EUROPEAN COMMISSION

Health & Consumer Protection
Directorate-General

Scientific Committee on Health and Environmental Risks

SCHER

Non surfactant Organic Ingredients and Zeolite-based Detergents

(RPA report J480b/detergents – 30 June 2006)

Scientific Committees
on consumer products
on emerging and newly identified health risks
on health and environmental risk

The SCHER adopted this opinion at its 17th plenary on 29 May 2007

About the Scientific Committees

Three independent non-food Scientific Committees provide the Commission with the scientific advice it needs when preparing policy and proposals relating to consumer safety, public health and the environment. The Committees also draw the Commission's attention to the new or emerging problems which may pose an actual or potential threat.

They are: the Scientific Committee on Consumer Products (SCCP), the Scientific Committee on Health and Environmental Risks (SCHER) and the Scientific Committee on Emerging and Newly-Identified Health Risks (SCENIHR) and are made up of external experts.

In addition, the Commission relies upon the work of the European Food Safety Authority (EFSA), the European Medicines Evaluation Agency (EMEA), the European Centre for Disease prevention and Control (ECDC) and the European Chemicals Agency (ECHA).

SCHER

Questions relating to examinations of the toxicity and ecotoxicity of chemicals, biochemicals and biological compound whose use may have harmful consequences for human health and the environment.

In particular, the Committee addresses questions related to new and existing chemicals, the restriction and marketing of dangerous substances, biocides, waste, environmental contaminants, plastic and other materials used for water pipe work (e.g. new organics substances), drinking water, indoor and ambient air quality. It addresses questions relating to human exposure to mixtures of chemicals, sensitisation and identification of endocrine disrupters.

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SCHER scientific opinion on non surfactant organic ingredients and zeolite-based Detergents, 29 May 2007

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1. BACKGROUND

In 2003, CSTEE adopted a scientific opinion on the environmental impact (reduction in eutrophication) that would result from banning sodium tri-polyphosphates (STPP) in household detergents. The opinion concluded, *inter alias*:

- *"that a quantitative assessment of the extent of eutrophication in EU waters in relation to phosphorus load from different sources, and in particular in relation to STPP contribution, should be performed on the basis of existing experimental and modelling information"*.

In order to further elucidate this issue, the relevant CEFIC sector group, CEEP (European Detergent Phosphate Industry) volunteered to carry out a study entitled: "Development of a European Quantitative Eutrophication Risk Assessment of Polyphosphates in Detergents", in collaboration with Green Planet Environmental Consulting SL and INIA (Spanish National Institute for Agriculture and Food Research and Technology). This report was completed in October 2006.

In addition, the same scientific opinion of SCTEE (2003, "eutrophication-polyphosphates in detergents") concluded that:

- *"that though zeolites (main alternative builders to STPP) do not pose a risk to health or the environment, it was also recommended that further consideration should be given to the risks associated with the co-builders (such as carboxylates, phosphonates etc.), proposing that a risk assessment of these should be conducted."*

Moreover, generally there are concerns over the potential impact on the environment associated with a wide range of non-surfactant substances added to detergents, in particular, organic compounds. As a consequence, DG-Enterprise contracted Risk and Policy Analysts Ltd (RPA) to review these issues and prepare a report with the relevant findings. It should be also noted that within the HERA (Human and Environmental Risk Assessment) project, the health and environmental risks of various types of zeolites (A, P, X) have been recently reviewed, but with no changes in the conclusions.

2. TERMS OF REFERENCE

DG Enterprise would therefore much appreciate further opinions of SCHER, based on the submitted reports. More specifically:

(1) SCHER is requested to assess the overall scientific quality of the RPA report and comment on the methodology and the assumptions used.

(2) SCHER is requested to comment whether the conclusions of the RA concerning the reviewed non-surfactant detergents ingredients (as summarised in Tables 4.11 and 4.12) are valid and in agreement with current literature. Particular consideration should be given to the results concerning the health and environmental risks of the following co-builders in detergents formulations (for which the RA indicates that either concern or some uncertainties exist):

(i) EDTA and EDTA tetrasodium salts (ii) Nitriloacetic acid (NTA) (iii) phosphonates (iv) polycarboxylates.

(3) SCHER is requested to comment on the following key observations of the RPA report (page-84), concerning the analysed non-surfactant organic ingredients: (i) the analysis presented in this report suggests that, for persistent ingredients, there maybe no associated risks (i.e. the PEC/PNEC ratio is less than one) and (ii) that for readily biodegradable substances there is no risk because they are rapidly removed from the environment by biodegradation.

(4) SCHER is requested to comment whether the substitution of phosphate-based detergents in the EU by zeolite-based detergents would lead to a significant increase in health or environmental risks.

3. OPINION

3.1 Question 1

SCHER is requested to assess the overall scientific quality of the RPA report and comment on the methodology and the assumptions used.

3.1.1 General comments

The RPA report gives an overview on the problem of non-surfactant ingredients of detergents used in the EU, with particular attention to the consequences of an increased use of phosphate-free detergents.

The first part of the report describes the situation of detergent uses in the EU-25. Not all information is very recent but, reasonably, in most cases more recent data are not available. So the report offers a good and quite complete picture, up to date as far as possible, of the European uses of detergents.

The second part describes the main non-surfactant chemicals used in Europe in the formulation of detergents. About 50 different ingredients are grouped into 12 main groups. These are briefly described in order to provide basic information on uses, degradation and a very preliminary idea of the potential risk for human health and environment. As a conclusion of this part, a preliminary screening of the chemicals that are likely to be of potential concern and, therefore, would require more attention, is proposed (Table 3.17). The SCHER agrees with this proposal.

In the third part of the report, a more detailed description of selected ingredients is given. This description is generally based on available risk assessment reports, some of them (e.g.: EDTA, NTA) already evaluated by European Scientific Committees (CSTEE, SCHER). A suitable synthesis of the available information is given. Some of the chemicals will be examined with more detail under Question 2.

