Peracetic Acid (CAS No. 79-21-0) and its Equilibrium Solutions

JACC No. 40

ISSN -0733-6339-40

Brussels, January 2001

ECETOC JACC No. 40

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EXECUTIVE SUMMARY

This report has been produced as part of the Joint Assessment of Commodity Chemicals (JACC) programme. It presents a critical evaluation of the physicochemical, ecotoxicity and toxicity data of peracetic acid (PAA) solutions. At present no other comprehensive review is available. A risk assessment, inter alia, will be required under the EU Biocidal Products Directive[a].

Most studies have been performed with different grades of equilibrium PAA solutions, i.e. formulations containing PAA, acetic acid and hydrogen peroxide dissolved in water in different concentration ratios. PAA solutions are clear, colourless and acidic liquids with a pungent vinegar-like odour. Upon dilution with water, their components tend to re-equilibrate slowly within several days. Solutions with a high (> 15%) PAA content can produce flammable vapours and exothermic decomposition can occur, liberating large volumes of oxygen gas. To guard against this, commercial PAA formulations are stabilised.

If released into the environment PAA will be distributed almost entirely to the aquatic compartment, where it is degraded by hydrolysis or decomposition. Hydrolysis is faster at high pH, such as in seawater. Biodegradation is rapid, although limited by the biocidal effect of PAA at higher concentrations. Bioaccumulation is not expected to occur.

PAA solutions are acutely toxic to aquatic organisms. The toxicity is related to the PAA content, except for solutions with a relatively high ratio of hydrogen peroxide. In those cases, the toxicity is attributable to the hydrogen peroxide.

The studies of acute mammalian toxicity do not reveal a clear dose-response that could be related to the PAA content or concentration alone. A particular problem with the inhalation studies is the instability of the vapour/aerosol phase. The available repeated-dose toxicity studies suffer from deficiencies in reporting, inadequate histopathological examination and limited number of dose levels tested. The presence of infectious disease in a number of the animal studies obscured and confounded the test findings. It was thus not possible to derive clear, no-adverse effect levels from the existing studies.

In spite of these limitations, it can be concluded that the main effect of PAA seen in experimental animals is severe irritation and corrosion of skin, eyes and mucous membranes. This is consistent with information on human exposure. However, the limited data available suggest that a systemic effect after repeated exposure to PAA cannot be completely excluded. The skin sensitisation potential of PAA appears to be low. The data do not raise immediate concern for mutagenicity, carcinogenicity or toxicity to reproduction.

[a] European Parliament and Council Directive 98/8/EC concerning the placing of biocidal products on the market (EU, 1998)

THE ECETOC SCHEME FOR THE JOINT ASSESSMENT OF COMMODITY CHEMICALS

This report has been produced by an ECETOC Task Force as part of the Joint Assessment of Commodity Chemicals (JACC) programme for preparing critical reviews of the toxicology and ecotoxicology of selected existing industrial chemicals. In the programme, commodity chemicals (i.e. those produced in large tonnage by several companies and having widespread and multiple uses) are jointly reviewed by experts from a number of companies with knowledge of the chemical. It should be noted that in a JACC review only the chemical itself is considered; products in which it appears as an impurity are not normally taken into account.

This report presents a critical evaluation of the ecotoxicology, toxicology and physicochemical properties of peracetic acid (PAA, CAS No. 79-21-0) and its equilibrium solutions. Commercial grades (formulations) of equilibrium PAA contain the main components PAA, hydrogen peroxide (H_2O_2) and acetic acid (HOAc) dissolved in water at a number of different concentration ratios. A distilled (non-equilibrium) solution containing PAA and water is also marketed. These PAA solutions are reviewed here together because they contain PAA and have similar physicochemical properties, environmental and (eco)toxicity profiles and use patterns.

In this report, for each study, the composition of the solution (formulated product) tested has been specified as far as possible in terms of its content of PAA, H_2O_2 and HOAc. In addition, for each of the toxicological and ecotoxicological studies the actual dose or concentration of the main component PAA is given.

Where relevant, the Task Force has assigned a Code of Reliability (CoR)[a] to (eco)toxicological studies to reflect the degree of confidence that can be placed on the reported results. The criteria used to assess and categorise reliability are included in Appendix B.

[a] A list of special abbreviations used throughout this report is at Appendix A

1. SUMMARY AND CONCLUSIONS

This report reviews the available physicochemical, ecotoxicity and toxicity data on different peracetic acid (PAA) solutions. PAA is completely soluble in water and solutions are clear and colourless with a pungent vinegar-like odour. PAA solutions are acidic (pH < 1).

PAA is produced commercially as a solution in which PAA is in equilibrium with hydrogen peroxide (H_2O_2), acetic acid (HOAc) and water, or as a distilled (non-equilibrium) solution containing primarily PAA and water. Equilibrium solutions are generally prepared by reacting glacial HOAc with H_2O_2 in the presence of a catalyst such as mineral acid. Specific grades are formulated by controlling the concentration and amount of H_2O_2 and HOAc used during the manufacturing process. Commercial PAA grades (formulations) are available in PAA concentrations ranging from about 0.3% to 40% by weight.

The production of non-equilibrium solutions involves the vacuum distillation of PAA from a mixture containing HOAc, H_2O_2, a catalyst (e.g. mineral acid) and de-ionised water. Final formulations contain only minor amounts of HOAc and H_2O_2. Distilled PAA solutions are produced on site or shipped, normally in concentrations ranging from 25 to 40%. These grades are usually shipped cooled (< 0°C) to slow down the hydrolysis reaction.

Major uses of PAA are in chemical synthesis, disinfection and bleaching. PAA is also generated *in situ* from laundry detergents containing sodium perborate or sodium percarbonate and tetra-acetyl ethylenediamine (TAED).

Emissions of PAA to the environment through production and use are considered negligible due to the processes applied. However, the current emission situation is not well described.

Possible routes of human exposure to PAA are by inhalation of vapours or aerosols during production and use as well as dermal contact, mostly to diluted solutions. The available data on workplace exposure are limited. This may be due partly to difficulties in the analytical determination of PAA in air samples and to the instability of PAA in air.

The decomposition of PAA is strongly exothermic, liberating large volumes of oxygen gas. Decomposition can be initiated by high temperatures, high pH, and contamination with metal catalysts such as copper, iron, chromium, and incompatible organic materials. To prevent decomposition, commercially available equilibrium and distilled formulations contain low concentrations of proprietary stabilisers, which protect against decomposition induced by metal ions and minor contamination.

Most of the equilibrium grades containing less than 15% PAA exhibit closed-cup flash points, but no open-cup flash point. Thus, these grades are not flammable where the liquid is open to the atmosphere. Grades containing greater than 15% PAA exhibit both open and closed-cup flash points and the vapours can be flammable.

