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

Sodium percarbonate

(CAS No. 15630-89-4)

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Executive Summary

Sodium percarbonate is mainly used as a bleaching chemical in laundry detergents, laundry additives and machine dishwashing products. The pure product (100 %) is also available for consumers as a laundry additive. Sodium percarbonate may also be used in products for drain cleaning, multipurpose cleaning or for denture cleansing. The amount of sodium percarbonate, which is used in household cleaning products in Europe, was estimated to be 100,000 – 150,000 tonnes in 2001 but the amount is expected to increase the coming years.

Environment

Sodium percarbonate rapidly dissolves in water and dissociates into sodium, carbonate and hydrogen peroxide. Acute ecotoxicity tests with fish and water fleas revealed LC50 values of 71 and 4.9 mg/l. The available data show that the observed aquatic toxicity of sodium percarbonate can be explained by the formation of hydrogen peroxide. Because sodium percarbonate dissociates into sodium, carbonate and hydrogen peroxide, the environmental risk assessment is based on the risk assessment of the individual components.

After use of the household cleaning product, the spent washing liquor (containing the sodium percarbonate) will be disposed via the drain. Neither hydrogen peroxide nor carbonate will be discharged to aquatic ecosystems. Hydrogen peroxide will degraded in the biological waste water treatment plant, while carbonate will be neutralised by the biological waste water treatment plant to bicarbonate. Sodium has a low toxicity and the emitted amount of sodium is relatively low compared to background concentrations and therefore the emitted amount of sodium will not have an effect on the aquatic organisms of the receiving water.

Based on the available data, the use of sodium percarbonate in household cleaning products has no adverse effect on the aquatic ecosystem.

Human health

Sodium percarbonate has a low acute toxicity via the oral and dermal route (LD50 > 1000 mg/kg bodyweight). The existing animal data on acute toxicity show that sodium percarbonate has a local effect. In animal tests a slight irritating effect on the skin was reported for solid sodium percarbonate and it was highly irritating to the rabbit eye (not rinsed). Sodium percarbonate did not have sensitising properties in a test with guinea pigs.

When consumers are exposed to sodium percarbonate, neither hydrogen peroxide nor sodium carbonate will be systemically available due to their effective detoxification (degradation or neutralisation) in the body. Consequently it is to be expected that the concentration of hydrogen peroxide and sodium in the blood and the pH of the blood will not be increased. Therefore, neither sodium percarbonate itself nor hydrogen peroxide or carbonate will reach the organs or the foetus and there is no risk for systemic, developmental or reproductive toxicity. With regard to genotoxicity and carcinogenicity the properties of sodium percarbonate also resemble those of hydrogen peroxide and it can be concluded that there is no concern for humans with regard to a possible genotoxicity or carcinogenicity of sodium percarbonate. The only critical endpoint for sodium percarbonate seems to be local irritation.

Consumers can be exposed to sodium percarbonate due to skin contact with solutions which contain sodium percarbonate, which can be laundry hand washing. However, the estimated concentrations of sodium percarbonate in these solutions are too low to cause skin irritation.

Accidental exposure of the eyes to dry products which contain sodium percarbonate or to solutions of household cleaning products which contain sodium percarbonate could result in eye irritation. Only if the sodium percarbonate concentration in the product or the solution is very high (> 25%) irreversible damage to the eye could occur if the product is not immediately washed out, which would normally be the case.

Acute cases of oral poisoning or effects on human eyes, due to accidental or intentional overexposure to sodium percarbonate, have not been found in the literature.

Based on the available data, the use of sodium percarbonate in household cleaning products has no adverse effect on consumers.

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This report has been prepared by Solvay S.A., Brussels, Belgium.

1. Introduction

1.1 Identity and physical/chemical properties

Sodium percarbonate is an addition compound of hydrogen peroxide and sodium carbonate. Based on the molecular formula, the pure substance sodium percarbonate contains 32.5 % hydrogen peroxide and 67.5 % sodium carbonate (based on weight). Sodium percarbonate is a white crystalline powder.

A melting and a boiling point can not be determined because sodium percarbonate decomposes when heated. The decomposition is exothermic and releases oxygen gas. Determination of log P_{ow} and vapour pressure are not applicable as sodium percarbonate is an ionisable, inorganic compound. The average particle size diameter of sodium percarbonate is in the range of 300 – 900 µm. Sodium percarbonate is readily soluble in water, producing a moderately alkaline solution. The pH is about 10.5 at 1 % concentration. The identity and several physical/chemical properties are summarized in Table 1.

Table 1: Identity and physical/chemical properties of sodium percarbonate

Property	**Results / Remarks**	**Reference**
Molecular formula	$2Na_2CO_3 \cdot 3H_2O_2$	
Molecular Weight	314.06	
CAS number	15630-89-4	
EINECS number	239-707-6	
Average particle size	300 – 900 µm	
Melting Point	Not applicable. Decomposition when heated.	
Density	2.14 g/cm^3	
Bulk density	900 – 1100 kg/m^3 [A]	Bertsch-Frank et al (1995)
Water Solubility	140 g/l	Bertsch-Frank et al (1995)
Vapour Pressure	Negligible	

[A] Data from sodium percarbonate producers show that the bulk density ranges between 900-1200 kg/m^3.

Based on the active oxygen content, the commercialised product sodium percarbonate has a purity of more than 85 %. The product sodium percarbonate can contain up to 15 % inorganic salts e.g. sodium carbonate, sodium chloride, sodium silicates, sodium sulfate, magnesium sulfate, sodium hexametaphosphate and borates. These inorganic salts are present as

impurities or are used as coatings. These coatings have been developed to maintain the stability of sodium percarbonate in household cleaning products.

1.2 Production

Globally sodium percarbonate is produced at 10 – 15 production sites and about half of them are located in Europe.

Sodium percarbonate is produced by the reaction of sodium carbonate with hydrogen peroxide, which can be done via dry, spray and wet processes. In the dry process aqueous hydrogen peroxide solution is sprayed on solid sodium carbonate; a solid-liquid reaction yields sodium percarbonate. In the spray process sodium percarbonate is produced by a fluid bed process. Solutions of sodium carbonate and hydrogen peroxide are sprayed into a drying chamber where the water is evaporated. In the wet process sodium percarbonate is usually prepared by cristallisation possibly in combination with salting out.

1.3 Use

The main user of sodium percarbonate is the household cleaning products industry, which is expected to use more than 95 % of the European sodium percarbonate demand.

Sodium percarbonate is mainly used as a bleaching chemical in laundry detergents (tablets, compact or regular powders), laundry additives and machine dishwashing products. The concentrations of sodium percarbonate in the different household cleaning products are presented in Table 2. However, higher concentrations are used also. Bleach booster products with a sodium percarbonate concentration between 65 and 85 % are placed on the market. Furthermore the pure product (100 %) is available for consumers as a laundry additive. Minor amounts of sodium percarbonate may be used in products for drain cleaning, multipurpose cleaning or for denture cleansing.

The amount of sodium percarbonate, which is used in household cleaning products in Europe, was estimated to be 100,000 –150,000 tonnes in 2001 but the amount is expected to increase the coming years. The amount of 150,000 tonnes will be used as a worst case scenario for the environmental assessment.

Table 2: Sodium percarbonate content in household cleaning products (AISE, 2002a)

Product	**Content sodium percarbonate (%)**	**Typical content (%)**
Laundry regular, powder	7-16	8-16
Laundry compact, powder Laundry compact, tablet	12-21 12-24	12-21 12-20
Laundry additive, powder bleach Laundry additive, tablet	20-40 25-56	23-31 28-56
Machine dishwashing, powder Machine dishwashing, tablet	3-21 8.5	21 8.5

2. Environmental Assessment

2.1 Environmental exposure assessment

In most cases the household cleaning products, which contain sodium percarbonate, are added to tap water during use. For example laundry detergents are dissolved in water during the laundry washing process, while machine dishwashing products are also added to water. After use, the spent washing liquor will be disposed via the drain and finally it will be discharged to aquatic ecosystems (e.g. rivers, lakes, estuaries, sea) after a treatment.

2.1.1 Environmental Fate

Sodium percarbonate rapidly dissolves in water and dissociates into sodium, carbonate and hydrogen peroxide.

$$2\ Na_2CO_3 \cdot 3H_2O_2 \rightarrow 4\ Na^+ + 2\ CO_3^{2-} + 3\ H_2O_2$$

Sodium, carbonate and hydrogen peroxide do not adsorb to sediment. Furthermore there is no distribution or transport to the atmosphere and therefore the environmental risk assessment can be focussed on the aquatic compartment. The environmental fate of hydrogen peroxide and sodium carbonate will be discussed below.

Hydrogen peroxide

Hydrogen peroxide is a reactive substance in the presence of other substances, elements, radiation, materials or cells. Both biotic and abiotic degradation processes are important routes in removal of hydrogen peroxide in the environment:

$$2\ H_2O_2 \rightarrow 2\ H_2O + O_2$$

All organisms contain catalase and other enzymes to degrade hydrogen peroxide. The stability of hydrogen peroxide has been studied extensively (ECETOC, 1993; European Commission, 2001). It's half-life in both surface water and sediment can be significantly less than 1 day but in some cases it can be up to 5 days.

Hydrogen peroxide is rapidly degraded in a biological waste water treatment plant. An activated sludge, respiration inhibition test was conducted according to OECD Guideline 209 (Groeneveld et al., 1999). The test was conducted at concentrations of 0, 1.0, 3.0, 10, 30, 100, 300 and 1000 mg/l. In all test solutions the half-life was less than 2 minutes and therefore it can be concluded that hydrogen peroxide is degraded completely in biological waste water treatment plants. Not only a biological waste water treatment plant but also other domestic clarifiers are able to degrade hydrogen peroxide (Guhl et al., 2001).