The fourth part describes the implications (advantages and disadvantages) of an increased use of zeolites, due to the increased use of phosphate-free detergents. Some chapters of this part are extremely synthetic. For example, the overview on eutrophication problems in Europe (Chapter 5.4) is too short for giving an adequate description of the problem. On the other hand, it is not the scope of the report to provide an exhaustive description on eutrophication, and some more detailed documents are quoted.

Finally, the fifth part is a synthesis of the main conclusions and recommendations.

As a general comment, it is the opinion of the SCHER that the overall quality of the report is good and that it could represent a suitable basis of information and most of the assumptions used are acceptable. However, there are some specific points that would require some more detailed comments.

3.1.2 Specific comments

At page 13, a comparison is made between phosphate uses in detergents and fertilisers, by concluding that phosphates used in detergents account for less than 10% of the phosphates used in fertilisers. The statement is misleading. It does not take into account that detergent phosphorus is totally discharged in water (with or without treatment) while phosphorus fertilisers are applied on soil, are partially assimilated by crops, can be strongly bound to soil, and only in part reach surface water. The contribution to surface water is very variable, as a function of many environmental characteristics (soil properties, slope, rain regime, etc) and must be evaluated case by case.

Most of the P from fertilizers is sorbed in soil and therefore normally the amount of P from fertilizers reaching the aquatic environment is below 1 % of the applied rates (exceptions are P-saturated soils and soils with high risks for erosion). If this is taken

into account, the amount of phosphates from detergents reaching the aquatic environment can be more than 10 times higher than the amount of P from fertilizers.

On the other hand, the emission of P from detergents depends on the level of implementation of WWTP.

In Chapter 5 it is not sufficiently clarified that the rules for defining "sensitive areas" are not the same in all member countries. Therefore, the level of tertiary treatment required according to the Urban Waste Water Directive, is different. It follows that some relevant endangered areas are not adequately protected (e.g.: Baltic Sea, Black Sea, Northern Adriatic).

Tables 5.4 and 5.5 (page 67) on the benefits of moving to P-free detergents are misleading. All P-free countries are indicated as having "Few benefits" from the implementation of P-free detergents use, which is obvious! Also this conclusion is misleading. Indeed, in all these countries, the benefits of a P ban have been already attained, and the classification and the scoring is not applicable. The assessment of benefits should be only based on the actual consequences (predicted or already attained) that a P ban would produce on eutrophication.

The partial or complete replacement of P in detergents was the main reason for the fast and large reduction of TP- loads of most of the Eastern European rivers since 1990. The TP concentration in the Danube has decreased from about 200 µg/l at the end of 1980s to about 120µg/l in the last years. This is followed by a large improvement of the ecological state of the Northwestern Black Sea. A complete replacement of P in detergents would be sufficient to reach a target concentration of below 100 µg/l, which corresponds to a good ecological status for many large river systems and to the status of the earlier 1960s (van Gils et al., 2005; Behrendt et al, 2005**).**

It must also be considered that the benefits of moving to P-free detergents are estimated based on a linear relationship, while, in reality, the relationship between phosphate concentrations and eutrophication risk follows a sigmoid curve similar to other biological responses such as toxicity, with threshold for no response and for the maximum potential response. Therefore, a reduction in P-load will only produce the desired benefits if the resulting concentration is below the maximum potential threshold. This issue has not been considered in the assessment, and therefore, the estimated benefits cannot be supported on scientific grounds.

In addition, it should be remembered that the biological response of P is mostly related to the soluble reactive P (SRP). The proportion of SRP at the TP differs for different water bodies but decreases with decreasing TP concentrations. A German survey indicates that average annual TP concentrations below 100 µg/l usually corresponds to SRP concentrations below 25 µg/l (Data of ARGE Elbe and Environmental agencies of German countries). Such low levels of average annual SRP concentrations would lead to very limiting concentrations at least in certain periods of the year (spring, early summer).

Moreover, any kind of intervention will apparently produce low effects if the eutrophication level is in the asymptotic part of the sigmoid curve. Therefore, in very highly eutrophic environments, a gap is possible between the reduction of P-load and the start of evident benefits in the water body. It must be highlighted that the level of eutrophication of most European water bodies is not so extreme and the benefits of P reduction can be evident, although highly variable among water bodies, river basins and regions. The SCHER is currently reviewing a proposal for estimating the benefits, in terms of eutrophication risk reduction, associated to reductions in P emissions.

3.2 Question 2

SCHER is requested to comment whether the conclusions of the RA concerning the reviewed non-surfactant detergents ingredients (as summarised in Tables 4.11 and 4.12) are valid and in agreement with current literature. Particular consideration should be given to the results concerning the health and

environmental risks of the following co-builders in detergents formulations (for which the RA indicates that either concern or some uncertainties exist):
(i) EDTA and EDTA tetrasodium salts (ii) Nitriloacetic acid (NTA) (iii) phosphonates (iv) polycarboxylates.

3.2.1 Risk for human health of non surfactant Organic Ingredients

3.2.1.1 EDTA and EDTA tetrasodium salt

Both chemicals have been subject of risk assessment reports (RAR) reviewed by the CSTEE (see the opinion in September 2003). The main conclusions of CSTEE where the following:

Consumer exposure

According to the RAR consumer exposure to EDTA results primarily by its use in cosmetics, care products, cleansing agents and dish washing products resulting in a total dermal exposure of ≈ 0.72 mg/kg bwt per day, to which household cleaners contribute about 0.12 mg/kg bwt. Since dermal absorption is about 0.001% this route of exposure is considered to be insignificant. As EDTA does not accumulate in biota the only relevant indirect consumer exposure for human occurs via drinking water. Model calculations result in a daily exposure between 0.003 and 0.4 mg/kg bwt. The upper value is based on a worst case scenario because EDTA drinking water levels in central Europe range between 0.5 to 9.6 microgram/L. In the Netherlands drinking water prepared from surface water contained 10 to 30 microgram/L. Even assuming a daily intake of 5 L drinking water containing 30 microgram EDTA/L would result in a daily exposure of about 2 microgram/kg bwt. Therefore the SCHER considers the estimated daily exposure of 0.003 mg/kg as a realistic estimate.