Volatilisation from aqueous solutions is relatively low, but dependent on the partial vapour pressure. When PAA formulations are diluted with water, the solution slowly begins to re-equilibrate in a temperature dependent reaction until a final equilibrium is attained. At ambient temperature re-equilibration usually takes several days.

Mackay level 1 calculations suggest that, once released into the environment, PAA is expected to partition mainly (> 99%) to the aquatic compartment, while a minor part (< 1%) will be distributed into the atmosphere. No partitioning of PAA into soil, suspended matter or biota is expected. Based on its chemical reactivity and short half-life, PAA is not expected to persist in the atmosphere. Airborne PAA vapours have a low stability, with a half-life of about 20 minutes at ambient temperature. When entering the aquatic environment, PAA is subject to a concentration-, pH- and temperature-dependent hydrolysis or decomposition; the half-life is lower as pH increases. At acidic pH, the half-life of PAA will be around 7 to 12 days, while at neutral or alkaline pH, half-lives may be 1 day or less. In seawater degradation is expected to be rapid (half-life < 1 h). In soil a diluted PAA solution will be rapidly degraded by hydrolysis and decomposition evoked by transition metals. At low PAA concentrations, biodegradation could contribute to degradation in soil and surface waters. In sewage treatment plants with adapted activated sludge PAA is rapidly biodegraded. The low octanol-water partition coefficient of PAA (log P_{ow} = -0.52) suggests that PAA has no potential to bioaccumulate.

Several studies on acute toxicity to aquatic species are available for all trophic levels. PAA formulations were toxic to algae. The lowest 120-h no-observed-effect concentration (NOEC) of 0.13 mg PAA/l was found for *Selenastrum capricornutum*, with an EC_{50} (median concentration expected to have an effect in 50% of the test organisms) value of 0.18 mg/l for growth inhibition. PAA was also toxic to *Daphnia magna* with 48-h EC_{50} values of 0.5 to 1.0 mg PAA/l. Toxicity to fish was lower and 96-h LC_{50} (median concentration expected to cause the death of 50% of the test organisms) values ranged from 0.9 to 3.3 mg PAA/l in most freshwater species. In general, the aquatic toxicity tests were reproducible if concentrations were expressed as PAA irrespective of the concentrations of H_2O_2 and HOAc. Thus, the PAA concentration alone may explain the toxicity of PAA formulations. However, when PAA concentrations are low compared to H_2O_2 concentrations, H_2O_2 apparently contributes to the toxic effects, in particular for algae and daphnids. In these cases, the effect concentrations of PAA formulations are close to those of H_2O_2 alone. For fish there was not always evidence of an additional toxic effect of H_2O_2. The results of the aquatic toxicity studies also suggest a relationship between the size of the organisms and their sensitivity. Small test organisms were more sensitive than larger organisms, probably because of their high body surface-weight ratio, which enables a relatively high uptake of the test substance (per gram body weight). This phenomenon can be related to the relatively non-specific mode of action of the compound, i.e. its oxidising properties, which is relevant to all organisms.

Only few data on the toxicokinetic properties of PAA in mammals are available. Due to the high water solubility and low octanol-water partition coefficients, absorption into the circulation would be expected to be limited. However, PAA seems to be rapidly absorbed through damaged skin when the skin barriers are destroyed due to the corrosivity of PAA solutions.

Distribution is only likely in body fluids and limited by the degradation of PAA. PAA may be degraded in the organism either non-enzymatically, by hydrolysis, dismutation or reaction with reducing agents such as cysteine and glutathione (GSH), or enzymatically by catalases or peroxidases. The catalase reaction with PAA is independent of the PAA concentration and may therefore be saturated. H_2O_2 is also degraded by peroxidases, catalases and a number of antioxidants and thus the equilibrium between PAA, H_2O_2 and HOAc will also be influenced by the continuous elimination of H_2O_2 from the equilibrium under physiological conditions.

PAA possesses a moderate acute toxicity via the oral route. The acute oral toxicity of PAA solutions is dependent on the composition (i.e. the relative content of PAA, H_2O_2 and HOAc) and concentration of the applied (diluted) test solution. Usually PAA solutions containing less than 10% of PAA are of low oral toxicity. The acute dermal toxicity of PAA solutions in rabbits is relatively low and depends upon the applied concentration and presence of local irritations. The available acute inhalation toxicity studies in rats and mice with aerosols and vapours derived from different PAA solutions suffer from difficulties in achieving and measuring constant PAA concentrations due to the instability of the substance itself and the aerosol droplets. Consequently, the LC_{50} values show a relatively wide variation, the main effect being local irritation of the respiratory tract. The predominant effect in all acute toxicity studies is local irritation at the site of contact, which strongly depends on the applied concentration.

PAA solutions containing > 10% PAA were severely corrosive to rabbit skin already 3 minutes after application. Formulations containing between 3.4 and 5% PAA were corrosive to rabbit skin after occluded exposure for 4 or 24 hours. Dilutions containing 0.034 to 0.35% PAA were reported to be not irritant or slightly irritant. PAA solutions are corrosive or severely irritant to the rabbit eye at concentrations of 0.2% and higher. A study of sensory irritation in rats revealed an RD_{50} (concentration inducing a 50% reduction of respiratory rate) value of 21.5 to 24.1 mg PAA/m^3.

No evidence for skin sensitisation was observed in two Bühler tests in guinea pigs with different solutions of PAA. In one guinea pig maximisation test a positive result was claimed, but the report does not allow a critical evaluation of the results. Despite the use of PAA in hand and surface disinfection no cases of skin sensitisation have been reported in humans. Taken together, there seems to be no indication for a skin sensitisation potential of PAA solutions in humans.

The available repeated dose toxicity studies in experimental animals suffer from deficiencies in reporting, including uncertainties about the composition, concentration and stability of the test substance, inadequate histopathological examination and limited number of dose levels tested. In a number of studies the test animals suffered from infectious diseases and it remains unclear to what extent the reported effects are the result of administration of PAA. It is not possible to derive clear, no-adverse effect levels from the existing studies. In spite of these limitations, the following conclusions may be drawn.

The predominant effects after repeated oral, dermal or inhalation exposure of experimental animals to PAA appear to be related to local irritation at the site of contact. The toxicokinetic data suggest that PAA might become available systemically when the detoxifying enzyme systems are saturated. The detoxification reaction could then be slower than the speed of distribution to organs, such as liver and kidney.

