergent powders and tablets as well as in automatic dishwashing detergents. Polycarboxylates are usually not contained in manual dishwashing detergents. A typical mean concentration of polycarboxylates is 3.0 % for P-AA/MA 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/MA 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/MA in laundry detergents in handwashing amounts to 3%.
- 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/MA:**
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 0.03 (fraction of P-AA/MA in detergent; 3%) = 0.059 mg / day

0.059 mg P-AA/MA 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, 0.059 mg is used in the assessment resulting in an estimated dose of (60 kg bw assumed):

$Exp_{sys(direct\ skin\ contact)}$ = 0.99 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/MA:
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 0.03 (fraction of P-AA/MA in detergent; 3%) = 1.5 mg / day

1.5 mg P-AA/MA 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, 1.5 mg is used in the assessment resulting in an estimated dose of (60 kg bw assumed):

$Exp_{sys(direct\ skin\ contact)}$ = 25 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)

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

Calculation for the systemic exposure:

F_1 = 3% for P(AA-MA)
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/MA) = 0.088 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 3 % of polycarboxylates. Thus, residual P-AA/MA 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/MA concentration is 349 mg/l during the first cycle. In the remaining washing liquor after the pumping-off process, 105 mg P-AA/MA remain in the dishwashing machine. The P-AA/MA concentration is decreased to 1.5 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/MA load of 0.82 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-AAMA)= F_1 x $C'_{P\text{-}AA/MA}$ x S x F'' x F_9/bw= **$7.3 * 10^{-2}$ µg/kg bw/day**

The terms are defined with the following values:

F1 = (weight fraction of substance in product; not used, already included in $C'_{P\text{-}AA/MA}$)
$C'_{P\text{-}AA/MA}$ = 0.82 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 dust per cup of product used for machine laundering, of which up to up to **3% eq. 0.008 µg/use** is P-AA/MA**.**

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

Exp/use = 0.00014 µg/kg bw P-AA/MA

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 89 % of P-AA/MA 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 $C_{local, water}$ of 0.124 mg/l for P-AA/MA 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:

$$\mathbf{Exp_{sys\ (oral\ route)}\ (P\text{-}AA/MA) = 124\ \mu g/l \times 2\ l/day/60\ kg\ bw = 4.133\ \mu g/kg\ bw/day}$$

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 3 % P-AA/MA 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/MA from their use in household cleaning products would be 28 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/MA
Direct skin contact via hand-washed laundry	0.99
Direct skin contact from pre-treatment of laundry	25
Indirect skin contact from wearing laundered clothes	0.088
Inhalation of laundry powder dust	1.4×10^{-4}
Indirect oral exposure from dish washing	7.3×10^{-2}
Oral exposure from drinking water	4.133
Total exposure	27.8 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

Table 14 summarises the acute toxicity of the copolymers with molecular weight up to 70,000 which demonstrates the low acute oral toxicity. No deaths occurred within the 14-day observation period and neither clinical nor any gross pathological findings were recorded.

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

Mean MW	Test species	Test Substance	LD_{50} [mg/kg bw]	Reliability	Reference
50,000	Rat	**undiluted**	$LD_{50} > 5{,}000$	2	**BASF, 1986**
70,000	Rat	No data	$LD_{50} > 5{,}000$	2	**BASF 1992**

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

Acute dermal toxicity data are not available for P-AA/MA.

5.2.1.1.3 Acute Inhalation Toxicity

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

5.2.1.2 Skin Irritation

Two studies with P-AA/MA 50,000 and P-AA/MA 70,000, both performed according to OECD Guideline 404, showed no skin irritation (BASF 1986i, BASF 1982a) (Table 15). The

test substances have been applied to the skin as a 45% aqueous solution. No erythema or oedema have been reported.

Table 15: Summary table of skin irritation data of copolymers (P-AA/MA)

Mean MW	Test species	Test Substance	Result	Reliability	Reference
50,000	Rabbit	**45% aq. solution**	Not classifiable as irritating	2	**BASF, 1986 i**
70,000	Rabbit	**40% aq. solution**	Not classifiable as irritating	2	**BASF, 1982 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

Conclusion

None of the copolymers tested at very high concentrations has been reported to be irritating to the skin.

5.2.1.3 Eye Irritation

A non-irritating effect has been observed in two studies performed according to standard OECD protocol, but not according to GLP. P-AA/MA50,000 and P-AA/MA70,000 have been applied in 40% and 45% aqueous solutions, respectively. In the case of P-AA/MA70,000 severe discharge and slight erythema have been noted (2/3), in the case of P-AA/MA50,000 only slight discharge has been reported (2/3). In both studies the effects were reversible after 24 h.