Sodium carbonate

The environmental fate of sodium carbonate is presented already in the HERA Sodium carbonate report (HERA, 2002) and for this reason only a short summary of the aquatic fate will be presented here.

An emission of sodium carbonate to water will result in an increase in alkalinity and a tendency to raise the pH value:

$CO_3^{2-} + H_2O \rightarrow HCO_3^- + OH^-$

However, the increase in pH depends on the buffer capacity of water which in most cases is determined by the natural background concentration of bicarbonate. To underline the importance of the buffer capacity, a table is included with the concentration of sodium carbonate needed to increase the pH to a value of 9.0, 10.0 and 11.0 at different bicarbonate concentrations. The data of Table 3 were based on calculations (De Groot et al., 2002).

Table 3: Concentration of sodium carbonate (mg/l) needed to increase the pH to values of 9.0, 10.0 and 11.0 (De Groot et al., 2002).

Buffer capacity[A]	**Final pH[B]**		
	9.0	**10.0**	**11.0**
0 mg/l HCO_3^- (distilled water)	1.1 (0.6)	16 (6.1)	603 (61)
15 mg/l HCO_3^- (10^{th} percentile of 21 European rivers)	2.3 (16)	28 (21)	725 (76)
128 mg/l HCO_3^- (mean value of 21 European rivers)	12 (129)	120 (134)	1646 (189)
233 mg/l HCO_3^- (90^{th} percentile of 21 European rivers)	20 (234)	206 (239)	2502 (294)

[A] The initial pH of a bicarbonate solution with a concentration of 15 – 233 mg/l is 8.3 (calculated).
[B] Between brackets the final concentration of bicarbonate is given.

2.1.2 Monitoring Data

Hydrogen peroxide, inorganic carbon and sodium are naturally present in the environment.

In natural water hydrogen peroxide occurs naturally as a result of dry and wet deposition, photochemical and biological formation or through the oxidation of metals (ECETOC, 1993; European Commission, 2001). Both field and laboratory studies indicate that the major pathway for production of hydrogen peroxide in natural waters is photochemical formation, although it is also introduced to water bodies through rain and biological processes. Natural background concentrations are normally less than 10 µg/l but concentrations significantly higher than 10 µg/l have been reported.

Normally the pH in aquatic ecosystems is significantly less than 10.3 and therefore carbonate is present in very low concentrations in aquatic ecosystems, which explains why monitoring data are not available for carbonate. However, for bicarbonate many monitoring data are available. On overview of the bicarbonate concentration in world river basins has been published by UNEP (1995). The concentration was measured in a total number of 21 rivers in Europe. The 10^{th}-percentile, mean and 90^{th}-percentile were 15, 128 and 233 mg/l,

respectively. The concentrations of the bicarbonate ion were strongly related to Ca^{2+} concentrations which reflect the weathering of rocks. The distribution of bicarbonate followed therefore the same pattern as that of the Ca^{2+} ion.

The sodium ion is ubiquitously present in the environment and it has been measured extensively in aquatic ecosystems. Sodium and chloride concentrations in water are tightly linked. They both originate from natural weathering of rock and from atmospheric transport of oceanic inputs and from a wide variety of anthropogenic sources. The anthropogenic sources of sodium are so pervasive that the concentrations of sodium in water have risen by a factor of 10 to 20 in many rivers in the 20th century. The sodium concentration was reported for a total number of 21 rivers in Europe, with a 10th percentile of 1.9 mg/l, mean of 56 mg/l and 90th percentile of 92 mg/l (UNEP, 1995).

2.1.3 Predicted Environmental Concentrations

To evaluate the potential effect of sodium percarbonate on the aquatic organisms, the concentration of sodium percarbonate in the receiving water (an aquatic ecosystem) must be determined. In other words, the Predicted Environmental Concentration (PEC) must be determined to know the exposure of the aquatic organisms to sodium percarbonate.

To estimate the PEC, computer models can be used. In the European Union the model EUSES has been used to calculate the PEC of organic compounds (Vermeire et al., 1994). In some cases it can also be used for inorganic compounds to obtain a preliminary idea about the order of magnitude of the PEC. Within HERA the EUSES model has been adapted to develop a specific scenario for detergents (HERA, 2001). The HERA detergents scenario assigns a value of 7% of the EU tonnage to the standard EU region, while the Technical Guidance Document (TGD) of the European Commission (1996) uses a default of 10%. Furthermore the HERA detergents scenario increases the emissions at local level by a factor of 1.5, instead of the TGD default factor of 4. These changes introduced by HERA more realistically represent the regional emissions and the local input of substances used in household detergents, as experimentally demonstrated (Fox, 2001).

The PEC_{added} has been calculated using a tonnage of 150,000 t/y and assuming that the compound is inert. There is no distribution to air or sludge and degradation in the waste water treatment plant does not occur. The HERA detergent scenario revealed a $PEC_{regional.added}$ and a $PEC_{local.added}$ of 0.5 and 1.6 mg sodium percarbonate per liter, respectively.

The previous calculations were reported to obtain a preliminary idea about the order of magnitude of the PEC_{added} when the substance would be discharged to aquatic ecosystems, without considering the fate of the compound, effluent treatments and other emission sources. Because sodium percarbonate rapidly dissociates into sodium, carbonate and hydrogen peroxide in water an individual exposure assessment (and risk characterisation) will be performed for these substances.

Hydrogen peroxide

Based on the HERA detergent scenario the $PEC_{regional.added}$ and the $PEC_{local.added}$ of hydrogen peroxide are 0.2 and 0.5 mg/l, respectively. However, hydrogen peroxide is unstable and will be degraded already for a significant extent during use. After disposal the degradation of hydrogen peroxide will continue and hydrogen peroxide will be completely degraded in a biological waste water treatment plant (see section 2.1.1). Not only a biological waste water

treatment plant but also other domestic clarifiers are able to degrade hydrogen peroxide (Guhl et al., 2001). For this reason it can be concluded that the emission of hydrogen peroxide to aquatic ecosystems is negligible.

Carbonate

Based on the HERA detergent scenario the $PEC_{regional.added}$ and the $PEC_{local.added}$ of the carbonate anion are 0.2 and 0.6 mg/l, respectively. However, in reality the total domestic discharge of carbonate to aquatic ecosystems will be completely different because :

- The final discharge of carbonate/bicarbonate will depend very significantly on the domestic waste water treatment method. Normally the pH of the untreated waste water is measured and adapted when necessary (to neutral pH) to optimise the conditions for the domestic waste water treatment plant (WWTP). This means that carbonate is already neutralised to bicarbonate before the domestic WWTP.
- The discharge of organic and inorganic carbon via faeces and urine is much higher than the discharge via household cleaning products. Based on a total amount of 150 million kg of sodium percarbonate used per year and based on 370 million inhabitants in the European Union, the daily use of inorganic carbon is 0.085 g per inhabitant per day. According to Directive 91/271/EEC the biodegradable organic load is 60 g oxygen per inhabitant per day in the EU. If this amount of oxygen is used for the formation of carbon dioxide then the discharge of organic carbon would be equal to 22.5 g per inhabitant per day. This shows that the amount of carbon, emitted via faeces/urine is much higher than the amount emitted via the use of sodium percarbonate in household cleaning products. Due to the biodegradation of organic carbon to inorganic carbon in the waste water treatment plant, it is unlikely that the sodium percarbonate of the household cleaning products has an effect on the final concentration of inorganic carbon in the effluent.

These 2 factors show that the use sodium percarbonate in household cleaning products has a negligible effect on the carbon chemistry of the aquatic ecosystems. The domestic effluent treatment method and the discharges of organic carbon are more important for the carbon chemistry of the receiving water. Even the effect of these 2 factors is questionable. Eutrofication, acidification, deforestation and agricultural practices are known to have an important effect on the carbon chemistry of aquatic ecosystems (Kempe, 1984).

Sodium

It is evident that effluent treatments do not affect the discharge of sodium. Therefore it can be assumed that the total quantity of sodium is emitted to the aquatic ecosystems. Based on the HERA detergents scenario this would result in a $PEC_{regional.added}$ and a $PEC_{local.added}$ for sodium of 0.1 and 0.5 mg/l, respectively.

Although the use of sodium percarbonate in household cleaning products results in an emission of sodium to aquatic ecosystems it is clear that other anthropogenic activitities, e.g. mining and use of road salt, result also in an emission of sodium to aquatic ecosystems. According to UNEP (1995) the sodium and chloride concentrations in water are tightly linked for the major rivers of the world. Furthermore it should be realised that sodium is taken up via food, excreted and emitted to aquatic ecosystems. A normal uptake of sodium via food is 3.1-6.0 g per inhabitant per day according to Fodor et al. (1999) and a similar amount will be emitted to aquatic ecosystems. The daily discharge of sodium, via sodium percarbonate containing household cleaning products, is only 0.3 g per inhabitant per day.

Overview of PEC_{added} values

An overview of the PEC_{added} values is presented in Table 4. Hydrogen peroxide is degraded before discharge to the aquatic ecosysem, while carbonate is neutralised to bicarbonate before emission and therefore the realistic PEC_{added} of these components is 0.