Toxicokinetics

After oral administration of edetic acid, gastrointestinal absorption is poor and accounts for < 20 % of dose. Absorbed material is rapidly excreted with urine and only negligible amounts are metabolised to CO2. Absorption after inhalation has not been studied.

Acute toxicity

In experimental animals, both edetic acid and the Na4EDTA show only low potential for toxicity and LD50 values are in the range of 2 g/kg and above.

Irritation, corrosivity and sensitisation

Both edetic acid and Na4EDTA are mild skin irritants, but comparatively potent eye irritants. Based on limited experimental data and lack of reports of skin and respiratory sensitisation during industrial use of edetic acid and Na4EDTA, the rapporteur concludes that both edetic acid and Na4EDTA do not cause sensitisation by skin contact or by inhalation. Based on the positive results with the Magnusson-Klingman test, the CSTEE has concluded that edetic acid salts may be weak skin sensitisers. Since there are some indications from human studies on skin sensitisation, this aspect should be investigated further. Therefore, CSTEE did not agree with conclusion ii) and proposed conclusion i).

Repeated dose toxicity

Based on a two-year study after dietary exposure, a NOAEL of 500 mg/kg/day is derived for Na3EDTA. Based on this study and a limited number of further non-standard repeated dose toxicity studies, it is concluded that both edetic acid and Na4EDTA have only a low potential for toxicity after repeated oral administration.

The CSTEE supported this conclusion and the derived NOAEL.

Genotoxicity and Carcinogenicity

No mutations were induced in bacteria. An increase in mutant frequency and DNA

damage were found in cultures of mammalian cells after exposure to high concentrations of the free acid which exceeded current recommendations for in vitro tests. In vivo, there was no indication of a clastogenic activity in somatic cells. At doses near the LD50 value, aneugenic effects were found in germ cells of mice.

The CSTEE agreed with the rapporteur that EDTA shows genotoxic activity at extremely high dose levels, most probably involving secondary mechanisms.

Na4EDTA has not been tested for its carcinogenic properties nor were epidemiological data available. There is, however, no evidence of carcinogenicity from lifetime studies conducted on Na3EDTA x 3 H2O in rats and mice.

Based on the available genotoxicity data for EDTA and its salts, the negative data from cell transformation assays and based on negative carcinogenicity data from studies with Na3EDTA x 3 H2O, the CSTEE agrees with the member states' rapporteur that there are no evident concerns regarding this endpoint.

The CSTEE therefore supported conclusion of (ii) for workers and consumers.

Reproductive and developmental toxicity

Conclusion ii) is reached regarding effects on development and fertility for workers and consumers despite a MOS of < 100 for scenario 1 regarding workplace exposure. The RAR again justifies reaching conclusion ii) by deriving a minimal acceptable MOS. Due to the conservative exposure assessment, the steep dose-response, and a plausible mechanism to explain teratogenicity of edetic acid salts (zinc depletion) the CSTEE supported this conclusion.

Conclusion

In repeated dose studies the kidney has been identified to be the most sensitive target organ. Since EDTA shows genotoxic activity at extremely high dose levels only, most probably involving secondary mechanisms, the negative data from cell transformation assays and the negative carcinogenicity data justify the conclusion, that there are no concerns regarding genotoxicity and carcinogenicity. The two-year dietary exposure study in rats showed a NOEL of 500 mg/kg bwt. Taking into account a daily human exposure of 3 microgram/kg bwt, the MOE between NOEL and human exposure is more than 150,000. Consequently, the SCHER does not consider the present use levels as a risk to human health.

3.2.1.2 Nitrilotriacetic Acid (NTA and salts)

So far, the human health part of the RAR has not been evaluated by SCHER. Summarizing information has been taken from the Danish report on non-surfactant organic ingredients (2001), the IARC (1999) documentation and the draft of the RAR (2002) and more recent scientific literature.

Consumer exposure

Exposure to nitrilotriacetic acid, and presumably also to its water-soluble metal complexes, occurs as a result of its presence in household detergents and in drinking water. In Canada the national mean value for NTA in drinking water was 2.82 pg/L (range <0.2 to 20.4 pg/L) with a standard error of f1.53, whereas, for the raw water, the mean concentration of NTA was 3.88 pg/L (range <0.2 to 33.5 pg/L) with a standard error of 2.55. Of a further 21 private well water samples analyzed, 20 samples

showed levels at the limit of detection (0.2 pg/L) and the remaining sample was found to contain 16.9 pg-L-1 of NTA (Malalyandi et al 1979).

According to the RAR consumer exposure in Europe results from the use of Na3NTA in machine dish washing (up to 40%), general cleaning agents (up to 10%), cleaners for disinfecting (up to 10%), oven cleaners (up to 8%), metal cleaners (up to 7%), sanitary cleaners (up to 40%), car care products (up to 8%), floor cleaners and polish (up to

8%), textile colouring agents (up to 7%), glass cleaner (up to 4%), carpet cleaners (< 3%) and plastics cleaners (< 0.5%). These applications result in a chronic dermal exposure of 77 µg/kg bwt/d.

Oral exposure due to use of machine dishwashing products is much lower (0.4 µg/kg bw/d). The use of textile colorants does not account for total exposure.

Indirect exposure via the environment is mainly due to drinking water and fish and has been estimated to be less than 10 microgram/ kg bwt per day.

Due to the physical nature of Na_3NTA inhalation exposure is unlikely.

Based on this information the SCHER estimates a daily consumer exposure is about 100 µg/kg bwt.