Limited information is available on the effects of PAA on deoxyribonucleic acid (DNA) and its potential to induce gene and chromosome mutations *in vitro* or *in vivo*. Bacterial tests showed predominately negative results. These tests are of limited value because PAA is a biocide and will exert cytotoxicity at low doses. In most cases, cytotoxicity could be diminished by the addition of an exogenous metabolic system. Two DNA repair tests in human foetal lung cells did not indicate a genotoxic potential of PAA. In the *in vitro* chromosome aberration test, positive findings were obtained only at cytotoxic concentrations. Under *in vivo* conditions, PAA did not produce micronuclei in two mouse micronucleus tests after oral administration. In one study, the authors claimed to have observed positive effects in a series of chromosomal aberration tests with single intraperitoneal and dermal administration. The validity of this test is however highly questionable due to serious deficiencies in the experimental procedure and reporting. In an *in vivo / ex vivo* assay of unscheduled DNA synthesis (UDS) in rats after oral administration, PAA did not show a genotoxic potential. Overall these data do not raise immediate concern with regard to the mutagenic potential of PAA.

No specific data are available on the carcinogenicity or chronic toxicity of PAA. A limited initiation-promotion study on mouse skin indicates that PAA might have a tumour-promoting potential, which is not unusual for a corrosive substance.

Limited data are available on reproductive toxicity of PAA in experimental animals. Summary publications on multiple-generation studies indicate no effect on reproduction and development, offering some reassurance for this endpoint.

Human experience with PAA is limited to reported effects seen after acute inhalation and dermal exposure. Vapour concentrations below 0.5 mg PAA/m^3 (0.16 ppm) seem to be well tolerated. Concentrations up to 1.2 mg/m^3 (0.38 ppm) were not immediately irritant but unpleasant after exposure for an extended time period. Human eye irritation seems to be the most pronounced effect after exposure to PAA vapours or aerosols. Washing hands with a 0.2% PAA solution was without effect; higher concentrations of 0.5% PAA caused skin irritation when used as a wash solution.

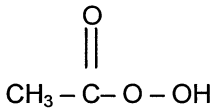
In conclusion, the main effect of PAA reported in mammalian toxicology studies was severe irritation and corrosion of skin, eyes and mucous membranes. This is consistent with reports of effects of human exposure. The skin sensitisation potential of PAA appears to be low. The limited data available from the experimental studies suggest that a systemic effect following repeated exposure to PAA cannot be completely excluded. The available data do not indicate an immediate concern for mutagenicity, carcinogenicity or toxicity to reproduction.

2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS

2.1 Identity

Name:	Peracetic acid
IUPAC Name:	Peroxyethanoic acid
Synonyms:	Acetyl hydroperoxide Ethaneperoxoic acid Peroxyacetic acid
Danish:	Pereddigesyre
Dutch:	Perazijnzuur
Finnish:	Peretikkahappo
French:	Acide peracétique
German:	Peressigsäure
Greek:	Υπεροξικό οξύ
Italian:	Acido peracetico Acetil-idroperossido
Norwegian:	Perettikusyre
Portuguese	Acido peracetico
Spanish:	Acido peracético
Swedish:	Perättiksyra
CAS Name:	Ethaneperoxoic acid
CAS Registry No.	79-21-0
Formula:	$C_2H_4O_3$

Structural formula:



Molecular Weight: 76.05

2.2 Conversion Factors

Conversion factors for concentrations of PAA in air at standard conditions (20°C and 1,013 hPa) are:

- 1 ppm = 3.162 mg/m^3
- 1 mg/m^3 = 0.316 ppm

In this report, converted values are given in parentheses.

2.3 EU Classification and Labelling

The following EU classification and labelling applies to pure PAA according to Directive 98/98/EEC, effective from 1 July 2000 (EC, 1998).

EC (EINECS) No. 201-186-8

Index No. 607-094-00-8

EEC classification: R 10, flammable

O, oxidising; R 7, may cause fire
Xn, harmful; R 20/21/22, harmful by inhalation / in contact with skin / if swallowed
C, corrosive; R 35, causes severe burns
N, dangerous to the environment; R 50, very toxic to aquatic organisms

EEC labelling: Symbols:	O, Oxidising C, Corrosive N, Dangerous to the environment
R-phrases:	R 10, flammable R 7, may cause fire R 20/21/22, harmful by inhalation / in contact with skin / if swallowed R 35, causes severe burns R 50, very toxic to aquatic organisms
S-phrases:	S 1/2, keep locked up / keep out of the reach of children S 3/7, keep in a cool place / keep container tightly closed S 14, keep away from ... (incompatible materials to be specified by the manufacturer) S 36/37/39, wear suitable protective clothing, gloves and eye/face protection S 45, In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible) S 61, Avoid release to the environment. Refer to special instructions/Safety data sheets

Preparations must be classified in accordance with Directive 1999/45/EC (EU, 1999). Specific concentration limits for health hazards of PAA in preparations are specified in Directive 98/98/EEC above.

Concentration ≥ 10%	C, corrosive; R20/21/22, harmful by inhalation / in contact with skin / if swallowed; R35, causes severe burns
5 ≤ Concentration < 10%	C, corrosive; R34, causes burns
1 ≤ Concentration < 5%	Xi, irritant; R 36/37/38, irritant to eyes / respiratory system / skin

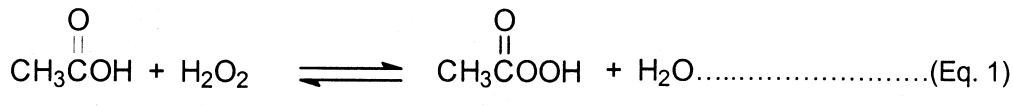
For the classification of equilibrium PAA solutions, the concentrations of hydrogen peroxide (H_2O_2) and acetic acid (HOAc) have to be considered as well following the same rules of the preparations Directive 1999/45/EEC.

2.4 Commercial Formulations

Peracetic acid (PAA) is produced commercially either as an equilibrium solution in which PAA is in equilibrium with H_2O_2, HOAc and water (Swern, 1970) or as a distilled product containing primarily PAA and water (Dalin, 1996; Jäkärä *et al*, 1998).

2.4.1 Equilibrium PAA solutions

Equilibrium PAA solutions are generally prepared by reacting glacial HOAc with H_2O_2 in the presence of a catalyst such as a mineral acid. The equilibrium reaction is shown in the following equation:



Specific grades are obtained by controlling the concentration and amount of H_2O_2 and HOAc used during the manufacturing process. Adding an acid such as sulphuric acid or increasing the temperature during the manufacturing process can accelerate the establishment of the final equilibrium concentration (grade). The final solution contains PAA in equilibrium with H_2O_2, HOAc and water. Commercial PAA grades are available in PAA concentrations ranging from about 0.3% to 40% by weight. For a given PAA formulation, the equilibrium concentration is temperature dependent, so that a decrease of temperature will increase the PAA content. The equilibrium aspects are further discussed in Section 2.5.