Table 4: Overview of Predicted Environmental Concentrations added (PEC_{added}) to the aquatic ecosystem

Component	**HERA Detergents scenario** **$PEC_{regional.added}$ (mg/l)**	**HERA Detergents scenario** **$PEC_{local.added}$ (mg/l)**	**Realistic scenario** **$PEC_{local.added}$ (mg/l)**
Sodium percarbonate	0.5	1.6	Not applicable
Hydrogen peroxide	0.2	0.5	Negligible
Carbonate	0.2	0.6	Negligible
Sodium	0.1	0.5	0.5

2.2 Environmental effects assessment

2.2.1 Toxicity

Effects on fish

A semi-static acute toxicity study with fathead minnow (*Pimephales promelas*) and sodium percarbonate has been conducted according to GLP (Good Laboratory Practice) and EPA (Environmental Protection Agency) test guidelines (Shurtleff, 1989a). The fathead minnow is a saltwater fish species. Test solutions were renewed daily and the hydrogen peroxide concentration was determined before and after renewal using a titration with potassium permanganate. The measured hydrogen peroxide concentration was used to calculate mean measured sodium percarbonate concentrations. Fish were exposed for 96 hours to mean measured sodium percarbonate concentrations of 0; 1.1; 7.4; 34; 81; 465 and 937 mg/l and observations were made after 24, 48, 72 and 96 hours. The LC50 and NOEC (No Observed Effect Concentration) of sodium percarbonate were 71 and 7.4 mg/l, respectively. No control mortality was observed.

Another fish toxicity test without any quality assessment was reported (Japanese Patent Office, 1989). The original reference was not available but the study was reported in the IUCLID published by the ECB (2000). The test was performed on fish infested with skin parasites. Fish were treated twice a weak for 3 minutes and the NOEC was ≥ 500 mg/l.

Effects on invertebrates

The effects of sodium percarbonate on the water flea *Daphnia pulex* have been studied by Shurtleff (1989b) according to GLP and EPA guidelines. Daphnids were exposed for 48 hours and they were transferred to fresh test solutions daily. The hydrogen peroxide concentrations were measured before and after each renewal using a titration with potassium permanganate.

The measured hydrogen peroxide concentration was used to derive mean measured sodium percarbonate concentrations. Mean measured test concentrations were 0; 2.0; 12; 46; 89; 416 and 835 mg/l. The EC50 and NOEC of sodium percarbonate were 4.9 and 2.0 mg/l, respectively. No control mortality was observed.

Effects in aquatic plants/ algae

Algal studies have been reported by Clarke (1991) but these studies were not performed according to GLP or standard guidelines. In these studies three green algae, *Chlamydomonas eugametos*, *Chlorella emersonii* and *Scenedesmus quadricauda* and three cyanobacteria, *Anabaena variabilis*, *Anabaena* A_4 and *Synechococcus leopliensis* were used. The algae were incubated in microtitre plates (300 µl). Analytical measurements were not available. Reported EC50 values ranged between 8-160 mg/l but these high values are not reliable. Probably hydrogen peroxide degraded during the test period, because the duration was too long for algal tests (140-240 hours). A significant recovery of the algal growth was seen in most cases during the test, which indicates a lack of exposure at the end of the test.

An algal study with *Chlorella vulgaris* has been conducted with hydrogen peroxide under standard test conditions (Degussa, 1991). The EC50 and NOEC of this study were 2.5 and 0.1 mg/l, respectively. Based on the study of Degussa (1991) predicted EC50 and NOEC values for a study with *C. vulgaris* and sodium percarbonate are 7.7 and 0.3 mg/l, respectively.

2.2.2 Derivation of PNEC

The results of ecotoxicity tests with sodium percarbonate, hydrogen peroxide and sodium carbonate are compared in Table 5. The results are expressed as sodium percarbonate, hydrogen peroxide and sodium carbonate concentrations, if applicable. The data of Table 5 show that the amount of hydrogen peroxide, which is released at EC50 concentrations of the fish and invertebrates tests with sodium percarbonate, is sufficient to explain the acute toxicity of sodium percarbonate. However, the amount of sodium carbonate, which is released at EC50 concentrations of the fish and invertebrates tests with sodium percarbonate, is not sufficient to explain the acute toxicity of sodium percarbonate.

Table 5: Comparison of acute toxicity of sodium percarbonate, hydrogen peroxide and sodium carbonate

Test substance	**Species**	**EC50 (mg/l)**			**Reference**
		SPC [A]	**H_2O_2 [A]**	**SC [A]**	
Sodium percarbonate	Fathead minnow	50-100	16-33	34-68	Shurtleff (1989a)
Hydrogen peroxide	Fathead minnow		13-21		Shurtleff (1989a)
Sodium carbonate	Freshwater fish			300-740	HERA (2002)
Sodium percarbonate	*Daphnia pulex*	2-12	0.7-3.8	1.4-8.0	Shurtleff (1989b)
Hydrogen peroxide	*Daphnia pulex*		1.0-5.5		Shurtleff (1989b)
Sodium carbonate	*Ceriodaphnia dubia*			200-227	HERA (2002)

[A] LC_{50} values are expressed as 95 % confidence intervals.

SPC = sodium percarbonate, H_2O_2 = hydrogen peroxide and SC = sodium carbonate.

Based on the results of Table 5, the acute toxicity of sodium percarbonate can be explained by the formation of hydrogen peroxide. The PNEC of hydrogen peroxide is equal to 10 µg/l and algae are the most sensitive species for hydrogen peroxide (European Commission, 2001).

A PNEC or a $PNEC_{added}$ has not been derived for sodium carbonate because (HERA, 2002):

- The natural alkalinity/pH of aquatic ecosystems can vary significantly between aquatic ecosystems and
- Also the sensitivity of the aquatic ecosystems to a change of the alkalinity/pH can vary significantly between aquatic ecosystems.

The increase in pH of the receiving water was used to obtain an idea of the acceptable amount of sodium carbonate which can be added to aquatic ecosystems. Depending on the buffer capacity of the aquatic ecosystem, an estimate of the acceptable amount ranges between 2 and 20 mg/l (see also Table 3). The PNEC of hydrogen peroxide is much lower (10 µg/l) and this confirms that hydrogen peroxide is the component which is responsible for the toxicity of sodium percarbonate.

There is no need to derive a PNEC of sodium percarbonate for risk characterisation because the risk characterisation should be based on the separate risk characterisations of hydrogen peroxide and sodium carbonate. However, to describe the general hazard of sodium percarbonate for aquatic ecosystems in a quantitative way it could be useful to calculate a PNEC. Because sodium percarbonate contains 32.5 % hydrogen peroxide, the PNEC of sodium percarbonate would be equal to 10/0.325 = 31 µg/l.

2.3 Environmental Risk Characterisation

To characterize the risk of sodium percarbonate, the exposure data (section 2.1.3) will be compared with the results of the effects assessment (section 2.2). The risk characterisation will be based on the risk characterisation for hydrogen peroxide, carbonate and sodium.

Hydrogen peroxide

Based on the HERA detergent scenario the $PEC_{regional.added}$ and the $PEC_{local.added}$ of hydrogen peroxide are 0.2 and 0.5 mg/l, respectively. However, hydrogen peroxide will be degraded during use, in the biological waste water treatment plant and even in domestic clarifiers and therefore the emission of hydrogen peroxide is considered negligible (Guhl et al., 2001). The concentration of hydrogen peroxide in the effluent will be similar to natural background concentrations of hydrogen peroxide and therefore there is no risk for the aquatic ecosystem. The PNEC of hydrogen peroxide is equal to 10 µg/l (European Commission, 2001).

Carbonate

Based on the HERA detergent scenario the $PEC_{regional.added}$ and the $PEC_{local.added}$ of the carbonate anion are 0.2 and 0.6 mg/l, respectively. However, the use of sodium percarbonate in household cleaning products will not result in an emission of carbonate to aquatic ecosystems because the domestic effluents are neutralised and because the organic carbon from faeces and urine have a more important effect on the carbon chemistry of the aquatic ecosystems (see section 2.1.3). Eutrofication, acidification, deforestation and agricultural practices are also known to have an important effect on the carbon chemistry of aquatic

ecosystems (Kempe, 1984). For this reason it can be concluded that the use of sodium percarbonate in household cleaning products has a negligible effect on the carbon chemistry of aquatic ecosystems.

The previous paragraph indicated that the acceptable amount of sodium carbonate which can be discharged to an ecosystem would be 2.3 to 20 mg/l (order of magnitude). This was based on the increase of the pH.

Sodium

Based on the HERA detergents scenario the $PEC_{regional.added}$ and the $PEC_{local.added}$ for sodium were 0.1 and 0.5 mg/l, respectively. It is evident that effluent treatments do not affect the discharge of sodium. Therefore it can be assumed that the total quantity of sodium is emitted to the aquatic ecosystems.

Concentrations of 0.1-0.5 mg/l are not expected to have an effect on aquatic organisms because reconstituted water for acute and chronic toxicity tests contain sodium concentrations which range between 3.3 and 105 mg/l (ASTM, 1996). These PEC_{added} values of sodium are also relatively low compared to measured concentrations of sodium in aquatic ecosystems. The sodium concentration was reported for a total number of 21 rivers in Europe, with a 10^{th} percentile of 1.9 mg/l, mean of 56 mg/l and 90^{th} percentile of 92 mg/l (UNEP, 1995). Other anthropogenic activities have most likely a more important effect on the sodium content of aquatic ecosystems. For this reason it can be concluded that the sodium, which originates from the use of sodium percarbonate in household cleaning products, has a negligible effect on the aquatic ecosystems.

2.4 Discussion and Conclusions

Sodium percarbonate rapidly dissolves in water and dissociates into sodium, carbonate and hydrogen peroxide. Acute ecotoxicity tests with fish and water fleas revealed LC50 values of 71 and 4.9 mg/l. The available data show that the observed aquatic toxicity of sodium percarbonate can be explained by the formation of hydrogen peroxide. Because sodium percarbonate dissociates into sodium, carbonate and hydrogen peroxide, the environmental risk assessment is based on the risk assessment of the individual components.

After use of the household cleaning product, the spent washing liquor (containing the sodium percarbonate) will be disposed via the drain. Neither hydrogen peroxide nor carbonate will be discharged to aquatic ecosystems. Hydrogen peroxide will degraded in the biological waste water treatment plant, while carbonate will be neutralised by the biological waste water treatment plant to bicarbonate. Sodium has a low toxicity and the emitted amount of sodium is relatively low compared to background concentrations and therefore the emitted amount of sodium will not have an effect on the aquatic organisms of the receiving water.