Table 16: Summary table of eye irritation data with copolymers (P-AA/MA)

Mean MW	Test species	Test Substance	Result	Reliability	Reference
50,000	Rabbit	45% aq. solution	Not classifiable as irritating	2	**BASF, 1986 j**
70,000	Rabbit	40% aq. solution	Not classifiable as irritating	2	**BASF, 1982 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

Conclusion

Based on the given data, the copolymers have no irritating property at similar high substance concentrations tested.

5.2.1.4 Sensitisation

P-AA/MA70,000 was tested in the Magnusson and Kligman Guinea pig maximisation assay.

Table 17: Summary table of sensitisation data with copolymers (P-AA/MA)

Mean MW	Test species	Test Method	Result	Reliability	Reference
70,000	Guinea pig	Maximisation test	not sensitising	2	**Rohm & Haas, 1988**

Mean MW	Test species	Test Method	Result	Reliability	Reference
70,000	Guinea pig	Maximisation test	not sensitising	2	**BASF, 1986 m**

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

I.d. induction was done with a 20% test substance preparation in aqua dest./Freund's adjuvans (1:1). Percutaneous induction was done with the neat test substance one week after i. d. Animals were exposed to about 0.3 g of the test substance. The duration of exposure was 48 h and readings were done about 48 h after the beginning of application. 1st and 2nd challenge were performed with 80% test substance in aqua dest. After i.d. induction with 0.1 ml of the test substance formulation, distinct erythema and oedema were observed at all injection sites of the test animals. Percutaneous induction led to incrustation, distinct erythema and oedema. Two separate challenge doses of 80% of the test substance formulation were applied and no sensitisation was observed. The challenges were given at day 19 and 26 following the induction phase (Rohm & Haas, 1988; BASF, 1986 m).

Conclusion

P-AA/MA 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 18: Summary table of the repeated dose toxicity tests with P-AA/MA

Mole-cular Weight	Test species	Duration	Route	Estimated NO(A)EL	Doses	Reliability	Reference
70,000	Rat	90 days	Oral drinking water	NOAEL> 16,000 ppm	1,000; 4,000; 16,000 ppm	**2**	**BASF, 1987 f**
70,000	Rabbit	28 days	dermal	NOEL= 2000 mg/kg bw/d	2000 mg/kg bw/d	**2**	**BASF, 1983**
70,000	Rat	91 days	Inhalation	$NOEC_{lung}$ = 1 mg/m^3 $NOEC_{syst.}$ = 5 mg/m^3	0.2, 1.0 and 5.0 mg /m^3	**2**	**Procter & Gamble, 1991**

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-AA/MA70,000 has been tested in a 91 d inhalation study (Table 18). 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 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 5 mg/m^3 P-AA/MA70,000. 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 1 mg/m^3 for respirable dust of P-AA/MA70,000 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.

5.2.1.5.2 Oral route

P-AA/MA70,000 has been tested according to OECD Guideline 408 under GLP conditions (Table 18). The test substance was administered to 10 male and 10 female Wistar rats for 90 d in drinking water at dose levels of 1,000; 4,000 and 16,000 ppm, the top dose being equivalent to 1,871 mg/kg bw/day for male rats and 2,216 mg/kg bw/day for female rats. At the beginning of the study the low-dose males consumed about 119 mg/kg bw/d and the mid-dose males about 445 mg/kg bw/d. The females with the low dose showed a substance intake of about 126 mg/kg bw/d and those with the mid dose about 499 mg/kg bw/d. Ophthalmoscopic investigations were performed on control and high-dose animals prior to and at the end of test substance administration. Clinical chemistry and urinalysis were performed in week 6 of the study and at the end. Furthermore, macroscopic and histopathological examinations were conducted. With the exception of increased water consumption in both sexes (more pronounced in the females) of the high-dose group, no other test substance related findings were reported. Especially, no adverse effects to the gonads were reported.

The NOAEL determined in this study was 16,000 ppm, which is equivalent to 1,871 mg/kg bw/d for male rats and 2,216 mg/kg bw/d for female rats (BASF, 1987 f).