Toxicokinetics

Na_3NTA is poorly absorbed from the gastrointestinal tract in humans. When absorbed the compound is rapidly excreted in the urine. About 87% of the absorbed dose was excreted within the first 24 h post dosing. NTA is not biotransformed and is excreted almost entirely unchanged in urine (Budny and Arnold 1973, Anderson et al 1985). Less than 0.1% of dermal doses are absorbed (Anderson and Alden 1989).

Acute Toxicity

The acute toxicity of NTA and its salts in animals are relatively low. In rats LD50 values after oral application range between 1.5 and 2.3 mg/kg, in mice the value is 3.1 mg/kg.

Irritation, corrosivity and sensitation

NTA is a skin irritant. The degree depends on the neutralization (Richardson 1992-1994). A 20% solution of Na_3NTA was not skin irritating in a patch test on 66 persons (Nixon 1971). NTA is a mild eye irritant (Grant and Schuman 1993).

Dermal exposure to NTA does not cause sensitization (Anderson and Alden 1989). A 20% solution of Na_3NTA was not allergenic in a patch test on 66 persons (Nixon 1971).

Repeated dose toxicity

Rats fed for 90 days with diets containing 2,000 ppm (0.2 g/kg bw/day) Na_3NTA and no effects were observed. Rats fed a diet containing 20,000 ppm (2 g/kg bw/day) had abnormal kidneys and a significant decrease in weight gain with a corresponding increase in organ/body weight ratios (liver and kidney) (Nixon 1971). In 12 months feeding study similar effects have been seen with an NOEL of 15 mg/kg per day (Nixon 1972).

Genotoxicity and carcinogenicity

NTA induces tumours only after prolonged exposure to higher doses than those producing kidney toxicity. The reported induction of tumours in rodents is considered to be due to cytotoxicity resulting from the chelation of divalent cationics such as zinc and calcium in the urinary tract (WHO 1996). Dosages of NTA that do not alter Zn or Ca distribution do not produce any urinary tract toxicity even after chronic exposure. When toxic doses are supplied chronically some of the severely damaged tissues may develop tumours (Anderson *et al*. 1985). Rats were given 0.1% NTA trisodium salt in drinking water for 2 years. The exposed animals showed an increase in hyperplasia and tumourigenesis in the kidney (Goyer *et al.* 1981). Nitrilotriacetic acid and nitrilotriacetic acid, trisodium salt were tested for carcinogenicity in mice and rats by oral administration and induced tumours of the urinary system (kidney, ureter and bladder). The monohydrate administered in the diet induced malignant tumours of the urinary system. When administered in drinking water to rats, it induced renal adenomas and adenocarcinomas (IARC 1990).

The mechanism of the renal toxicity and carcinogenicity can be partly explained by chelation of essential divalent metal ions such as Ca^{++}, Mg^{++} and Zn^{++}. In repeated dose

studies in rats daily doses of about 10 mg NTA/kg bwt primarily NTA or its sodium salt are excreted in the urine. At doses of 75 and 250 mg/kg a dose dependent increase in CaNTA and ZnNTA is observed. Whereas the Zn^{++} mostly likely originates from the diet the Ca^{++} is extracted from the epithelia of the nephron, which at least partially explains the nephrotoxicity of NTA (Anderson et al., 1985; Leibold et al., 2002). Renal excretion of carcinogenic FeNTA has not been observed at even higher doses (Anderson et al 1985; Anderson und Kanerva 1979; Leibold et al 2002).

The potential of NTA to cause chromosome abnormalities was investigated in cell culturs (human lymphocytes and Chinese hamster ovary cells) and *in vivo* in mice (micronucleus test). NTA was not found mutagenic in any of the three test assays (Monaldi *et al.* 1988, Loveday *et al.* 1989).

Reproductive and developmental toxicity

The effect on reproduction and development of Na_3NTA in the diet was studied in rats for two generations and in rabbits during a single pregnancy. Na_3NTA was fed to rats either continuously or only during organogenesis (from day 6 to 15) in each pregnancy at one or two dietary levels, 0.1 and 0.5%. For the rabbits doses of 2.5, 25, 100 and 250 mg Na_3NTA/kg body weight were given by stomach tube during organogenesis (on day 7 to 16 of pregnancy). Na_3NTA caused no effects on reproduction or embryonic development in either rats or rabbits.

The only effects of Na_3NTA on the rats were some growth depression in both adults and wealing animals fed 0.5% (Nolen *et al.* 1971). Pregnant mice were given 0.2% NTA in the drinking water from day 6 to 18 of pregnancy. The fetuses were examined for malformations. Skeletal or visceral examination did not reveal any teratogenic effects, although NTA also accumulated in the foetal skeleton (Tjälve 1972).

Conclusion

The kidney is the primary target for NTA toxicity in animals. There is a clear evidence of carcinogenicity in rats and mice, causing kidney, bladder and urinary tract tumours in high doses and after long-term exposure. No human carcinogenic data are available. There is no evidence of teratogenicity and mutagenicity. The 12 months feeding study in rats resulted in a NOEL of 15 mg/kg bwt per day.

A daily human exposure of about 100 microgram/kg bwt has been estimated, to which dermal exposure contributes 77 microgram/kg bwt. Since dermal absorption is about 0.1% and gastrointestinal absorption is poor as well the SCHER estimates a realistic daily exposure of about 10 microgram/kg bwt. The MOE between NOEL and human exposure is about 1500.

Consequently, the SCHER does not consider the present use levels as a risk to human health. However, the SCHER recommends a more precise estimate of human exposure to better estimate the consequences of any increased use of NTA.

3.2.1.3 *Phosphonates*

Phosphonates contain one or more $-C-PO_3-H_2$ groups and are synthesized from phosphorous acid by reaction with formaldehyde and either ammonia or amines.