Based on the available data, the use of sodium percarbonate in household cleaning products has no adverse effect on the aquatic ecosystem.

3. Human Health Assessment

3.1 Consumer Exposure

Based on information from AISE (2002a) the concentrations of sodium percarbonate in laundry detergents, laundry additives and machine dishwashing products are 7-24, 20-56 and 3-21 %, respectively. However, higher concentrations are used also. A bleach booster tablet with 85 % sodium percarbonate is commercialised also in Europe. The pure product (100 %) is also available for consumers as a laundry additive.

As relevant consumer contact scenarios, skin contact, inhalation, oral uptake and accidental or intentional overexposure of sodium percarbonate were identified and assessed.

3.1.1 Skin contact

Consumers may be exposed to sodium percarbonate via skin contact with solutions which contain sodium percarbonate. A common exposure scenario seems to be laundry hand washing with a detergent and therefore this scenario will be discussed below. Other applications, resulting in exposure to solutions of sodium percarbonate, do exist but they are probably less common or the exposure will be lower.

Laundry hand washing

There is a consolidated overview concerning habits and uses of detergents and surface cleaners in Western Europe issued by AISE (2002b). This list reflects the consumer`s use of detergents in g/cup, tasks/week, duration of task and other uses of products. This overview of AISE (2002b) has been used to calculate the exposure.

The concentration of laundry detergent in the hand washing solution is approximately 1 % (10 g/l). The highest concentration of sodium percarbonates in laundry detergents amounts to 24 % (see Table 2). For this reason the hands and forearms of the consumer are exposed to an estimated sodium percarbonate concentration of 2.4 g/l (= mg/ml). However, a quantity of 15 gram of pure sodium percarbonate can be added as a laundry bleaching additive according to label information from a pure sodium percarbonate product available for consumers in Europe. Based on a volume of 10 liter this would result in an additional concentration of 1.5 g/l. For this reason, in a worst case assumption, the hands and forearms of the consumer are exposed to an estimated sodium percarbonate concentration of 3.9 g/l (= mg/ml).

Using the equations of the HERA guidance document (2001) the following exposure can be derived:

$C_{sodium\ percarbonate}$ = Maximum concentration of sodium percarbonate : 3.9 g/l (= mg/ml)

T_{der} = Thickness of layer on skin: 0.01 cm (HERA 2001; European Commission, 1996)

S_{der} = Exposed area of hands and forearms of adult male: 1980 cm^2 (EPA, 1997)

F = Fraction absorbed in 24 h exposure period: 0.001 (Schaefer et al., 1996).

$EXP_{sys} = C_{sodium\ percarbonate} \times T_{der} \times S_{der} \times F$

$EXP_{sys} =$ 3.9 mg/ml (cm^3) x 0.01 cm x 1980 cm^2 x 0.001 =

0.077 mg sodium percarbonate absorbed in 24 hours

As this is calculated for a 24 h exposure and the exposure time is normally 10 minutes (AISE, 2002b) this has to be corrected by a factor of (24x60/10) yielding an assumed absorption of 5.4×10^{-4} mg per event.

Based on a body weight of 60 kg the estimated systemic dose of sodium percarbonate would be equal to $5.4 \times 10^{-4} / 60 = 8.9 \times 10^{-6}$ mg/kg body weight per event.

Contact with solid product

Another scenario would be dermal contact to a fraction of the solid (0.1%) when filling the washing machine. In this case it can be assumed that the contact lasts less than 1 minute (AISE, 2002b) and only affects a fraction of the hand surface (palms of the hands). According to EPA (1997) the surface of the hands would constitute ca. 840 cm^2, the palms would then be one half, 420 cm^2. Only a fraction of the amount would be soluble and available for absorption. The maximum amount of detergent powder used per event was 150 g. With a maximum amount of 24% sodium percarbonate this would contain 36 g sodium percarbonate. If about 0.1% comes into contact with the skin, this would constitute 36 mg. It can be assumed that only a fraction of this will be soluble and available on the skin for absorption.

Given the very short duration of exposure and the very low levels of material expected to be available for skin absorption, this exposure scenario can be expected to be negligible. In the case of the use of tablets the exposure would be even lower as only the thumb and the index finger of one hand (approximately 2 cm^2) are in contact with the products.

Pure sodium percarbonate is also available as a laundry additive and therefore there could some skin contact with pure sodium percarbonate. Given the very short duration of exposure and the very low levels of material expected to be available for skin absorption, also this exposure scenario can be expected to be negligible.

3.1.2 Inhalation

The dust formation from products containing sodium percarbonate, is so small that the amount is considered negligible for consumers. The negligible inhalation has been confirmed for the laundry washing scenario. According to Van de Plassche et al. (1998) studies indicate an average exposure of about 0.27 µg dust per cup of product used for machine laundering, of which up to 24 % or 0.06 µg is sodium percarbonate. Based on the large particle size of the pure sodium percarbonate, which is available as a laundry additive, the inhalation exposure is considered negligible.

3.1.3 Oral uptake

Oral uptake of sodium percarbonate by consumers via the use of household cleaning products is considered negligible under normal handling and use conditions.

3.1.4 Accidental or intentional overexposure

Accidental or intentional overexposure to sodium percarbonates may potentially occur via:

- oral exposure to products which contain sodium percarbonate,
- oral exposure to solutions of these products in water,
- exposure of the eyes to products which contain sodium percarbonate,
- exposure of the eyes to solutions of these products in water (e.g. due to splashing) and
- inhalation exposure to products which contain sodium percarbonate.

No fatal cases arising from oral uptake of sodium percarbonate (solutions) have been found in the literature. Furthermore case reports related with high exposure to sodium percarbonate (solutions) have not been reported in the medical literature. The German Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV, 1999) published recently a report on products involved in poisoning cases. No fatal case of poisoning with detergents was reported in this report. Detergent products were not mentioned as dangerous products with a high incidence of poisoning.

Accidental spillage may cause eye contact of sodium percarbonate. Cases of eye irritation, which were caused by sodium percarbonate (solutions), have not been found in the literature.

Cases of accidental inhalation exposure to the product sodium percarbonate have not been found in the literature but inhalation of laundry detergent powder by children has been reported in the Unites States (Einhorn et al., 1989). The predominant symptoms were stridor, drooling and respiratory distress. It is unknown if similar cases of accidental inhalation exposure have occurred in Europe.

3.2 Hazard Assessment

3.2.1 Toxicokinetics, metabolism and mechanism of action

Sodium percarbonate is an inorganic, water soluble solid of relatively low molecular weight. Dermal absorption is assumed to be low due to the hydrophilic character and the ionic structure of the substance.

When sodium percarbonate is getting into contact with body fluids it will dissociate into hydrogen peroxide, carbonate and sodium. All three substances are naturally present in the human body. The substances will be discussed separately below.

Hydrogen peroxide

The toxicokinetics, metabolism and distribution of hydrogen peroxide has been described in detail by the European Commission (2001). Hydrogen peroxide is a normal metabolite in the aerobic cell, but there is uncertainty about the true levels of the substance in biological media due to analytical difficulties. The steady state level appears to depend on the balance between its generation and degradation. There are two main hydrogen peroxide metabolizing enzymes,

catalase and glutathione peroxidase, which control the hydrogen peroxide concentration at different levels and in different parts of the cell as well as in the blood. At the site of contact hydrogen peroxide will in part be decomposed by the cells of the tissue of first contact. Remaining hydrogen peroxide diffusing into the capillaries will be immediately decomposed in the blood. Red blood cells remove hydrogen peroxide efficiently from the blood due to a very high catalase activity whereas in the serum catalase activity is low. In view of the high degradation capacity for hydrogen peroxide in tissues and blood it is unlikely that the endogenous steady state level of the substance is affected. In other words, hydrogen peroxide is not expected to be systemically available in the body.

Carbonate

The toxicokinetics, metabolism and distribution of carbonate has been described by the HERA report on sodium carbonate (HERA, 2002) but it will be summarized below. The carbonate could potentially increase the pH of the blood.

$CO_3^{2-} + H_2O \rightarrow HCO_3^- + OH^-$

The major extracellular buffer in the blood and the interstitial fluid of vertebrates is the bicarbonate buffer system, described by the following equation:

$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$

The blood plasma of man normally has a pH of 7.4. Should the pH fall below 7.0 or rise above 7.8, irreversible damage may occur. Compensatory mechanisms for acid-base disturbances function to alter the ratio of HCO_3^- to PCO_2 , returning the pH of the blood to normal. Thus, metabolic acidosis may be compensated for by hyperventilation (increased excretion of carbon dioxide) and increased renal absorption of HCO_3^-. Metabolic alkalosis may be compensated for by hypoventilation (decreased excretion of carbon dioxide) and the increased excretion of HCO_3^- in the urine (Johnson and Swanson, 1987). Therefore, if carbonate is absorbed its concentration will be regulated by these physiological mechanisms and therefore elevated amounts of carbonate are not expected to be available in the body. In other words, carbonate is not expected to be systemically available in the body.

Furthermore it should be realised that an oral uptake of sodium percarbonate results in a neutralisation of carbonate in the stomach by the gastric acid. Significant amounts of gastric acids are present in the stomach (pH about 2) which will result in a formation of bicarbonate and/or carbon dioxide. Therefore it is very unlikely that an oral uptake of sodium percarbonate will result in a pH increase of the blood.

Sodium

Sodium is an essential element in the diet but a high intake of sodium has been accociated with cardio-vascular diseases (Fodor et al., 1999). Sodium is readily absorbed throughout the small intestine and is subject to rapid exchange by the large majority of cells in the body. The main regulation of the body concentrations of sodium takes place in the kidney. The consumer exposure to household cleaning products results in a relatively low exposure to sodium (compared to dietary uptake) and therefore elevated amounts of sodium are not expected to be available in the body. In other words, sodium is not expected to be systemically available in the body.