5.2.1.5.3 Dermal route

P-AA/MA70,000 has been examined in a 28-day rabbit dermal study (Table 18). Groups of 15 male and 15 female rabbits received 10, 25 and 50% aq. solutions of the test material at a dosage of 2 g/kg bw on to shaved and abraded skin (open application). For comparison, a group of 5 animals per sex was used as control and treated with aqua dest. All test sites were washed with lukewarm water approx. 7 h after treatment and gently dried with disposable paper towels. Examinations of the body weight, for clinical signs and skin irritation as well as haematological, gross pathological and histopathological examinations were carried out. The concentrations selected for the present investigation were determined in a pre-test with 16 rabbits, which received the neat test substance, 50, 25, 10, 5, 2.5 and 1% aqueous solutions of the test substance applied topically on the shaved and abraded skin 5d/wk for two weeks. At the beginning of the test substance application mean weights of the rabbits were 2.68 kg for male and 2.78 kg for female animals. Statistical evaluation of the data was performed.

In all high-concentration animals slight erythema was seen commencing in the third week and persisting until the end of the study. No effects on the skin were observed in the low concentration group animals and in the control animals. There were no changes in the remaining investigated parameters of the treatment groups when compared with the concurrent control animals. The minimum slightly irritant concentration was 25%. In the 50% concentration group the irritation was also reported to be slight. In view of the test substance to the abraded skin and taking into account that the treatment was repeated work daily for 4 weeks, the observation of slight skin irritation is in accord with the study results obtained for short term skin irritation (BASF, 1983).

The NOAEL for systemic toxicity upon short term repeat dose dermal exposure to the abraded skin was 2,000 mg/kg bw/d.

Conclusion

Table 19

Test Substance	Duration	Route of Exposure	Species	NOAE(L)C_{syst}	NOAE(L)C_{local}
P-AA/MA70,000	13 wks	Oral drinking water	Rat	1,871-2,216 mg/kg bw/d	
P-AA/MA70,000	4 wks	Dermal (abraded skin)	Rabbit	2,000 mg/kg bw/d (limit dose)	
P-AA/MA70,000	13 wks	Inhalation	Rat	5 mg/m^3	1 mg/m^3

5.2.1.6 Genotoxicity

5.2.1.6.1 In vitro

Table 20: Summary table of the genotoxicity in vitro of P-AA/MA

Mean MW	Test system	Test Substance	Metabolic Activation	Result	Reliability	Reference
12,000	Ames Test	45% aq. solution	With and without	negative	2	Thompson, 1983
12,000	Mouse lymphoma assay	45% aq. solution	With and without	negative	2	Thompson, 1983
12,000	Cytogenetic Assay (CHO)	45% aq. solution	With and without	negative	2	Thompson, 1983
12,000	Unscheduled DNA synthesis	45% aq. solution	Without	negative	2	Thompson, 1983
70,000	Ames Test	No data	With and without	negative	2	BASF, 1984
70,000	Cytogenetic Assay (CHO)	No data	With and without	negative	2	BASF, 1985
70,000	Unscheduled DNA synthesis	No data	Without	negative	2	BASF, 1984

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

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. In an HGPRT assay with Chinese hamster ovary (CHO) cells the test substance (P-AA/MA65,000) was applied to the cells at 0, 1.0, 4.64, 6.81, 10.0, 21.5 and 46.4 mg/ml with and without metabolic activation. Toxicity to CHO cells was observed at approximately 10 mg/ml in the absence of S-9 mix and > 46.6 mg/ml in the presence of S-9 mix. An increase of mutants at certain toxic dose levels was observed, but this was not clearly dose related and was considered due to other effects, e. g. calcium chelation, cytotoxicity and precipitation out of solution of the test substance (BASF, 1985) .

Neutralised test substances of aqueous solutions containing 45 % P-AA/MA12,000 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 (Thompson et al, 1983).

Unscheduled DNA Synthesis

Neutralised test substances of aqueous solutions containing 45 % P-AA/MA12,000 have been tested for induction of UDS (Unscheduled DNA Synthesis) in primary rat hepatocytes following the methods described by Williams et al. (1977). P-AA/MA12,000 was tested to a maximum concentration of 4 µl/ml. The test substance showed appreciable toxicity at the highest concentrations tested. No evidence of UDS was observed (Thompson et al, 1983).

Under GLP conditions, a study with P-AA/MA70,000 did not induce significant changes in the nuclear labelling of primary rat hepatocytes for the concentration range 25 to 5,000 µg/ml (0.025 - 5.0 -µl/ml). 8 treatments in this range resulted in a cell survival range of 102% to 73.8 %. Treatment with 10,000 µg/ml (10µl/ml) was excessively toxic (BASF, 1984).