Examples are **A**mino **t**ris **m**ethylene**p**hosphonic acid (**ATMP**; CAS No. 6419-19-8) or **E**thylene**d**iamine **t**etra **m**ethylene**p**hosphonic acid (**EDTMP**; CAS No. 1429-50-1), **H**examethylene**d**iamine **t**etra **m**ethylene**p**hosphonic acid (**HDTMP**; CAS No. 23605-74-5), **D**iethylene**t**riamine **p**enta **m**ethylene**p**hosphonic acid (**DTPMP**; CAS No. 15827-60-8). 1-Hydroxy ethane diphosphonic acid (**HEDP**; CAS No. 2809-21-4) is formed from PCl_3 and acetic acid (Gledhill and Feijtel 1992).

Consumer exposure

According to the HERA draft report (6/09/2004)10,000 to 50,000t/year is used in Europe, preferentially HEDP and DTFMP, about 12,000 t of this in household products.

The use pattern resembles that of NTA. The range of phosphonate levels in the different products is given as follows: carpet cleaner 2-4%, machine dishwashing detergent 0.2%, laundry additives 0.1-1.9%, compact laundry detergents 0-2.3%, regular laundry detergents 0.02-1.3%, hand dishwashing detergents 0.002-0.04%. The total daily exposure due to the use in the different products is about 0.5 microgram/kg bwt including residues on eating utensils and dishes.

The direct skin contact from laundry tablets and powder is considered to be insignificant. Exposure via drinking water is 0.0032 microgram/kg bwt. Similarly, inhalation of aerosols and powder is about 0.003 microgram/kg bwt.

Based on this information the SCHER estimates a total daily exposure of about 0.5 microgram/kg bwt including drinking water, residues on eating utensils and dishes.

Toxicokinetics

HEDP is poorly absorbed in from the gastrointestinal tract (Caniggia and Gennari 1977). In humans 70-90% of the oral dose of ^{32}P–labelled HEDP was found in faeces after 6 days. After intravenous administration 35-50% of the administered ^{32}P-labelled HEDP dose was excreted in the urine after 6 days. Similarly ^{14}C-labelled EDTMP was poorly absorbed from the gastrointestinal tract and most of the absorbed dose was rapidly excreted by the kidneys or sequestered in bone (Calvin *et al*. 1988). In both studies no metabolism has been detected. Percutaneous absorption has not been studied.

Acute Toxicity

In rats and rabbits phosphonates show low oral and dermal toxicity. In rats oral application of ATMP resulted in LD50 between 2.1 and 2.9 g/kg body weight (SFT 1991, RTECS), after dermal application it was > 6,3 g/kg (RTECS). The pentasodium salt revealed dermal and oral LD50s beyond 15 g/kg (RTECS). Oral and dermal LD50 of HEDP, EDTMP, DTPMP and 1,2,4-Butantricarboxylic acid, 2-phosphono, tetrasodium salt (IUCLID 2000) were > 5.0 g/kg (SFT 1991, RTECS 1997) except an oral LD50 of HEDP of 2.4 g/kg (SFT 1991)

Skin and eye irritatio, sensitizationn

Only moderately skin and eye irritation have been seen with concentrated ATMP and HEDP (SFT 1991).

In Guinea pig maximization test 1,2,4-butantricarboxylic acid, 2-phosphono, tetrasodium salt in a 32% solution was not sensitizing (IUCLID 2000), nor did ATMP, HEDP and EDTMP show sensitizing effects (SFT 1991).

Mutagenicity and carcinogenecity

EDTMP did not show mutagenicity in the Ames test, in the mouse lymphoma assay, unscheduled DNA synthesis and *in vivo* cytogenetics assays (Calvin *et al*. 1988). Similarly HEDP was negative in the Ames test and in mouse lymphoma assay (SFT 1991). In vivo a single oral administration of a 50% solution of 1,2,4-butantricarboxylic acid, 2-phosphono was negative in the mouse micronucleus test " (IUCLID 2000). In a 2 years study in rats EDTMP in the diet up to 100 mg/kg/day did not show carcinogenic or other effects (Calvin *et al*. 1988).

Reproductive toxicity

No differences between the controls and the treated animals were seen with respect to teratogenicity and maternal toxicity, when rabbits were given HEDP by gavage at doses of 25, 50 and 100 mg/kg/day from day 2 to 16 of gestation (Nolen and Buehler 1971). In rats oral doses of 100, 300 or 1,000 mg 1,2,4-butantricarboxylic acid, 2-phosphono/kg given from day 6 to 15 of gestation did not reveal teratogenicity, embryotoxicity or maternal toxicity (IUCLID 2000).

Conclusions

Phosphonates show no sensitizing, mutagenic or reproductive effects and the acute oral and dermal toxicity is low. Based on a long term carcinogenicity study in rats a NOEL of 100 mg/kg bwt has been determined.

a total daily exposure of about 0.5 microgram/kg bwt. Taking into account a daily human exposure of 0.5 microgram/kg bwt, the MOE between NOEL and human exposure is 200,000. Consequently, the SCHER does not consider the present use levels as a risk to human health.

3.2.1.4 Polycarboxylates

Consumer exposure

Except some estimated concentrations in surface water and drinking water there is no appropriate data to assess human exposure. Based on usage and per capita water consumption ECETOC (1993) reported polycarboxylate concentrations in West Germany and Italy to be 30 microgram/L in surface water and less than 3 microgram/L in drinking water. Since dermal absorption of polycarboxylates is 0.3%. the SCHER considers the oral route of exposure to be more relevant and estimates a daily exposure via 2.1 L drinking water of about 0.1 microgram/kg bwt.

Toxicokinetics

When 25 mg/kg bwt of ^{14}C-labelled polycarboxylates P(AA-P)2,500 was given to rats by gavage in the concentrations of 25 mg/kg body weight 0.35% of the administered dose was recovered in expired air, 0.47% in the urine, and 82-94% in the faeces after 4 days. This result indicates a very little absorption from the intestinal tract (ECETOC 1993). In a skin penetration study only 0.3% of the administered polycarboxylates P(AA-P) was recovered after 2 days in expired air, urine and faeces.