Conclusion

Under normal handling and use conditions hydrogen peroxide, carbonate and sodium are not expected to be systemically available in the body. Hydrogen peroxide is rapidly degraded in the tissues of first contact and the blood by catalase, carbonate will be neutralised in the blood to bicarbonate. The sodium uptake, due to sodium percarbonate exposure, is relatively small to dietary uptake and the body concentration of sodium will be regulated mainly by the kidney.

3.2.2 Acute Toxicity

Oral toxicity

An acute oral study has been conducted with rats according to EPA test guidelines and EPA GLP guidelines (Glaza, 1990a). Sodium percarbonate was mixed with deionised water and the resulting suspension was administered. The study was conducted at sodium percarbonate dose levels of 700, 1000 and 1500 mg/kg bw (body weight). A total number of 30 rats was used for this study. The LD_{50} was 1034 mg/kg bw. Mortality occurred within 3 days of test material administration. Coloration changes in the glandular portion of the stomach were observed at necropsy and the walls of these stomachs were occasionally thickened as well.

Rats were dosed with sodium percarbonate, as a 10 % suspension in maize oil, at dose levels of 1000, 1700, 2900 and 5000 mg/kg bw (Chater, 1978). This study was not performed according to GLP or standard test guidelines. A total number of 24 rats was used in this study. The LD_{50} was 2000 mg/kg bw. Necropsy findings indicated that an effect was present in the stomach. Inflammation and necrosis were observed. Death was always found to be associated with the stomach and intestine being enlarged and filled with gas.

Another acute oral study has been conducted with mice and sodium percarbonate (Momma et al., 1986). This study was not performed according to GLP or standard test guidelines. A total number of 130 female and male mice were dosed with a solution of sodium percarbonate in water at dose levels of 1500 – 3040 mg/kg bw. The LD50 value was 2050 mg/kg for the males and 2200 mg/kg for the females. At necropsy, dead animals presented a slight degree of congestion or blood spots in the stomach mucosa, and blood was mixed with the stomach contents. Furthermore distension of the gastro-intestinal tract was observed.

Dermal toxicity

A single dose of 2000 mg/kg bw sodium percarbonate was administered to the intact skin of 10 New Zealand White rabbits according to EPA test guidelines and EPA GLP guidelines (Glaza, 1990b). The rabbits were exposed to the test substance for 24 hours. No mortality or test material related clinical signs were observed during the study. The level of dermal irritation was severe. Dermal irritation consisted of slight to severe erythema and oedema and slight to marked atonia, desquamation, corioceousness and fissuring. No other macroscopic findings were observed at necropsy.

Inhalation toxicity

The following data was reported without any quality assessment: LC_0 rat > 4.58 mg/l at an exposure time of 1 hour (ICI, 1977). The original reference was not available but the study was reported in the IUCLID published by the ECB (2000).

Conclusion

Standard acute oral and dermal toxicity studies with a high reliability are available. Acute oral LD50 values in rats and mice were 1034 and 2000 mg/kg body weight, while the acute dermal LD50 in rabbits was > 2000 mg/kg bw respectively. The acute oral toxicity is dependent on the concentration of the administered solution and the vehicle and is due to the local irritating/corrosive effects of the substance. The existing animal data on acute toxicity show that sodium percarbonate has a local effect and that systemic effects are not to be expected.

3.2.3 Skin Irritation

A skin irritation study was conducted with 6 New Zealand White rabbits according to EPA test guidelines and EPA GLP guidelines (Glaza, 1990c). Application of sodium percarbonate to rabbits under 4-hour semi-occluded conditions resulted in reversible slight erythema (mean grade 0.8) and oedema (mean grade 0.1) reactions.

Another skin irritation study was conducted with rats exposed to repeated applications (12 days) of sodium percarbonate, either as solid or as a 1 % aqueous solution (Chater, 1978). This study was not performed according to GLP or standard test guidelines. The powder caused slight to mild irritation to rat skin. Slight erythema and desquamation developed by the 4th application but this did not progress during the remainder of the test period. The 1 % aqueous solution appeared to be non-irritant to rat skin, slight erythema and desquamation only becoming apparent during the last 2 days of the test.

The irritant effect of sodium percarbonate can be explained by the presence and formation of hydrogen peroxide. The available irritation and corrosivity studies of hydrogen peroxide have been reviewed by the European Commission (2001). Furthermore the evaluation of hydrogen peroxide by the EU Commission Working Group on the Classification and Labelling of Dangerous Substances has been finalised in 2001. Based on this evaluation a hydrogen peroxide concentration of 50 % and higher is corrosive, while concentrations of 35-50 % are irritant to the skin. Sodium carbonate (solid) and sodium carbonate solutions are essentially non-irritant for the skin (HERA, 2002). Sodium percarbonate itself is only slightly irritant to the skin, which is consistent with the hydrogen peroxide content being just below the irritation limit of hydrogen peroxide.

3.2.4 Eye Irritation

The eye irritation studies conducted with sodium percarbonate (solutions) are summarized in Table 6.

An eye irritation study was performed with New Zealand White rabbits (Chater, 1978). Ocular irritancy was tested by introducing sodium percarbonate into the rabbit eye, either in powder form, or as 1 % aqueous solution. Initial pain and irritancy were recorded over a period of 7 days. The 1 % aqueous solution was considered not irritant while the powder was considered a severe irritant.

An eye irritation study was conducted which was comprised of three groups of three rabbits (Momma et al., 1986). This study was not performed according to GLP or standard test guidelines. Quantities of 100 mg of the solid test substance were instilled in the rabbit left eyes and the eyes were submitted to three different treatments. One group's eye was left unrinsed, one group's left eye was rinsed after 4 seconds and the third group's eye was rinsed

Table 6: *In vivo* eye irritation tests with sodium percarbonate

Species	**Protocol**	**Test material and concentrations**	**Result**	**Reference / CoR** [A]
Rabbit	Sodium percarbonate was tested Either As 1 % Aqueous Solution Or In Powder Form	1 % Solution and powder	1 %: Slight irritation Powder: severe irritation	Chater (1978) CoR = 2
Rabbit	Dose of 100 mg , rinsed (after 4 and 30 s) and unrinsed eyes OECD Guideline 405	White granules, test material contained several percent of non-ionic surfactant	Without rinse: severe irritation Rinsed after 4 s: no irritation Rinsed after 30 s: mild irritation	Momma et al. (1986) CoR = 1
Rabbit	Dose of 100 mg, exposure for 96 hours, not rinsed EPA OPP 81-4	White granules	Highly irritating	Glaza (1990d) CoR = 1
Rabbit	Dose of 100 mg, exposure for 24 hours, not rinsed OECD Guideline 405	White granular solid, ground to a fine powder before use	Highly irritating	Driscoll (1985a) CoR = 1
Rabbit	Dose of 100 mg, exposure for 24 hours, not rinsed OECD Guideline 405	White granular solid, ground to a fine powder before use	Highly irritating	Driscoll (1985b) CoR = 1
Rabbit	Dose of 10 and 50 mg, exposure for 21 days and 48 hours, respectively, not rinsed OECD Guideline 405	White granular solid, ground before use	Corrosive (10 mg), irreversible effect in one treated eye (three eyes were treated)	Driscoll (1985c) CoR = 1

[A] CoR = Code of Reliability (Klimisch et al., 1997)
Reliability : 1 = valid without restrictions, 2 = valid with restrictions, 3 = invalid and 4 = not assignable.

after 30 seconds. Severe irritation was observed in the eye of the group of animals which had not been rinsed. When the eyes had been rinsed after 4 seconds no lesion in the cornea and iris was observed. Redness, oedema of conjunctiva disappeared after 7 days. When the eyes had been rinsed after 30 seconds no effect on the iris was observed. Redness, oedema of conjunctiva persisted up to day 7.

Rabbit eyes were exposed to 100 mg sodium percarbonate in powder form according to EPA test guidelines (Glaza, 1990d). The eyes were exposed for 96 hours and not rinsed. Necrosis of the conjunctivae was seen in one animal at 48 hours and in six animals at 72 and 96 hours. Sodium percarbonate was considered highly irritating.

A dose of 100 mg sodium percarbonate was instilled in the eye of a female rabbit (Driscoll, 1985a). The eye was exposed for 24 hours without washing. The eye was examined after 1 and 24 hours. A similar study was conducted in which 100 mg sodium carbonate was instilled in the eye of a male rabbit without washing (Driscoll, 1985b). The study was stopped after 5 hours and the eye was examined after 1 and 5 hours. In both studies translucent corneal

opacity, iridial inflammation, moderate to severe conjunctival irritation was observed and sodium percarbonate was considered to be highly irritating.

Amounts of 10 and 50 mg sodium percarbonate were instilled into the eyes of rabbits (Driscoll, 1985c). At the 10 mg dose level observations were made 1, 24, 48 and 72 hours following treatment. Additional observations were made on day 7, 14 and 21 to assess the reversibility of the ocular effects. At the 50 mg dose level observations were made 1, 24 and 48 hours following treatment and this study was stopped after 48 hours. A single 10 mg application of the test material to the non-irrigated eye of three rabbits produced translucent corneal opacity, irridial inflammation, moderate conjunctival irritation and vascularisation of the cornea. Two treated eyes appeared normal 7 days after treatment. Corneal opacity and vascularisation persisted in one treated eye at the 21-day observation and these effects were considered to be irreversible. A single 50 mg application of sodium percarbonate to the non-irrigated eye of one rabbit produced translucent corneal opacity, irridial inflammation and moderate to severe conjunctival irritation. Sodium percarbonate (10 mg) was considered to be corrosive to the eye due to irreversible effects noted in one treated eye.