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

Cytogenetic Assay

P-AA/MA70,000 has been tested for chromosome aberrations in the bone marrow of male and female Chinese hamsters following a single i.p. injection of 200; 600 and 1,780 mg/kg bw. The doses were applied in a volume of 10 ml/ kg bw.

For control purposes, a solvent control group and a positive control group (cyclophosphamide) were used. 20 animals (10 animals of each sex) were used for the solvent control, 10 animals (5 of each sex) for the positive control and the low- and mid-dose groups, respectively, and 30 animals (15 of each sex) for the high dose group . High-dose animals were killed and bone marrow was examined at 6, 24 and 48 h after dosing (10 animals at each time point). The animals (10 per group, 5 of each sex) from the other two dose groups and the solvent and positive control groups were killed 24 h after dosing.

No increase in aberrant metaphases and no significant differences in the types and frequency of aberrations between the dose groups and the solvent control group were observed. No chromosome-damaging effects were seen under the present study conditions (BASF, 1985a).

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/MA. P-AA/MA is, however, devoid of any genotoxic potential in-vitro and in-vivo. Apart from some indication of cellular pneumocyte hyperplasia in a 90 d inhalation study, these polymers did not show other cellular hyperplasias upon other routes of exposure. As acrylic copolymers 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 21: Summary table of developmental toxicity data for P-AA/MA

Mean MW	Test Species	Route	Test Substance	Doses [mg/kg]	NOAEL (mg/kg)	Reliability	Reference
12,000	Rat	Gavage	44.9 % aq. solution	67 ; 667 ; 6,670	M: >= 6,670 **T: >= 6,670**	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-AA/MA12,000 was administered to four groups of 25 female rats each by gavage at dose levels of 67; 667 and 6,670 mg/kg bw/day during days 6-15 of gestation. On day 20 of gestation the dams were killed. One half of each litter was examined for visceral findings by the Wilson (1965) method and the other half by the Dawson (1926) method for skeletal findings. Conception was considered day 0. There were no deaths in the high-dose group but in the low-dose group there were 8 malformed foetuses all from 1 litter and all with short thickened bodies with numerous malformations. Animals from the other 23 litters in this test group showed no developmental toxic effects (no foetotoxicity and no teratogenicity). This singular finding was therefore considered to be incidental and not to be treatment-related. All other findings with respect to malformations or variations were scattered randomly throughout the groups with no pattern or increased incidence. Therefore the NOEL for maternal toxicity and developmental toxicity was determined to be 6,670 mg/kg bw/d (Nolen, 1989).

Conclusion

P-AA/MA did not show developmental toxicity or embryotoxic effects in rats.
In a ninety days repeat dose study with substance application via drinking water no effects on the reproductive organs of the test animals were reported for P-AA/MA.
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

P-AA/MA 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 mg/kg bw for molecular weights ranging from 50,000 to 70,000 g/mol.

Data for acute dermal toxicity for P-AA/MA are not available.

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

The results obtained for a P-AA/MA70,000 with a 4 weeks repeat dose exposure to the abraded skin of rabbits at 2,000 mg/kg bw/d which did not show any signs of systemic toxicity support this argument.

Data on acute inhalative toxicity are not available. In the absence of any spray application products with P-AA/MA, 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/MA, respectively, in the molecular weight range from 50,000 to 70,000 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 after 24 hours. Therefore the effects were assessed as being not classifiable as irritating.

P-AA/MA have been demonstrated to be not skin sensitising on the basis of a study performed with P-AA/MA70,000 in the guinea pig maximization test (GPMT).

Two P-AA/MA of 70,000 molecular weight have been tested in repeat dose studies via drinking water and inhalation as dust aerosols. Exposure times were from 4 – 13 weeks.

A subchronic drinking water study in rats, performed according to the OECD test guideline 408 is available. Apart from an increase of water consumption in the high dose group, no other test substance related effects were identified. The NOAEL identified in this study was approx. 2,000 mg/kg bw/d for both genders.

In a 28 d non-guideline study in rabbits with substance application to the abraded skin of rabbits, a systemic NOEL of 2,000 mg/kg bw/ d was determined.

Both studies confirm a low repeat dose toxicity by the oral and dermal route.
P-AA/MA of molecular weight of 70,000 was tested by inhalative exposure for 13 weeks with dust aerosols. This study shows 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/MA is not considered to be mutagenic or genotoxic. P-AA/MA 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/MA with a molecular weight of 12,500 has been tested for developmental toxicity in rats. No significant embryotoxicity or developmental toxicity was detected in this study. Furthermore, in a subchronic oral 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 for these two polymer classes.