Acute toxicity

The LD50 values by oral administration for rats and mice are over 5 g/kg body weight and by dermal administration for rabbits over 5 g/kg body weight (ECETOC 1993), which indicates a low acute oral and dermal toxicity.

Skin and eye irritation

The available data are summarized by ECETOC (1993). A 40% active solution of P(AA)7,000 and a 45% solution of P(AA)8,000 were not irritant to the skin of rabbits. When applied to the eyes P(AA)1,000 or P(AA)1,200 did not damage the cornea or iris. A slight conjunctivae irritation was observed but this cleared within 24 hours after administration. The concentrations of the applied compounds have not been reported. P(AA) with different molecular weights were not found to be sensitising .

Subchronic toxicity

No serious adverse effects were observed by oral, dermal or pulmonal administration (ECETOC 1993). In a 90 days drinking water study in rats at dose levels of 1000, 4000 and 10,000 ppm (62.5, 250 and 1000 mg/kg bwt) the NOEL was 1000 mg/kg bwt.

Mutagenicity and carcinogenicity

No evidence of mutagenic potential for polycarboxylates P(AA) and P(AA-MA) tested in a variety of genetic tests, such as Ames test, gene mutation in mammalian cells (mouse lymphoma), UDS (unscheduled DNA synthesis) assay and micronucleus test (Thompson *et al.* 1989). The International Agency for Research on Cancer (IARC) has evaluated polyacrylic acid and the data available to the working group did not permit an evaluation of the carcinogenicity to humans of polyacrylic acid (IARC 1979).

Reproductive toxicity

P(AA)90,000 and 4,500 and P(AA-MA)12,000 have been administrated by gavage to rats during days 6 to 15 of gestation at dose levels of 500 – 7,000 mg/kg bw/day. No treatment related adverse effects on foetal development (skeletal abnormalities and soft tissue) have been reported (Nolen *et al*. 1989).

Conclusions

P(AA) and P(AA-MA) have a low acute toxicity after oral and dermal administration. Some P(AA) were slightly irritating to rabbit eyes. No sensitizing potential has been identified. There is no indication of genotoxic or teratogenic effects. A long term carcinogenicity study is not available. The NOEL in the 90 days drinking water study is 1000 mg/kg bwt. Due to the low dermal absorption the SCHER concludes that oral ingestion is the predominant route of exposure. Since exposure via drinking water is about 0.1 microgram/kg bwt the MOE is 10,000,000. However, this estimate needs to be confirmed by appropriate data on concentrations in drinking water, food and other possible contributors to human exposure.

3.2.2 Risk for the environment of non surfactant Organic Ingredients

3.2.2.1. EDTA and EDTA tetrasodium salt

Both chemicals have been subject of risk assessment reports (RAR) reviewed by the CSTEE (see the opinion in September 2003).

For surface water, the following concentrations were calculated as PEC regional and PEClocal due to use in household detergents:

PECregional = 95 μg/L

PEClocal = 195 μg/L

Main conclusions of the RAR, for the aquatic compartment where:

1. Conclusion (ii)[1] for most production and use patterns, including the use in household detergents;
2. Conclusion (iii) for :
   - use in industrial detergents
   - use by paper mills
   - use by circuit board producers
   - recovery of EDTA containing wastes.

The CSTEE endorsed these conclusions with the following comments to bullet 2:

'*'For some uses (in particular: industrial detergents, pulp and paper, metal plating, disposal) a PEC/PNEC higher than 1 has been calculated and a risk to aquatic organisms cannot be excluded. Therefore, the CSTEE agrees with conclusion iii) as a preliminary approach.*

Nevertheless, as previously mentioned, exposure assessment is controversial and probably overestimated. Therefore the CSTEE supports the need for a better assessment of exposure by suitable ad-hoc experimental monitoring in relevant emission sites.''

[1] *According to the Technical Guidance Document on Risk Assessment – European Communities 2003:*

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

The final version of the RAR has been published in 2004 (ECB, 2004), but up to now, no additional information has been provided for a more precise exposure assessment. Therefore the SCHER supports the conclusions of the CSTEE.

3.2.2.2 Nitrilotriacetic Acid (NTA and salts)

Trisodium Nitrilotriacetic Acid has been subject of risk assessment reports (RAR) reviewed by the SCHER which expressed an opinion in December 2004.

For surface water, concentrations were calculated as PECregional and PEClocal; the latter was calculated as a worst case due to industrial uses, being impossible a breackdown between uses in industrial and household detergents; the following values were calculated:

PECregional = 4.2 μg/L

PEClocal = 500 μg/L

For the aquatic compartment, the RAR proposed Conclusion (ii) for all production and use patterns.

The SCHER endorsed this conclusion.

3.2.2.3 Phosphonates

The information included here has been mostly taken from the RPA report and from the HERA report, a voluntary initiative conducted by the industry.

Phosphonates are multifunctional acids, which structurally have the phosphonic acid group $-PO_3H_2$ in common. Phosphonates forms salts or complexes of different composition, depending on the chemical composition and the pH of the environment. In detergent formulations these substances are used primarily as acids and as sodium salts.

Phosphonates most commonly used in the detergent industry are described under chapter 3.2.1.3.

Environmental fate and behaviour

Phosphonates are water soluble, with very low Kow values and low volatility. They are not ready biodegradable and the limited information shows some differences in the inherent biodegradability and in the aerobic degradation in soil. ATMP and HEDP seem to be very persistent in soil.

Despite their very low Kow, the potential for binging to sludge in the WWTP is reported as very high, being this mechanism the main responsible for the removal of these chemicals from wastewater to sludge.