Conclusion

Results in this section show that the powder sodium percarbonate is highly irritating to corrosive to the eye (not rinsed). The irreversible effect on one rabbit eye was observed when the granular solid was ground before use.

The irritant/corrosive effect of sodium percarbonate can be explained by the presence and formation of hydrogen peroxide. The evaluation of hydrogen peroxide by the EU Commission Working Group on the Classification and Labelling of Dangerous Substances has been finalised in 2001. Based on this evaluation a hydrogen peroxide concentration of 5-8 % will be labelled with “irritating to eyes” (R36), a concentration of 8-50 % will be labelled with “risk of serious damage to eyes” and concentrations higher than 50 % will be “corrosive”. Sodium carbonate (solid) is also irritating for the eye (HERA, 2002).

3.2.5 Sensitisation

A skin sensitisation test was conducted on 24 guinea pigs according to EPA test guidelines and EPA GLP guidelines (Buehler method) (Glaza, 1990e). A naive control group of 10 animals was included. The animals received one application (0.4 ml of a 75 % w/v mixture) per week for 3 weeks for a total of three applications, the naive control animals were not treated during this phase. Two weeks following the third induction dose, a challenge dose (0.4 ml of a 25 % w/v mixture) was administered to the test animals and the naive control animals. Application sites were examined and scored for erythema and oedema at 24 and 48 hours following the induction and challenge applications. Very faint to faint dermal reactions were elicited from all test animals during the induction phase. None of the test or naive control animals reacted to the challenge application of the test. Sodium percarbonate was classified as not-sensitising.

3.2.6 Repeated Dose Toxicity

No animal data are available on repeated dose toxicity studies by oral, dermal or inhalation exposure routes for sodium percarbonate. However, repeated dose toxicity data are available for hydrogen peroxide, carbonate and sodium. The data for hydrogen peroxide have been reviewed by the European Commission (2001).

In a 90-day study with hydrogen peroxide mild duodenal mucosal hyperplasia was seen in catalase deficient mice given hydrogen peroxide in drinking water in concentrations between 100 and 3000 ppm resulting in doses between 78 and 260 mg/kg (Freeman et al, 1997). Both males and females receiving 3000 ppm exhibited significant reductions in body weight and food and water consumption. Animals receiving 300 and 1000 ppm displayed intermittent reductions in food and water consumption. No biologically significant differences in haematology parameters were noted among treated animals relative to controls. Males receiving 3000 ppm displayed significant reductions in total protein and globulin levels (clinical chemistry parameters) in the blood possibly attributed to reduced food consumption or reduced protein absorption caused by mucosal hyperplasia observed in the duodenum of these animals. No treatment-related significant differences in absolute or relative organ weights were noted.

Necropsy revealed no treatment-related gross lesions. Macroscopic evaluation of tissue slides indicated an increase in the cross sectional diameter and wall thickness of the duodenum. Subsequent microscopic evaluation of the duodenum revealed minimal to mild mucosal hyperplasia in eight of nine males receiving 3000 ppm and in seven of ten males receiving 1000 ppm. Minimal mucosal hyperplasia was noted in one of ten males receiving 300 ppm. Minimal to mild mucosal hyperplasia was also noted in ten of ten females receiving 3000 ppm and in eight of ten females receiving 1000 ppm. No duodenal mucosal hyperplasia was noted neither among females receiving 300 ppm nor among males or females receiving 100 ppm. Duodenal mucosal hyperplasia is defined as an increase in mucosal area and an increase of villi size. No other areas of the gastrointestinal tract were affected. Microscopically, no evidence of cellular atypia or architectural disruptions nor any other indications of neoplastic changes were observed; therefore, the treatment-related mucosal hyperplasia noted in this study is not considered to be a pre-neoplastic lesion.

After a 6-week recovery period no significant differences in haematology, clinical chemistry or organ weight parameters were noted among recovery animals. No treatment-related gross lesions were noted during necropsy of animals following the recovery period. No histopathological findings were noted that were attributed to previous treatment among any recovery animals following the recovery period. No mucosal hyperplasia was noted among recovery animals.

Based on dose-related reductions in food and water consumption, and the observation of duodenal mucosal hyperplasia for hydrogen peroxide, the Lowest Observed Adverse Effect Level (LOAEL) was 300 ppm and the No Observed Adverse Effect Level (NOAEL) was 100 ppm (26 and 37 mg/kg/day for males and females, respectively). The food and water consumption decreases among animals receiving 300 and 1000 ppm were intermittent and reversible. Histopathological effects were not present in any organ other than the duodenum. Microscopically, neither evidence of cellular atypia or architectural disruptions nor any other indications of preneoplastic lesions were observed.

All effects noted during the treatment period of the study were reversible. Animals sacrificed following the recovery period were considered biologically normal. No clinical signs of toxicity or morphological effects on any organ systems other than the local effects on the gastrointestinal tract were noted during the study.

In another study on hydrogen peroxide, rats were given by gavage solutions of 0.1 to 1.1 % (v/w), 56-506 mg/kg bw, in water 6 days per week for 12 weeks. At the high dose group of

506 mg/kg bw lesions of the gastric mucosa were reported while the NOAEL was 169 mg/kg bw (0.34 %) (Ito et al., 1976).

If the lowest NOAEL of the study in catalase deficient mice, a very sensitive animal model is considered, the dose of 37 mg/kg/day of hydrogen peroxide is equivalent to a sodium percarbonate dose of 114 mg/kg/day. As the local effect is more dependent on the concentration than on the administered dose the no effect concentration of 100 ppm for hydrogen peroxide would be equivalent to a concentration of 308 ppm of sodium percarbonate.

An oral uptake of carbonate will result in a neutralisation in the stomach by the low pH of the gastric juice and therefore neither local nor systemic effects are expected after oral exposure. Also via other exposure routes (inhalation, dermal exposure) carbonate is not expected to be systemically available in the body due to the limited uptake compared to the neutralisation capacity of the blood.

The effect of repeated exposure of humans to sodium has been studied extensively and has mainly focussed on the effects of sodium on the prevention and control of hypertension. Recommendations on daily dietary sodium intake were reported to be 2.0-3.0 g for a moderately restricted intake and 3.1-6.0 g was considered to be a normal intake (Fodor et al., 1999).

Although a repeated dose study is not available for sodium percarbonate, an additional repeated dose toxicity study in rats with sodium percarbonate is not necessary because the effects can be predicted based on the release of hydrogen peroxide, carbonate and sodium.

3.2.7 Genetic toxicity

Studies with sodium percarbonate are not available but the mutagenicity of hydrogen peroxide has been tested extensively. A review has been presented for example by ECETOC (1996) and the European Commission (2001). A genotoxic potential was found for *in vitro* tests but there was no evidence for *in vivo* mutagenicity. Due to the rapid degradation in the whole body, hydrogen peroxide has no systemic genotoxic potential. Also for sodium carbonate there was no concern with regard to a possible genotoxicity. In contact with body fluids sodium percarbonate dissociates into hydrogen peroxide and sodium carbonate and for this reason sodium percarbonate is considered non-mutagenic under *in vivo* conditions.

3.2.8 Carcinogenicity

Carcinogenicity studies with animals and sodium percarbonate are not available. The only component that could give rise to some concerns with regard to this endpoint is hydrogen peroxide that has been intensively studied for possible carcinogenic effects.

For hydrogen peroxide several studies show that long-term oral administration of 0.1-0.4 % hydrogen peroxide causes an inflammatory response in gastroduodenal tissue of mice. The response is limited to the glandular stomach and, to a lesser extent, to the peri-pyloric and proximal portion of the duodenum. No inflammatory response was observed in the oral cavity, forestomach or distal intestinal tract. The incidence was higher in strains of mice with a low catalase activity. Studies by Ito et al (1982) revealed that cessation of hydrogen peroxide administration causes a regression of lesions induced by prolonged (up to 180d) administration of hydrogen peroxide in drinking water.

The investigations by Ito et al (1981a,b) suggest that this inflammatory response may progress to carcinogenic changes in mice that are catalase deficient. In rats, hydrogen peroxide induced only papillomas; no malignant tumours of the forestomach were seen, even at nearly lethal concentrations (1-1.5% hydrogen peroxide in drinking water). Initiation-promotion studies suggest that hydrogen peroxide is not an initiator in skin, but may be a weak promoter of tumours in the rat at high (>15%) concentrations on the skin, or nearly lethal concentrations (1.5%) in drinking water.

In the 90-d study performed on catalase-deficient, C57BL/6NCrlBR mice that received constant concentrations of 0, 100, 300, 1000, or 3000 ppm of hydrogen peroxide in distilled drinking water for approximately 90 days, microscopically, no evidence of cellular atypia or architectural disruptions nor any other indications of neoplastic changes were observed. Therefore, the treatment-related mucosal hyperplasia noted in this study is not considered to be a neoplastic lesion. This reinforces the conclusion from the data of Ito suggesting that only inflammatory changes seen at nearly lethal concentrations in particularly catalase-deficient species or individuals could possibly lead to local tumours.

In vivo genotoxicity data currently point strongly to the fact that hydrogen peroxide is not an *in vivo* genotoxin. The induction of carcinogenicity by a non-genotoxic mechanism has been proposed (Troll and Wiesner, 1985). The fact that tumours were induced only at the sites where high concentrations of H_2O_2 came directly into contact with the tissues and that the tumours were associated with persistent local inflammation supports a non-genotoxic mechanism for the gastrointestinal tract tumours. It can be underlined also here that three recent studies demonstrated the lack of genotoxicity of hydrogen peroxide when administered *in vivo* at the maximally tolerated dose by different routes (intra-peritoneal, oral (2-wk via drinking water), i.v.). Consequently it can be concluded that hydrogen peroxide is unlikely to be carcinogenic under relevant human exposure conditions.