2.4.2 Distilled PAA solutions

The production of distilled solutions involves vacuum distillation of PAA from a mixture containing HOAc, H_2O_2, a catalyst (e.g., mineral acid) and de-ionised water. Final formulations contain only minor amounts of HOAc and H_2O_2. Distilled solutions of PAA in water are produced on site or shipped in concentrations normally ranging from 25 to 40%. These grades are usually shipped cooled (< 0°C) to slow down the hydrolysis reaction, which in effect slows down the formation of HOAc and H_2O_2.

2.5 Physical and Chemical Poperties

All PAA solutions are clear, colourless liquids with a pungent vinegar-like odour and are soluble in polar solvents, aromatics and acetates (Swern, 1970). Physical and chemical properties characteristic of the component PAA are shown in Table 1.

Table 1: Physical and Chemical Properties of PAA

Property	Value, unit	Reference
pH	< 1	Safety data sheets[a]
Solubility in water at 20°C	1,000 g/kg[b]	Swern, 1970; Safety data sheets[a]
pK_a at 20°C	8.2	Swern, 1970
Partition coefficient, log K_{ow} (octanol/water) at 25°C	- 0.52[c] - 1.25[d]	Byers, 1998 Thus, 1994
Odour threshold	50 ppb	Ancker and Zetterberg, 1997
Henry's law constant at 25°C	0.22 Pa·m^3/mol[e]	Lind and Kok, 1986

[a] Ausimont, 1997a,b; Bactria, 1995, 1997; Bioxal, 2000a,b; Chemoxal, 1997; Degussa, 1996a,b, 1997; FMC, 1998a,b,c; Henkel, 1995, 1997a,b; Solvay, 1997a,b,c,d

[b] Reported as 100%

[c] Measured, reported as $K_{ow} = 0.30$

[d] Calculated

[e] Measured, reported as 467.6 mol/l·atm

Other physical and chemical properties are specific to the concentration ratio of the individual components in the formulation.

2.5.1 Equilibrium PAA grades

Equilibrium grades of PAA are produced in various concentrations ranging from about 0.3% to 40%. Many of the chemical and physical properties are specific to the concentrations (ratios) of each component, i.e. PAA, H_2O_2, HOAc and water, in the different grades. Generally, most commercial 5% to 35% equilibrium grades from different producers have similar compositions and physico-chemical properties. Table 2 shows chemical and physical properties specific for equilibrium grades of 5%, 15% and 35% PAA. Producers' material safety data sheets should be consulted for data pertaining to their commercial grades.

Table 2: Physical and Chemical Properties of Three Equilibrium Grades of PAA

Property		Value, unit			Reference
		5%	15%	35%	
Ratio components PAA: H_2O_2:HOAc:H_2O		5 : 22 : 10 : 63%[a]	15 : 20 : 15 : 50%[a]	35 : 7 : 40 : 18%[a]	Safety data sheets[b, c, d]
Melting point		-26 to -30°C[e]	-30 to -50°C[e]	-44°C[e]	Safety data sheets[b, c, d]
Boiling point		99 to 105°C	> 100°C	> 105°C	Safety data sheets[b, c, d]
Relative density D_4^{20} at 20°C (density of water at 4°C is 1,000 kg/m^3)		1,120 kg/m^3	1,150 kg/m^3	1,130 kg/m^3	Safety data sheets[b, c, d]
Vapour Pressure at 20°C		21 to 27 hPa	25 hPa	17 hPa	Safety data sheets[b, c, d]
Partial pressure at 20°C	PAA	0.3 hPa (4%)	1.1 hPa (14%)	2.7 hPa (32%)	Caropreso, 2000
(vapour phase concentrations)	H_2O_2	0.4 hPa (2%)	0.5 hPa (3%)	0.2 hPa (1%)	
	HOAc	0.8 hPa (9%)	1.6 hPa (16%)	4.1 hPa (38%)	
	H_2O	25.0 hPa (85%)	21.8 hPa (67%)	10.1 hPa (28%)	
Flash point,	open cup closed cup	No data 74 to 83°C	> 100°C 68 to 81°C	No data 46 to 62°C	Safety data sheets[b, c, d]
Auto ignition temperature		270 to 430°C	≈ 265°C	≈ 218°C	Safety data sheets[b, c, d]
SADT[f] (55 US gallons[g] drum)		> 55 to > 65°C	> 50°C	> 55°C	Safety data sheets[b, c, d]
Sustained flammability		No	No	Yes, flammable	FMC, 1998[a, b, c]

a Each producer will have specified concentrations
b 5% PAA grade: Bactria, 1995; Henkel, 1995; Ausimont, 1997a; Degussa, 1997; Solvay, 1997a,b ; FMC, 1998a; Bioxal, 2000a
c 15% PAA grade: Henkel, 1995; Degussa, 1996a; Ausimont, 1997b; Bactria, 1997; Chemoxal, 1997, 1999; Solvay, 1997c,d; FMC, 1998b; Bioxal, 2000b
d 35% PAA grade: Degussa, 1996b; Henkel, 1997b; Akzo Nobel, 1998; FMC, 1998c.
e Decomposes
f Self-accelerating decomposition temperature
g One US gallon = 3.758 l

However, there are formulations on the market which have the same PAA concentration but different concentrations of HOAc and H_2O_2, so that the physico-chemical properties may be completely different. The equilibrium equation (Eq. 1, Section 2.4) shows that by changing the concentration of one component in a PAA formulation, the concentration of the other components will also change to re-establish the equilibrium (Section 2.4.1). Examples of formulations with the same PAA concentrations but with different concentrations of the other components are given in Tables 3 and 4.

Table 3: Composition of Two Commercial PAA 10% Formulations *(Steiner, 2000)*

	PAA (%)	**H_2O_2 (%)**	**HOAc (%)**	**H_2O (%)**
Formulation 1	10	1	78	11
Formulation 2	10	18	18	52

According to the UN classification system for transport of dangerous goods (UN, 1995), formulation 2 in Table 3 is an organic peroxide type F, while formulation 1 is an organic peroxide type D that is also flammable because of the high HOAc content. The UN system is explained in Section 3.4.

Table 4: Composition of Two Commercial PAA 15% Formulations *(Block, 1991)*

	PAA (%)	**H_2O_2 (%)**	**HOAc (%)**	**H_2O (%)**
Formulation 1	15	23	16	45
Formulation 2	15	14	25	42

Although the composition of these two 15% PAA grades is different, the formulations exhibit similar physical properties and both are classified as organic peroxide type F.

As soon as water is added, the solution slowly begins to re-equilibrate until a new final equilibrium composition is attained. Usually, re-equilibration takes several days. If the diluted solution is not going to be used within a few days, the amount of water needed to halve the concentration of PAA will be different from that calculated by simple material balance. Cooling to about 20°C can decrease the rate at which equilibrium is established. Conversely, increasing the temperature can increase the rate. As can be seen in Table 5, the PAA concentration of a 1:1 dilution mixture of a commercial 15% PAA acid formulation with water dropped from 7.3% to 2.8% after 12 days storage at 20°C. The active oxygen concentration remained constant, i.e. no decomposition occurred.