PEC calculations

PECs have been estimated using the information included in the RPA report, the TGD default values and HERA parameters. The bases for these calculations are briefly presented below:

- Detergent consumption: Maximum 10kg per person and year; EU average: 7 kg/person and year for Zeolite-based detergents.
- % of phosphonate in detergents
  - Zeolite-based compact powers: 0,2%
  - P-based detergents: 0%
- Phosphonate removal at the WWTP: between 60 and 90 %

If the maximum consumption values are employed, the phosphonate PEC for Zeolite-based compact powers ranges from 11 to 2.7 μg/l depending on the proportion selected for the sludge retention, and reaches 27 μg/l for direct emissions not passing through a WWTP.

For the EU averages, the phosphonate PEC for Zeolite-based compact powers ranges from 7.7 to 1.9 µg/l

Risk for aquatic organisms

The amount of information is limited but overall suggests a relatively low toxicity of phosphonates to aquatic organisms despite the effects related to metal chelating activity and its effects on algal growth. There is however a test showing a high chronic toxicity of HEDP to *Daphnia magna*. If the results of this test are used for the PNEC derivation, a risk for Zeolite-based compact powers is predicted even assuming a 90% removal at the WWTP. Obviously, the risk is higher for direct discharges of untreated effluents. Thus it is really essential to obtain additional information on the chronic toxicity of phosphonates to aquatic invertebrates as promised by industry.

Risk for terrestrial (soil) organisms

The approach selected in the HERA report using NOECs from acute toxicity tests for the PNEC derivation is not acceptable. If the TGD approach is used, a potential risk is observed even for a single application of sludge to agricultural soils, and considering the low biodegradation in soil of some phosphonates, a risk for accumulation in soil should also be considered. Due to the specific properties of phosphonates the use of the equilibrium partitioning method should be applied with care, thus the SCHER strongly recommends the need for conducting chronic toxicity tests on soil organisms.

Risk for secondary poisoning

The Kow of phosphonates is very low and would suggest no bioaccumulation at all. However, the HERA report presents some BCF values which, although below the threshold, indicate a higher potential than expected. These reports should be carefully considered to check that steady-state conditions had been reached.

Conclusions

The amount of information available for conducting a risk assessment of phophonates is very limited and only preliminary assessments can be conducted.

Applying the TGD approach, a potential risk for phosphonates used in Zeolite-based compact powers has been identified for the aquatic and terrestrial (agricultural soil) compartments. The risk for aquatic organisms depends on the validation of contradictory data on the chronic toxicity on aquatic invertebrates, and the risk for soil must be refined using additional ecotoxicity data.

It should be stressed that, as for other chemicals widely used by consumers, the risk should not be related to a few locations related to industrial facilities but could cover a large proportion of the EU territory (water bodies receiving municipal discharges and agricultural soil receiving municipal sludge).

The persistence of these substances and the inconsistencies regarding its bioaccumulation potential recommend a further assessment of long-term and secondary poisoning.

3.2.2.4 Polycarboxylates

The information related to polycarboxylates is even more limited than for phosphonates and no HERA is available.

PEC calculations

PECs have been estimated using the information included in the RPA report, and the TGD default values. The bases for these calculations are briefly presented below:

- Detergent consumption: Maximum 10kg per person and year for Zeolite-based, and 8kg per person and year for P-based detergents. EU averages: 7 kg/person and year for Zeolite-based and 3.9 kg/person and day for P-based formulations
- % of polycarboxylates in detergents
    - Zeolite-based compact powers: 5%
    - Zeolite-based tablets: 3%
    - P-based compact powers: 0%
    - P-based tablets: 2%
- Polycarboxylates removal at the WWTP: 0% (unrealistic worst case for WWTP and realistic case for direct emissions of untreated municipal effluents) and 60% (model estimated value from the USA).

The polycarboxylates worst case PECs for the different detergent formulations are summarised below:

- Zeolite-based compact powers: 0.68 mg/l
- Zeolite-based tablets: 0.41 mg/l
- P-based compact powers: 0
- P-based tablets: 0.22 mg/l

If EU averaged consumption data are employed, the concentrations are reduced to the following figures:

- Zeolite-based compact powers: 0.48 mg/l
- Zeolite-based tablets: 0.29 mg/l
- P-based compact powers: 0
- P-based tablets: 0.11 mg/l

If a 60% of reduction at the WWTP is considered as suggested by Hamilton et al. (1996), the concentrations would be

- Zeolite-based compact powers: 0.19 (EU average)-0.27 (maximum) mg/l
- Zeolite-based tablets: 0.12 (EU average)-0.16 (maximum) mg/l
- P-based compact powers: 0
- P-based tablets: 0.04 (EU average)-0.09 (maximum) mg/l

According to Jop et al. (1997), the removal in the WWTP is explained by sorption to sludge, with, adsorption coefficients, Koc, measured in isotherm tests, of 1060 and 2730 for a resin polymer (RP: a low-molecular-weight polymer MW 4500 to 9000) and for a polymer emulsion (PE: a high-molecular-weight polymer MW 50,000-60,000), respectively; and no evidence of significant biodegradation, although small amounts of radiolabeled CO_2 were produced.

Risk for aquatic organisms

The information compiled in the RPA report indicates a full data set (acute and chronic) with a lowest chronic value of 1.3 mg/l (chronic NOEC for aquatic invertebrates). The validity of these data cannot be confirmed by SCHER but assuming that the data is acceptable a PNEC of 0.13 mg/l should be considered.

A potential risk for polycarboxylates is therefore obtained for Zeolite-based compact powers, Zeolite-based tablets, and P-based tablets using the maximum detergent consumption figures and no retention at the WWTP. If the EU average detergent consumption figures are used the PEC/PNEC ratios are still above 1 for Zeolite-based formulations but not for P-based formulations.

In addition, assuming a degradation/reduction at the WWTP of 60% a potential risk for some Zeolite-based formulations is also identified.