All recent evaluations have concluded that hydrogen peroxide is of no concern with regard to a possible carcinogenicity in humans (ACGIH, 1995; US FDA, 1991; European Commission, 2001; EPA, 2002).

3.2.9 Toxicity to Reproduction

An animal reproduction study with sodium percarbonate is not available. However, under normal handling and use conditions (non-irritating), sodium percarbonate will not reach the male and female reproductive organs when exposed orally, dermally or by inhalation, as it does not become available systemically (see section 3.2.1). For this reason the substance is not considered toxic to reproduction and it is considered not useful to perform a reproduction study with animals.

An animal reproduction study is not available for hydrogen peroxide. However, a reproduction toxicity study was not required because it is not systemically available in the body (European Commission, 2001).

3.2.10 Developmental Toxicity / Teratogenicity

An animal developmental/teratogenicity study with sodium percarbonate is not available. However, under normal handling and use conditions (non-irritating), sodium percarbonate does not become systemically available (see section 3.2.1). For this reason the substance is not considered toxic to the foetus and it is considered not useful to perform further studies with animals.

An animal developmental toxicity study is not available for hydrogen peroxide. However, a developmental toxicity study was not required because it is not systemically available in the body (European Commission, 2001).

3.2.11 Experience with human exposure

A poison centre report under the UK home accidents surveillance scheme has been prepared by DTI (1998). It summarises an analysis of accidents with household products for the year 1998, which were the most recent data available. However, the report included a survey from 1991 to 1998, which showed that the numbers were relatively constant. Of a total number of accident records of 145,361 only 59 accidents were related to laundry and dishwashing agents. Of these 59 accidents 30 were related with detergents/wash powder, 21 to dishwasher products and 8 to clothes wash liquid.

The accidents with laundry detergents and dishwashing agents mainly involved small children in the age group of 0-4 years. In this age group 5 accidents occurred with wash liquid, 17 with wash powder and 15 with dishwasher products. In the age group 5-14 years only 1 accident each with laundry detergents and dishwashing liquids occurred. For the age group of 15-64 years 2 accidents with washing liquids, 10 with laundry detergents and 5 with dishwashing agents were reported. In the age group of >65 years only 3 accidents were observed.

Poisoning, ingestion and skin contact (referred to as chemical injury) were the main causes of these accidents. Foreign body/eye injuries were reported in 4 cases for washing or dishwasher detergents, thereof 3 in children aged 0-4 years and one in the age group of 15-64 years.

The severity of the accidents seems rather low. No fatalities were reported and 59% of the accidents involving laundry and dishwashing agents could be treated at home. Further 46% could be treated ambulantly by a doctor. None of the patients involved in laundry detergent/dishwashing agent accidents was treated in a hospital. The majority of the accidents in the household with products that could contain sodium percarbonate consist of accidental ingestion or skin contact in particular of small children with seemingly slight effects only. No firm conclusions on the involvement of percarbonate can be drawn, but it is noteworthy that only very few cases of eye irritation were observed.

3.2.12 Identification of critical endpoints

The existing animal data on acute toxicity show that sodium percarbonate has a local effect. In animal tests a slight irritating effect on the skin was reported for solid sodium percarbonate and it was highly irritating to the rabbit eye (not rinsed). The local effect of sodium percarbonate in the eyes can be explained by the presence of hydrogen peroxide because hydrogen peroxide causes irreversible damage to the eye in experimental animals at concentrations of 8 % and higher. A skin sensitisation study was negative.

When sodium percarbonate is getting into contact with body fluids it dissociates into hydrogen peroxide, carbonate and sodium. All three substances are naturally present in the human body. Under normal handling and use conditions (non-irritating) hydrogen peroxide, carbonate and sodium are not expected to be systemically available in the body. For this reason there are no concerns with regard to possible mutagenic, reproductive, teratogenic or

other systemic effects. The only critical endpoint for sodium percarbonate seems to be local irritation.

3.3 Consumer Risk Characterisation

Based on normal habits and uses, the consumer exposure to sodium percarbonate by inhalation, oral uptake and skin contact to solid sodium percarbonate is negligible and therefore the associated risk is also negligible. However, two relevant exposure scenario's were identified and the potential risks will be characterized for both scenario's.

3.3.1 Skin contact with sodium percarbonate via solutions

The estimated exposure to sodium percarbonate due to laundry hand washing was 5.4×10^{-4} mg per event. This is equal to an exposure of 0.54 µg sodium percarbonate, which is equivalent with 0.18 µg hydrogen peroxide, 0.21 µg carbonate and 0.16 µg sodium. Due to the rapid degradation the amount of 0.18 µg will not increase the concentration of hydrogen peroxide in the blood. The amount of 0.21 µg carbonate will not affect the pH of the blood, while the amount of 0.16 µg sodium is negligible compared to the normal daily dietary uptake of sodium of 3.1- 6.0 g (Fodor et al., 1999). For this reason it can be concluded that the exposure to sodium percarbonate via solutions has no systemic effect on the consumers.

Data about the relationship between sodium percarbonate concentration and skin irritation potential are not available. However, to predict the skin irritation potential of sodium percarbonate solutions the hydrogen peroxide concentration could be used. Based on the evaluation of the EU Commission Working Group on the Classification and Labelling of Dangerous Substances a hydrogen peroxide concentration of 50 % and higher is corrosive, while concentrations of 35-50 % are irritant to the skin.

Because sodium percarbonate contains 32.5 % hydrogen peroxide, irritant levels of hydrogen peroxide can not be achieved in solutions. Based on the laundry hand washing scenario (with sodium percarbonate as extra laundry additive) the sodium percarbonate concentration in the solution would be 0.4 %, which is equivalent with a hydrogen peroxide concentration of 0.13 %. When humans are exposed to such a solution the hydrogen peroxide content in the solution is still about 250 times lower than the lower irritation limit of hydrogen peroxide (32.5 %). Therefore it can be concluded that local effects on the skin are not expected when consumers are exposed to sodium percarbonate via solutions (e.g. laundry hand washing).

3.3.2 Accidental or intentional overexposure

Accidental or intentional overexposure to sodium percarbonate may occur via the oral route, via exposure of the eyes (e.g. due to splashing) or via inhalation.

Acute oral LD50 values were 1034 and 2000 mg/kg body weight, while the acute dermal LD50 was > 2000 mg/kg body weight. Based on these LD50 values the uptake of sodium percarbonate by humans must be very high (> 50 g) to reach acute lethal effects. The amount of the household cleaning product which must be ingested is even higher and or this reason it is very unlikely that accidental overexposure results in lethal or severe effects. Typically one would estimate that not more than 5 g of detergent or 1.25 g of sodium percarbonate could be swallowed. For a 10 kg child this would result in a dose of 125 mg/kg bw. Lethal effects in animals occur from 1034 to 2000 mg/kg bw in rodents. However, it is likely that due to the

liberation of hydrogen peroxide in the stomach humans will vomit and not be able to take up lethal amounts of detergents. The poison centre records that have not registered any fatal poisonings due to the swallowing of detergents, and normally only immediately reversible irritation reactions of relatively benign nature corroborate this. Furthermore acute cases of oral poisoning, due to sodium percarbonate ingestion, were not found in the literature.

In vivo eye irritation tests show that the powder sodium percarbonate is highly irritating to corrosive to the eye (not rinsed). Therefore solid sodium percarbonate or household cleaning products which contain sodium percarbonate (e.g. detergents) could potentially result in eye irritation. However, the eye irritation potential of products which contain sodium percarbonate depends on many factors e.g. the sodium percarbonate content, the other components and also the particle size distribution.

An evaluation of hydrogen peroxide by the EU Commission Working Group on the Classification and Labelling of Dangerous Substances revealed that concentrations of 5-8 % will be labelled as “irritating to eyes” (R36), concentrations of 8-50 % will be labelled with “risk of serious damage to eyes” and concentrations higher than 50 % will be “corrosive”. Based on these data “risk of serious damage to eyes” would only occur if the sodium percarbonate concentration is higher than 25 % in a solution.

A solution used for laundry hand washing contains only 0.39 % sodium percarbonate (= 0.13 % of hydrogen peroxide) and for this reason there is no risk for eye irritation if eyes were accidently exposed to such a solution (e.g. due to splashing). Effects on human eyes, due to exposure to sodium percarbonate as such, were not found in the literature. However, a few cases of relatively mild eye irritation have been reported after exposure to detergents (DTI, 1998).

Although accidental oral, eye or inhalation exposure to the product sodium percarbonate has not been found in the literature, ingestion and inhalation of laundry detergent powder by children has been reported in the Unites States (Einhorn et al., 1989). The predominant symptoms were stridor, drooling and respiratory distress. It is unknown if similar cases of accidental inhalation exposure have occurred in Europe.

3.4 Discussion and conclusions

Sodium percarbonate has a low acute toxicity via the oral and dermal route (LD50 > 1000 mg/kg bodyweight). The existing animal data on acute toxicity show that sodium percarbonate has a local effect. In animal tests a slight irritating effect on the skin was reported for solid sodium percarbonate and it was highly irritating to the rabbit eye (not rinsed). Sodium percarbonate did not have sensitising properties in a test with guinea pigs.

When consumers are exposed to sodium percarbonate, neither hydrogen peroxide nor sodium carbonate will be systemically available due to their effective detoxification (degradation or neutralisation) in the body. Consequently it is to be expected that the concentration of hydrogen peroxide and sodium in the blood and the pH of the blood will not be increased. Therefore, neither sodium percarbonate itself nor hydrogen peroxide or carbonate will reach the organs or the foetus and there is no risk for systemic, developmental or reproductive toxicity. With regard to genotoxicity and carcinogenicity the properties of sodium percarbonate also resemble those of hydrogen peroxide and it can be concluded that there is

no concern for humans with regard to a possible genotoxicity or carcinogenicity of sodium percarbonate. The only critical endpoint for sodium percarbonate seems to be local irritation.