Table 5: Re-equilibrium of PAA 15%[a] after Dilution with Deionised Water at 20°C *(Reinold, 2000)*

Dilution:	**1:1**	**1:2**	**1:3**
Time after dilution	**PAA concentration (%)**		
1 min	7.3	4.9	3.7
12 d	2.8	1.2	0.8

[a] Measured composition of test solution: 14.7% PAA and 21.9% H_2O_2

2.5.2 Distilled aqueous PAA grades

Table 6 shows chemical and physical properties for a 38% distilled aqueous grade of PAA. Producers' material safety data sheets should be consulted for data specific to their commercial grades.

Table 6: Physical and Chemical Properties of Distilled PAA (38%) *(Akzo Nobel, 1998)*

Property		**Value, unit**
Ratio Components PAA: H_2O_2 :HOAc		38 : < 1 : < 3%
pH		≈ 2
Melting point		≈ -12°C
Boiling point		105 - 110°C[a]
Relative density at 20°C		1,070 kg/m^3
Vapour pressure at 20oC		No data
Flash point	open cup	No data
	closed cup	≈ 65 to 70°C
Auto ignition		No data
SADT (55 gal drum)		No data
Sustained flammability		Not flammable

[a] Decomposes

2.5.3 Flashpoint and autoignition temperature

A comparison of producers' safety data sheets shows considerable scatter in measured flashpoints (Table 2). This scatter may be attributed to several factors e.g., PAA reacting with the sample container used in the flash point determination, thermal instability of the PAA solutions, loss of volatile material during analysis due to decomposition and excessive gassing, releasing oxygen and water which tend to extinguish any flame. While the reported flash point value may not be exact, it is an indication of the temperature at

which vapours can ignite. Most of the PAA equilibrium grades ranging from 5% to 15% exhibit closed-cup flash points but no measurable open-cup flash points. Thus, these grades are not flammable under conditions where the liquid is open to the atmosphere. However, a sustained flame is possible in a closed system. Decomposition of PAA produces oxygen. A closed system prevents the release of the oxygen, which in the presence of the organic (acetic acid) can sustain a flame. Thus, all the gases produced remain in the system and they can burn. Equilibrium grades of concentrations ≥ 30% PAA or higher exhibit both open and closed-cup flash points and are flammable.

Equilibrium PAA grades exhibit autoignition temperatures ranging from 218 to 430°C (Table 2).

2.6 Stability

The decomposition of PAA is strongly exothermic, liberating large volumes of oxygen gas. Decomposition can be initiated by high temperatures, high pH, and contamination with metal catalysts such as copper, iron and chromium, and incompatible organic materials.

2.6.1 Stabilisers and impurities

To prevent decomposition, commercially available equilibrium and aqueous formulations contain low concentrations of proprietary stabilisers, which protect against decomposition induced by metal ions and minor contamination. The concentration of impurities in commercially available PAA solutions is generally low. Common stabilisers include dipicolinic acid and phosphonates.

2.6.2 Decomposition of PAA in air

PAA vapour in air is found to have limited stability. For example, measurements taken at ambient temperature showed a decrease in concentration from 1 ppm (3.16 mg/m^3) to 0.5 ppm (1.58 mg/m^3) in 22 minutes (Ancker and Zetterberg, 1997).

2.6.3 Decomposition of PAA in aqueous solutions

Yuan *et al* (1977a,b) reported that decomposition of PAA solutions can involve three competitive reactions:

Spontaneous $2\ CH_3C(O)OOH \longrightarrow 2\ CH_3C(O)OH + O_2$ ..... (Eq. 2)

Metal [M] catalysed $2CH_3C(O)OOH + [M] \rightarrow 2CH_3C(O)OH + O_2 + [M]$ ..... (Eq. 3)

Hydrolysis $CH_3C(O)OOH + H_2O \rightarrow CH_3C(O)OH + H_2O_2$ ..... (Eq. 4)

Increasing temperature or pH will result in accelerated decomposition (Mücke, 1977; Yuan *et al*, 1977a). For example, Mücke (1977) showed that in the absence of heavy metal ions, dilute PAA solutions undergo hydrolytic decomposition (Eq. 4) in a manner that is the reverse of the formation reaction, to form HOAc and H_2O_2. The rate of hydrolysis increases with increasing temperature and pH.

Drimus and Matasa (1966) studied the thermal decomposition of PAA solutions. Analysis of the gas evolved during decomposition suggested that the decomposition process consisted of several distinct reactions, such as:

$$2\ CH_3C(O)OOH \longrightarrow 2\ CH_3C(O)OH + O_2 \quad \text{(Eq. 2)}$$

$$CH_3C(O)OOH \longrightarrow CH_3OH + CO_2 \quad \text{(Eq. 5)}$$

2.7 Chemical Reactivity

2.7.1 Compatibility

Good stability has been achieved in the presence of certain surfactants, mineral acids, thickening agents and perfumes (James and Shehad, 1995). However, it is important that all materials are tested for compatibility and stability in the presence of the specific PAA solution before being added to the formulation. Incompatible materials could cause the PAA solutions to decompose rapidly with the evolution of large quantities of oxygen and other vapours.

2.7.2 Chemical characteristics

PAA is a strong oxidising agent. For that property, it is used commercially in a variety of applications (Section 3.5).

2.8 Analytical Methods

An EU Project with the objective to develop methods for the quantitative determination of PAA in air and aqueous solutions will be finalised by the end of year 2000 and public reports will follow (Euperox, 1997). Several publications mentioned in this section originate from this project. One of these (Effkemann *et al*, 1999b) includes useful recommendations on choice of analytical methods for different purposes, as explained below.

Concerning animal experiments and other studies in air or in water, one has to consider that if the (diluted) PAA formulation used contains H_2O_2 it is necessary to record both compounds using a method that fits from the viewpoint of sensitivity and accuracy. Even when a H_2O_2-free PAA formulations is used, it might be necessary to record the levels of both compounds since H_2O_2 may be formed as a hydrolysis product of PAA. Due to the instability of PAA (and H_2O_2) in vapours and also in water, it is important to record continuously or regularly the concentrations of the components.

2.8.1 In aqueous solutions

Table 7 gives a summary of analytical methods for concentrated and diluted PAA solutions.