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 an 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/MA 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.

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/MA a NOEL of 2000 mg/kg bw/d for dermal exposure during 28 days has been shown in rabbits (BASF 1983) and a NOAEL of 1,871 to 2,216 mg/kg bw/day has been determined on the basis of a 90 d oral drinking water study in rats (BASF, 1987f).

NO(A)ELs for MOE Calculations:

- NOEL rabbit, dermal, 28 d study: **2,000 mg/kg bw/d for P-AA/MA**
- NOAEL rat, oral drinking water, 90 d study: **1,871 mg/kg bw/d for P-AA/MA**

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

For calculation of the MOE for P-AA/MA, the NOEL of **2,000** mg/ kg bw/d from the 28 day rabbit dermal study was divided by the daily systemic dose of 26 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/MA: $MOE_{\text{direct skin hand-washed laundry}}$ = 2000,000/26 = **7.7×10^4**

5.3.1.2 Exposure scenario: indirect skin contact wearing clothes

For calculation of the MOE for P-AA/MA, the NOEL of 2,000 mg/ kg bw/d from the 28 day rabbit dermal study was divided by the daily systemic dose of 0,088 µg/kg bw/d.

P-AA/MA: $MOE_{\text{indirect skin contact wearing clothes}}$ = 2000,000/0.088 = **2.2×10^7**

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

For calculation of the MOE, the NOAEL of 1,871 mg/ kg bw/ day of PAA-MA was divided by the daily systemic dose of 7.3 x 10^{-2} µg/kg bw/ day, respectively (cf. section 5.1.3.5).

P-AA/MA: MOE $_{\text{oral route from residues on dishes and eating utensils}}$ = 1,871,000 /0.073 = **2.6 x 10^7**

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

For calculation of the MOE for P-AA/MA, the NOAEL of 1,871 mg/ kg bw/ day is divided by the daily systemic dose of 4.133 µg/kg.

P-AA/MA: MOE $_{\text{oral route via drinking water}}$ = 1,871,000/4.133 = **4.5 x 10^5**

5.3.1.5 Exposure scenario: inhalation of dust during washing process

The systemic dose of P-AA/MA via inhalation of detergent dust during the washing process was estimated to amount to 1.4 x 10^{-4} µg/ kg bw/ day for P-AA/MA.

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 NOEC of 1.0 mg/m^3 for P-AA/MA 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/MA** a daily exposure to the NOEC of 1.0 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] = 0.024 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 MOEs for inhalative exposure are calculated as follows:

P-AA/MA: MOE $_{\text{dust inhalation}}$ = 0.024 x 10^3/1.4 x 10^{-4} = **1.7 x 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/MA: ($0.99_{\text{Hand washed laundry}} + 25_{\text{pretreatment laundry}} + 0.088_{\text{wearing clothes}}$) [µg / kg bw/day]
= 26 µg/ kg bw/ day

P-AA/MA: MOE $_{\text{skin contact}}$ = 1,871,000/26 = **7.2×10^4**

Exposure by ingestion:

P-AA/MA: ($0.073_{\text{residues on dishes}} + 4.133_{\text{drinking water}}$) [µg / kg bw/day]
= 4.21 µg/ kg bw/ day

P-AA/MA: MOE $_{\text{ingestion}}$ = 1,871,000/4.21 = **4.4×10^5**

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 copolymers via intended use of polycarboxylate-containing products. As a result, the MOEs for the total estimated systemic dose of copolymers are very high

(P-AA/MA: **MOE $_{\text{skin contact}}$ = 7.2×10^4**; **MOE $_{\text{ingestion}}$ = 4.4×10^5; MOE$_{\text{inhal}}$ = 1.7×10^5**)

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/MA in consumer washing and automatic dishwashing detergents are not considered to cause any risk to human health.

5.3.3 Summary and Conclusion

The polycarboxylates P-AA/MA are widely used in laundry detergents (regular and compact powder) and dishwashing tablets. Thus, consumers are exposed to P-AA/MA 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/MA through residues remaining on eating utensils and dishes after running a typical dishwashing programme.

P-AA/MA have 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/MA demonstrates no irritating potential on rabbits' skin and eyes. Beyond that, there is no indication that P-AA/MA is skin sensitising. Local dermal effects due to direct skin or indirect skin contact with P-AA/MA- containing solutions in hand-washed laundry are not of concern because P-AA/MA 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 1.0 mg/m^3 for P-AA/MA 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 in other studies as the 90 days drinking water study with rats for P-AA/MA at exposure levels well beyond the limit dose, 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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