Consumers can be exposed to sodium percarbonate due to skin contact with solutions which contain sodium percarbonate, which can be laundry hand washing. However, the estimated concentrations of sodium percarbonate in these solutions are too low to cause skin irritation.

Accidental exposure of the eyes to dry products which contain sodium percarbonate or to solutions of household cleaning products which contain sodium percarbonate could result in eye irritation. Only if the sodium percarbonate concentration in the product or the solution is very high (> 25%) irreversible damage to the eye could occur if the product is not immediately washed out, which would normally be the case.

Acute cases of oral poisoning or effects on human eyes, due to accidental or intentional overexposure to sodium percarbonate, have not been found in the literature.

Based on the available data, the use of sodium percarbonate in household cleaning products has no adverse effect on consumers.

4. References

ACGIH (American Conference of Governmental Industrial Hygienists) (1995). Threshold limit values (TLVs) for chemical substances and biological exposure indices (BEIs), 1995-1996. ACGIH, Cincinatti, OH, 23.

AISE (2002a). Table with concentrations of sodium percarbonate in household cleaning products. Received by e-mail from AISE on 23 May 2002.

AISE (2002b), Table of Habits and Practices for consumer products in Western Europe, 19.04.02.

ASTM (1996). Annual Book of ASTM Standards – Volume 11.05. Standard E 729-88a : Standard Guide for Conducting Acute Toxicity Tests with Fishes, Macroinvertebrates, and Amphibians.

Bertsch-Frank B, Dorfer A, Goor G and HU Süss (1995). Hydrogen peroxide and inorganic peroxy compounds. Ind. Inorg. Chem.: Prod. Uses, 175-198.

BgVV (Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin) (1999). Ärztliche Mitteilungen bei Vergiftungen. ISBN 3-931675-59-9.

Chater BV (1978). Sodium Percarbonate, Acute Oral Toxicity with Histology, Skin and Eye irritation. ICI Report CTL/T/1151.

Clarke CA (1991). The Anti-Algal Activity Of Peroxygen Compounds. Thesis.

De Groot, WA et al. (2002). Addition of sodium carbonate to a solution with sodium bicarbonate to a fixed pH. Solvay Pharmaceuticals Int. Doc. No. 8320/48/01.

Degussa (1991). Chlorella vulgaris, Algenwachstumshemmtest mit Wasserstoffperoxid 35 % G. Bericht Nr. 91/11/01.

Driscoll R (1985a). Acute Eye Irritation Test in the Rabbit. Solvay Duphar Int. Doc. No. 56352/55/95.

Driscoll R (1985b). Acute Eye Irritation Test in the Rabbit. Solvay Duphar Int. Doc. No. 56352/57/95.

Driscoll R (1985c). Acute Eye Irritation Test in the Rabbit. Solvay Duphar Int. Doc. No. 56352/56/95.

DTI (Department of Trade and Industry) (1998). Home accident and surveillance system including leisure activities, 22nd annual report 1998 data, tables 1 to 9.

ECB (2000). IUCLID of sodium percarbonate. CDROM.

ECETOC (1993). Joint Assessment of Commodity Chemicals No. 22 – Hydrogen peroxide. European Centre for Ecotoxicology and Toxicology of Chemicals, Brussels, Belgium.

Einhorn A, Horton L, Altieri M, Ochsenschlager D, Klein B, (1989) Serious respiratory consequences of detergent ingestions in children. Pediatrics 84(3):472-474.

EPA (1997). Exposure Factors Handbook, Volume 1, Table 6-4.

EPA (2002). 40 CFR part 180 [OPP–301217; FRL–6822–7], RIN 2070–AB78, Hydrogen Peroxide; An Amendment to an Exemption from the Requirement of a Tolerance, 9214 Federal Register / Vol. 67, No. 40 9214-9218.

European Commission (1996). TGD - Technical Guidance Document (Parts I-IV) in Support of Commission Directive 93/67/EEC on Risk Assessment for New Notified Substances and Commission Regulation (EC) No 1488/94 on Risk Assessment for Existing Substances.

European Commission (2001). Risk assessment Hydrogen Peroxide, according Regulation (EEC) 793/93 on the evaluation and control of the risks of "existing" substances, Final Draft of 24.04.2001. Available on website: http://ecb.jrc.it/existing-chemicals/

Fodor et al. (1999). Recommendations on dietary salt. Canadian Medical Association Journal, 160, S29-S34.

Fox KK (2001). Environmental risk assessment under HERA: challenges and solutions, Jorn. Com. Esp. Deterg. 31: 213-223.

Freeman C (1997). Hydrogen Peroxide 13-Week Drinking Water Study With 6-Week Recovery Period In C57bl/6ncrlbr Mice. FMC Study Number: I95-2039

Glaza SM (1990a). Acute Oral Toxicity Study Of Sodium Percarbonate In Rats (EPA Guidelines). Sponsored by Solvay Interox. Hazleton Laboratories America Inc., Winsconsin, USA, report no. 90903986.

Glaza SM (1990b). Acute Dermal Toxicity Study of Sodium Percarbonate in Rabbits. Sponsored by Solvay Interox. Hazleton Laboratories America Inc., Winsconsin, USA, report no. HLA 90903987.

Glaza SM (1990c). Primary Dermal Irritation Study of Sodium Percarbonate in Rabbits. Sponsored by Solvay Interox. Hazleton Laboratories America Inc., Winsconsin, USA, report no. HLA 90903988.

Glaza SM (1990d). Primary Eye Irritation Study of Sodium Percarbonate in Rabbits. Sponsored by Solvay Interox. Hazleton Laboratories America Inc., Winsconsin, USA, report no. HLA 90903989.

Glaza SM (1990e). Dermal Sensitization Study of Sodium Percarbonate in Guinea Pigs - Closed Patch Technique. Sponsored by Solvay Interox. Hazleton Laboratories America Inc., Winsconsin, USA, report no. HLA 90903990.

Groeneveld, AHC and WA de Groot (1999). Activated sludge, respiration test with hydrogen peroxide. Solvay Pharmaceuticals, report A.SOL.S.003.

Guhl W & Berends AG (2001). Degradation of perborate in domestic waste water. Tens. Surf. Det. 38, No. 2: 98-102.

HERA (2001). Guidance Document – Methodology. June, 2001. Available on website: http://www.heraproject.com/

HERA (2002). HERA report on sodium carbonate (CAS No. 497-19-8). March, 2002. Available on website: http://www.heraproject.com/

ICI, unpublished report, 1977.

Ito A, Naito M and Watanabe H (1981a). Implication of chemical carcinogenesis in the experimental animal. Tumorigenic effect of hydrogen peroxide in mice. Ann Rep of Hiroshima Univ Res Inst. Nuclear Medicine and Biology, 22, 147-158 [Japanese].

Ito A, Naito M, Naito Y and Watanabe H (1982). Induction and characterization of gastro-duodenal lesions in mice given continuous oral administration of hydrogen peroxide. Gann 73, 315-322.

Ito A, Watanabe H, Naito M and Naito Y (1981b). Induction of duodenal tumors in mice by oral administration of hydrogen peroxide. Gann 72, 174-175.

Ito R, Kawamura H, Chang HS, Toida S, Matsuura S, Hidano T, Nakai S, Inayoshi Y, Matsuura M and Akuzawa K (1976). Oral safety of hydrogen peroxide acute and subacute toxicities. Toho Igakki Zasshi (J Medical Soc Toho), 23, 531-537 [Japanese, English translation].

Japanese Patent Office (1989). A method of eliminating the ectoparasitic sucking parasites which infest marine-type cultivated fish. The laid-open patent gazette, 22nd December. Publication number 1-317346.

Johnson W, Swanson K (1987). Final report on the safety assessment of sodium sesquicarbonate, sodium bicarbonate, and sodium carbonate. J. Am. College Toxicol., 6, 121-138.

Kempe, S (1984). Sinks of the anthropogenically enhanced carbon cycle in surface fresh water. Journal of Geophysical Research, Vol. 89, No. D3, page 4657-4676.

Klimisch HJ et al. (1997). A systemic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regulatory Toxicology and Pharmacology 25, 1-5.

Momma J, Takada K, Suzuki Y and M Tobe (1986). Acute Oral Toxicity and Ocular Irritation of Chemicals in Bleaching Agents. Shokuhin Eiseigaku Zasshi, 27 (5), p. 553-560.

Shurtleff LE (1989a). Solvay Interox America Sodium Percarbonate And Hydrogen Peroxide - Acute Toxicity To The Freshwater Fish - Pimephales Promelas. Burlington Research Inc., 1-32.

Shurtleff LE (1989b). Solvay Interox America Sodium Percarbonate And Hydrogen Peroxide - Acute Toxicity To The Freshwater Invertebrate - Daphnia Pulex. Burlington Research Inc., 1-40.

Troll W and Wiesner R (1985). The role of oxygen radicals as a possible mechanism of tumor promotion. Ann Rev Pharmacol Toxicol 25, 509-528.

US FDA (Food and Drug Administration) (1991) Hydrogen peroxide, affirmation of GRAS status as a direct human food ingredient with specific limitations. Fed Reg 48, 223, 52323-52333.

UNEP (1995). Water quality of world river basins. UNEP Environment Library 14, Kenya.

Van de Plassche et al. (1998). Moret Ernst & Young Management Consultants. Second Draft, Rep. No. 601503 013, Nov. 1998 1-64.

Vermeire, TG et al. (1994). Uniform system for the evaluation of substances: principles and structure. Chemosphere, Vol. 29, No. 1, pp. 23-38.

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