Table 7: Analysis of PAA in Aqueous Solutions

Analytical technique	Range (mg PAA/l)	Detection limit (mg PAA/l)	Reference
Concentrated (and diluted) products			
Titration with cerium sulphate (for H_2O_2) followed by iodometric titration (for PAA)	10 - 50,000	10	Greenspan and MacKellar, 1948
Titration at 0°C with $KMnO_4$ in presence of NaF (for H_2O_2) followed by iodometric titration (for PAA)	10 - 50,000	10	Senf, 1984
Dilute solutions			
Colorimetric oxidation of DPD[a] reagent (Merckoquant test strips)	5 - 50	5	Merck, 1995, 1998
Colorimetric oxidation of tetra-methylbenzidine in buffered potassium iodide (RQflex[b] photometer with Reflectoquant test strips)	1 - 100	1	Fischer *et al*, 1989; Merck, 1994
Successive reaction of PAA with MTS[c] and of H_2O_2 with triphenylphosphine, HPLC[d] analysis	0.1 - several 1,000	0.1	Pinkernell *et al*, 1994, 1997a
Selective oxidation of enzyme substrate ABTS[e], HPLC analysis	Not stated	0.1	Pinkernell *et al*, 1997b
Oxidation of ADS[f]. HPLC , detection at 410 nm	0.007 - 0.7	0.002	Effkemann and Karst, 1998
HPLC with electrochemical detection on line (Prominent Perox Controller)	10 - 200 or 100 - 2,000	10	Pinkowski, 1995; Prominent, 1997
HPLC with electrochemical detection	Not stated	0.1	Kirk *et al*, 1992; Qi and Baldwin, 1993

a N,N'-diethyl-*p*-phenylenediamine
b Reflectometer Quality flexible (strips)
c Methyl *p*-tolyl sulphide
d High performance liquid chromatography
e 2,2´-Azino-*bis*-(3-ethyl-benzo-thiazoline)-6-sulphonate
f 2-((-3(2-(4-Amino-2-(methylsulphanyl)phenyl)-1-diazenyl)phenyl)sulphonyl)-1-ethanol

The generally accepted method, suitable for concentrated solutions (10 - 500,000 mg PAA/l), starts with the determination of the concentration of H_2O_2 by cerium sulphate titration. The PAA content is then measured by iodometric titration with sodium thiosulphate. This procedure is carried out at low temperature (< 0°C) to prevent re-equilibration (Greenspan and MacKellar, 1948). An alternative method is to determine the H_2O_2 content by titration with potassium permanganate ($KMnO_4$) at 0° C, and then determine the PAA content with iodometric titration as described above (D'Ans, 1912 as quoted in Swern, 1970; Senf, 1984). The cerium-based method is regarded as more accurate and less dependent on operator skill compared to the $KMnO_4$/iodometric method.

The method according to Pinkernell (1994, 1997a) is suitable for the analysis of PAA + H_2O_2 in dilute solutions but too cumbersome for determination of PAA alone. The Merck RQflex-Reflectoquant test is considered more selective than the DPD method, which cannot be used in the presence of active chlorine compounds. The electrochemical method of Prominent (1997) is easy to use (e.g. calibration) and useful, amongst others, for on-line control of disinfectant solutions in the food industry.

2.8.2 In air

Table 8 summarises analytical methods for the determination of PAA in air. All of these methods are selective for PAA, rather than determining total PAA + H_2O_2 concentrations. An overview of nine existing gas monitoring methods for PAA has been made, including applicability of the methods and costs (Solvay, 1999). Five of these are included in Table 8.

Table 8: Analytical Methods in Air

Analytical technique	Detection limit (mg PAA/m^3)	Air sample volume (l)	Reference
Iodide catalysed oxidation of ABTS[a] in coated test tubes or impingers	0.35	3 - 5	Effkemann *et al*, 2000
Oxidation of ADS[b] on coated test tubes or impingers. HPLC[c], detection at 410 nm	0.13	5	Effkemann *et al*, 1999a
Oxidation of MTS[d], HPLC, UV detection	0.035[e]	NS	Thus *et al*, 1996
Impinger. Amine colour reaction (Merck PAA test 15975)	0.5	20	Fischer *et al*, 1989, Solvay 1999
Direct measurement in vapour phase with FTIR[f] and Michelson interferometer	0.15	1,000[g]	Ancker and Zetterberg, 1997
Photo-acoustic FTIR	0.09[h]	NS	Solvay, 1999

NS Not Stated
a 2,2´-Azino-*bis*-(3-ethyl-benzo-thiazoline)-6-sulphonate
b 2-((-3(2-(4-Amino-2-(methylsulphanyl)phenyl)-1-diazenyl)phenyl)sulphonyl)-1-ethanol
c High performance liquid chromatography
d Methyl *p*-tolyl sulphide
e H_2O_2 0.16 mg/m^3
f Fourier transform infrared (spectroscopy)
g Range 0.15 - 100 mg PAA/m^3 or higher
h H_2O_2 0.1 mg/m^3

For ambient workplace air and personal measurements at the workplace, the method by Thus *et al* (1996) provides high sensitivity for both PAA and H_2O_2 without interference between PAA and H_2O_2. Another sensitive and portable technique is the photo-acoustic Fourier transform infrared (FTIR) spectroscopy technique of Solvay (1999). Among the two methods developed by Effkemann *et al* (1999a, 2000), the ABTS test tube method is recommended for screening purposes. The ABTS impinger method and also the ADS impinger or test tube methods are more selective and accurate. The direct FTIR spectroscopic method according to Ancker and Zetterberg (1997) is suitable for personal and area measurements at the workplace, indoors and outdoors.

There are few methods available which are sensitive enough for atmospheric PAA measurements. An enzyme fluorometric method developed mainly for H_2O_2 (Lazrus *et al*, 1986) might be further developed for such a purpose.

3. PRODUCTION, STORAGE, TRANSPORT AND USE

3.1 Production

3.1.1 Industrial production

In general, peroxycarboxylic acids can be made by numerous methods generally involving the reaction of H_2O_2 with the corresponding carboxylic acid or carboxylic acid derivatives (Klenk *et al*, 1991; Swern, 1970).

Peroxyacetic acid (PAA) solutions are produced by three industrial methods. Equilibrium mixtures of PAA are obtained by reacting HOAc, H_2O_2 in the presence of an acid catalyst, normally sulphuric acid. Equilibrium PAA grades of this type are commercially available with a PAA content of up to 40%.

Optionally, PAA can be distilled from equilibrium mixtures of HOAc and H_2O_2 to yield an aqueous PAA solution with low residual H_2O_2 and HOAc. Commercially, distilled PAA is available with a content of 25-40% PAA.

Alternatively, PAA is produced by the oxidation of acetaldehyde in the presence of a solvent, e.g. ethylacetate, yielding a product with approximately 25% PAA content (Swern, 1970).

Accurate data on the quantities of PAA produced in Europe or USA are not available. CEFIC (2000a) estimated a figure of > 32,430 tonnes for western Europe.