Risk for terrestrial (soil) organisms

Not enough information is available for estimating a PNEC. A potential for accumulation in sludge must be considered.

Risk for secondary poisoning

No information is available

Conclusions

A potential risk for aquatic communities due to polycarboxylates used in Zeolite-based detergent formulations has been identified under worst-case and realistic average conditions. A potential risks for P-based detergents can be identified for worst-case direct discharges but not when the EU average consumption figure is considered or the municipal effluent is discharged through a WWTP.

A proper risk assessment for the terrestrial (soil) compartment cannot be conducted with the available information but accumulation in sludge can be predicted.

It should be stressed that, as for other chemicals widely used by consumers, the risk should not be related to a few locations related to industrial facilities but could cover a large proportion of the EU territory (water bodies receiving municipal discharges and agricultural soil receiving municipal sludge).

3.4 Question 3

SCHER is requested to comment on the following key observations of the RPA report (page-84), concerning the analysed non-surfactant organic ingredients: (i) the analysis presented in this report suggests that, for persistent ingredients, there maybe no associated risks (i.e. the PEC/PNEC ratio is less than one) and (ii) that for readily biodegradable substances there is no risk because they are rapidly removed from the environment by biodegradation.

The answer to this question can be derived from the answers to question 2.

A synthesis of degradation properties for the non-surfactant organic ingredients of major concern is the following:

- Readily biodegradable: NTA
- Non readily biodegradable: EDTA, phosphonates, polycarboxylates.

For the readily degradable NTA, it has been concluded that there is no risk for the environment.

For the non readily degradable, the problem can be summarised as follows:

- EDTA: there is no risk deriving from the use in household detergents; for some other uses risk is unlikely, but a more precise exposure assessment is needed to exclude it;
- Phosphonates: the available information is not sufficient to exclude a potential risk at European level. In fact a potential risk for terrestrial organisms related to the use of sludge as fertilizer has been estimated, as well as a potential risk for aquatic organisms pending on the confirmation of their chronic toxicity to aquatic invertebrates;
- Polycarboxylates: as for phosphonates, the information available is not complete; therefore a possible risk cannot be excluded. In fact the combination of the toxicity data reported in the RPA report and the TGD scenarios, indicates a PEC/PNECaquatic organisms higher than 1 for some zeolite-based detergents under worst-case and realistic scenarios and for some P-based detergents under worst-case scenarios.

It follows that the key observations of the RPA report must be considered with care. Before a conclusive statement on the absence of risk, some additional information must be provided.

3.5 Question 4

SCHER is requested to comment whether the substitution of phosphate-based detergents in the EU by zeolite-based detergents would lead to a significant increase in health or environmental risks.

Among the 50 different non-surfactant ingredients that can be added to detergents, only a few of them will substantially increase their use and emissions as a consequence of the substitution of phosphate-based detergents in the EU by zeolite-based detergents.

In particular, among the chemicals of major concern, it has been envisaged that the use of EDTA and NTA will not significantly change with the move to zeolite-based detergents. Zeolite-based detergents will increase the use of polycarboxylates and, in minor extent, of phosphonates. Minor amounts of these chemicals are already present in some formulations of phosphate-based detergents.

As a consequence of the conclusions on risk assessment for human health and the environment, highlighted in the answer of Question 2, it can be concluded that a significant increase in health risks is unlikely to occur; however, a potential environmental risk for polycarboxylates and phosphonates is possible, and based on the detergent compositions mentioned in the RPA report the potential risks would be higher for zeolite-based than for P-based detergents. Due to a lack of information, some open points have been underlined, and should be addressed for conducting a more thorough comparison of the risks associated to both types of formulations. .

In addition, as stressed in the SCHER Opinion on "Environmental Risk Assessment of non Biodegradable Detergent Surfactants under Anaerobic Condition", it should be noted that the environmental risk assessment conducted for the surfactants are based on the assumption that that effluents are treated through a "generic" WWTP facility before reaching water bodies. As the RPA report indicates that the amount of surfactant is different for zeolite-based and P-based detergents, the surfactant associated risk for direct emissions may also be different.

Therefore, the SCHER recommends that additional information should be provided for a more thorough and complete risk assessment. This is particularly needed for phosphonates and polycarboxylates. It will also imply to complete the surfactant risk assessment with a direct emission scenario representative for the European conditions and refined risk assessment, in particular in relation to soil. The latter will be important for locations where sewage sludge is used in agriculture.

The ban of P detergents or a mixed use of detergents with and without P as well as the use of both substances in both detergent compositions will, in SCHER's view, lead to limited increases of the amount of these substances in relation to a complete replacement of P in detergents for most of the European water bodies.

Then, an assessment of the situation in countries where P-free detergents are in use since a long time would be very helpful.

4. LIST OF ABBREVIATIONS

ATMP	Amino tris methylenephosphonic acid
DTPMP	Diethylenetriamine penta methylenephosphonic acid
EC50	median Effect Concentration
EDTA	Ethylendiammine tetra acetate
EDTMP	Ethylenediamine tetra methylenephosphonic acid
EUSES	European Union System for the Evaluation of Substances

HDTMP	Hexamethylenediamine tetra methylenephosphonic acid
HEDP	1-Hydroxy ethane diphosphonic acid
HERA	Human and Environmental Risk Assessment
LC50	median Letal Concentration
MOS	Margin of safety
NOAEL	no observed effect level
NTA	Nitriloacetic acid
P(AA)	Polyacrylic acid
P(AA-P)	Polyacrylic-propenoic acid
P(AA-MA)	Copolymer of acrylic acid and maleic acid
PEC	Predicted Environmental Concentration
PNEC	Predicted No Effect Concentration
RAR	Risk Assessment Report
SRP	Soluble reactive phosphorus
STPP	Sodium tri-polyphosphates
TGD	Technical Guidance Document
TP	Total Phosphorus
WWTP	Waste Water Treatment Plant

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