3.1.2 Generation *in situ*

PAA acts as a low temperature bleaching agent and is generated *in situ* during the washing process from sodium perborate / percarbonate and TAED (Jakobi and Löhr, 1991). In Europe, powder detergents with bleach typically contain 15-25% persalt and up to 5% TAED corresponding to approximately 3.5% PAA equivalent (100%) (Jakobi and Löhr, 1991).

Minor quantities of PAA precursors such as TAED, acetyl salicylic acid or HOAc anhydride are used for generation *in situ* of PAA in the sterilisation of medical instruments and in the textile industry (Wurster, 1992).

In 1999, approximately 48,500 tonnes of TAED (corresponding to 32,300 tonnes PAA (100%) generated *in situ*) were employed in European detergents (Battelle, 1999). AISE (2000) estimated that approximately 60,000 tonnes PAA is generated in this way worldwide, excluding South America and Africa.

3.1.3 Quantities used

In Europe, the equilibrium PAA consumption (as such) is estimated at 25,000 t/y. This is mainly used for disinfection and does not include use in chemical synthesis (CEFIC, 1998). In Scandinavia the consumption of distilled PAA in pulp bleaching is estimated at 2,000-3,000 tonnes (100%) mainly driven by demand for total chlorine free (TCF) pulp grades (Sandström *et al*, 1999).

In the USA, the PAA consumption is estimated to be less than 10,000 t/y (as such) for non-synthesis applications (CEFIC, 1998). Approximately 20,000 tonnes of PAA were produced in the USA by autoxidation of acetaldehyde (Johnson, 1995).

Worldwide consumption in chemical synthesis including captive use and *in situ* generation has been estimated at 45,000-50,000 tonnes (PAA 100%) in 1998 (CEFIC, 2000b). In 1999 the worldwide consumption of acetaldehyde for PAA production was expected to be 41,000 tonnes corresponding to 72,500 tonnes PAA (100%) (Tecnon Consulting, 1999). The Task Force was not aware of any production by this route in Europe.

3.2 Compatibility

3.2.1 Storage and transportation containers

Generally, PAA is stable in containers made from glass, certain high density linear polyethylene grades, polyvinylchloride, poly-*tetra*-fluoroethylene and properly passivated stainless steel 304L and 316. However, it is important to check the compatibility and stability with all containers before long-term use; PAA can degrade (embrittle) plastics with extended contact time. Degradation rates are enhanced by elevated temperature. The German authorities have restricted the maximum storage time for PAA > 17% in standard polyethylene containers to 6 months from the day of filling. Extensions can be obtained for containers that exhibit long-term storage stability with PAA by passing the required tests (drop test) after contact with PAA for a defined time period (BAM, 1999).

PAA solutions are capable of leaching metal ions from stainless steel. This effect is enhanced by some of the mineral acids (e.g. H_2SO_4) added as catalysts. Many of these metal ions, e.g., iron, nickel, chromium, and molybdenum can cause product instability.

3.2.2 Non-compatible materials

Concentrated PAA is not compatible with aluminium, carbon steel, some cross-linked polyethylene and metal alloys containing copper. It is important to determine compatibility before using PAA with any material. PAA is rapidly decomposed upon contact with metal salts, alkalis and activated carbon.

3.3 Storage

Equilibrium PAA is stabilised and stored at ambient conditions in certain polyethylene, polyvinylidene fluoride containers, or passivated stainless steel tanks, with the appropriate safety measures e.g. pressure relief. PAA should be kept away from metals, metal salts, alkalis and reducing agents. PAA storage containers made of polyethylene are protected from UV radiation. Storage temperature conditions are determined individually for every formulation depending on the physical properties, in particular flash point and self-accelerating decomposition temperature (SADT).

Distilled PAA is typically stored and transported in cooled (< 0°C) stainless steel containers, in order to prevent an equilibrium shift from PAA to H_2O_2 and HOAc. For storage in stainless steel containers the addition of special corrosion inhibitors may be required in order to prevent accelerated leaching of metals into the product causing enhanced decomposition (see also Section 3.2).

Several national regulations apply for the storage and handling of PAA, e.g. in Germany on precautions for the handling of organic peroxides (BG Chemie, 1993) and on explosive substance regulations in other countries. In Germany, PAA is listed as water polluting in "Wassergefährdungsklasse (WGK) 2" (Bundesminister, 1999; Umweltbundesamt, 2000).

3.4 Transportation

Mixtures of H_2O_2 and PAA ≤ 5% may be classified as Oxidiser in division 5.1 of UN Recommendation 3149, provided they are thermally stable, do not detonate in the cavitated state, do not deflagrate at all, nor show any effect when heated under confinement nor any explosive power (UN, 1995; ECE, 1996). PAA solutions > 5% or not meeting the above-mentioned provision are classified as organic peroxides in division 5.2 (type D = UN 3105, type E = UN 3107 or type F = UN 3109). The appropriate type has to be determined by testing pursuant to the UN Recommendations on the Transport of Dangerous Goods, Manual of Tests & Criteria, Part II (UN, 1995; ECE, 1996).

In the USA, a mixture of PAA 6% and H_2O_2 may be classified as Oxidiser in division 5.1 (UN 3149) pursuant to an approval of the national competent authority (US-DOT, 1995).

PAA solutions are subjected to temperature control during carriage if the SADT is ≤ 45°C for type E and F, or ≤ 50°C for type D showing a medium effect when heated under confinement, or ≤ 45°C for type D showing a low or no effect when heated under confinement.

Equilibrium PAA is permitted for transport by road, rail and sea in plastic drums made of high-density polyethylene. Intermediate bulk containers (IBCs) made of stainless steel or rigid plastic (high-density polyethylene) and portable tanks made of stainless steel are permitted for type F for European and US American land transport with an upper limit of 43 % PAA. Transport by portable tanks requires approval of the competent authorities of the country of origin. For transport by sea, IBCs made of stainless steel or rigid plastic (high-density polyethylene) and portable tanks made of stainless steel are permitted for type F with an upper limit of 17% PAA only. Approval of the competent authorities is required for both IBCs and portable tanks.

At present distilled PAA is permitted for transport by road and rail, pursuant to an exemption of the competent authority of Finland, which submitted the content of the approval as proposal document ST/SG/AC.10/C.3/2000/10 to the 18th session of the UN Sub-Committee of Experts session held in Geneva on July 2000. Depending on the concentration and the individual product properties cooling may be required.

3.5 Use

Major uses of PAA are in chemical synthesis, disinfection and bleaching (Table 9). Low concentrations (1-15%) are used as sanitisers, disinfectants and sterilants in the food, beverage and medical industries. Concentrated (> 15%) solutions are used for the oxidation of organic compounds.

Table 9: Applications Ranked by Decreasing Quantity

Application	Method of use	Reference
Food Industry		
Clean-in-place (breweries and dairies)	In-line into closed vessels or pipework	Lever Industrial,
Surface cleaning	High or low pressure spray systems	1987; Lenahan,
Fish/meat/poultry processing	In process water	1992
Vegetable processing	In process water	
Sugar beet processing	In-line into process liquors	Bowler *et al*, 1996
Starch processing	In-line into process liquors	Pehrsson *et al*,
Bottle cleaning	Spray into bottles	1995
Agriculture / horticulture		
Animal house and glasshouse surface disinfection	High or low pressure spray and fogging	
Equipment disinfection	Open bath	
Animal waste / slurry	In slurry or liquid waste	
Irrigation water	Loosely covered tanks and pipelines	
Harvested fruit and vegetables	Open bath or spray	
Pulp and paper		
Chemical pulp bleaching	In-line into pulp	Kramer, 1997;
White water	In-line into white water	LaZonby, 1997
Pulp de-inking	In-line into pulp	
Health		
Renal dialysis machines and cartridges	Open baths or soak treatment or in line in pipework	Fischbach, 1985; Crow, 1992
Endoscopes	Open baths or automated washing systems	
Dental instruments	Open baths	
Consumer		
Household cleaners	Open operations	
Chemical Industry		
Oxidiser during synthesis of chemicals	Closed reaction vessels	
Miscellaneous		
Effluent treatment	In-line in open pipes or lagoons	Baldry *et al*, 1990,
Sludge debulking	In-line in pipework, sump or lagoon	1991, 1995;
Algal control	Low pressure spray onto water or solid surface	Rudd, 1989
Industrial laundries	Into closed washing machines	

PAA is employed as a sanitiser in the food processing and beverage industry. This includes meat and poultry processing plants, canneries, dairies, animal houses, green houses breweries, wineries and soft drink plants where it is used in clean-in-place (CIP) systems at concentrations of 50 to 200 ppm PAA (158 - 632 mg/m^3) (Jäger and Püspok, 1980; Schröder, 1982; Lever Industrial, 1987; Baldry and Fraser, 1988; Dychdala, 1988; Cords and Dychdala, 1993; Cords, 1994; Mrazek, 1996). At lower temperatures (up to

40°C), PAA (0.04-0.1%) is an alternative for H_2O_2 in aseptic packaging (Mrazek, 1996; Blakistone *et al*, 1999).

Another major use of PAA is as a bleaching and disinfecting agent in industrial and hospital laundries (Potokar *et al*, 1996).

PAA has been found useful in the disinfection of vegetables, fruits, starch products and plant growing media such as coir (strong fibre of coconut husk) (Chalkley, 1992). PAA is permitted in the US as a secondary and indirect food additive (US-FDA, 1996a,b) at concentrations up to 100 mg/l. PAA is also used as a disinfectant in sugar beet extraction (Bowler *et al*, 1996).

Because PAA has agricultural applications, residues potentially could be found in animals. Council Regulation 2377/90 of 26 June 1990 established a Community procedure for maximum residue limits of veterinary medicinal products in foodstuffs of animal origin (EEC, 1990). According to Commission Regulation 1433/96 of 23 July 1996, PAA is not subject to these limits (EC, 1996).

PAA has found applications in sewage sludge oxidation (Fraser, 1986) and municipal wastewater treatment (Baldry *et al*, 1991). Treatment of municipal wastewater with 10 mg PAA/l for 30 minutes proved sufficient to meet WHO faecal coliforms guideline values and for the water to be reused in agricultural irrigation (Liberti *et al*, 1998, 1999). PAA has also been evaluated for the disinfection of drinking water (Profaizer *et al*, 1997). In process water of paper mills PAA is employed as a slimicide in order to avoid corrosion and odour problems (Klahre, 1996a,b). PAA is also effective in removal and growth inhibition of biofilms and algae in cooling systems (Kramer, 1997).

PAA based systems are used for the sterilisation of medical equipment (Block, 1991; Malchesky, 1993). Pyrogens were significantly reduced at a concentration of 0.1% PAA for 30 minutes (Werner, 1988).

PAA is also applied for disinfection of stables and for drinking water conservation in animal farming (Krüger *et al*, 1977; Kurzweg *et al*, 1988). It has been employed for farm effluent disinfection where concentrations of up to 0.4% (PAA 100%) are applied for 15 minutes (Meyer, 1976). In greenhouses, PAA is used as a cleaner and disinfectant in water circuits.

Distilled PAA has found application as a bleaching agent mainly in TCF cellulose pulp production processes replacing chlorine dioxide (Basta *et al*, 1995; Thomasfolk *et al*, 1996; Ruohoniemi *et al*, 1998; Sandström *et al*, 1999). Small quantities of PAA are used in the bleaching of recycled fibres, de-inking and in textile finishing (Steiner, 1995).

High-strength equilibrium (> 15%) and distilled PAA products are in general employed as oxidising agents in the manufacture of organic chemicals and pharmaceuticals. Examples of oxidation reactions include the epoxidation of olefins and the production of sulphoxides and sulphones, such as in the synthesis of cephalosporins. Other examples are ε-caprolactone, epoxidised soybean oil (Swern, 1970), modified starch products and penicillin (V) sulphoxide, a key intermediate in the synthesis of cephalosporin antibiotics (Feigenbaum, 1997).

4. ENVIRONMENTAL DISTRIBUTION AND TRANSFORMATION

4.1 Emissions

4.1.1 Natural sources

Organic hydroperoxides such as PAA are thought to be formed in air by the reaction of peroxyl and hydroxyl radicals as follows (Gunz and Hoffmann, 1990).

$$R - C = OO^{\bullet} + HO^{\bullet}{}_2 \longrightarrow R - C = OOH + O^{\bullet}{}_2 \quad \text{(Eq. 6)}$$

The origin of these atmospheric radicals in polluted and unpolluted air has been reviewed (Wayne, 1991; Thompson, 1994).

The formation of PAA and other hydroperoxides has been demonstrated in smog chamber studies using chlorine atoms as initiator (e.g. Hanst and Gay, 1983).

Traces of PAA were found in mountain air, but have not been demonstrated in ambient air or atmospheric deposition samples (Section 5.1.1).

4.1.2 Emissions during production and use

Emissions to the atmosphere during production are normally avoided by scrubbing the exhaust using an alkaline scrubber. For the manufacture of equilibrium PAA an effluent-free process is applied. Thus no emissions to the aquatic environment are expected under normal operating conditions.

In the manufacture of distilled PAA, a minor liquid effluent flow essentially free of PAA is produced.

Water emissions during bleaching of pulp with distilled PAA are expected to be negligible due to the low stability of PAA in the bleaching liquids.

In the USA, the Toxic Release Inventory lists the reported releases (annual quantities emitted) from industrial facilities having 10 or more full-time employees and manufacturing or processing ≥ 25,000 lbs (11,364 kg)[a] or otherwise using ≥ 10,000 lbs (4,545 kg). The latest available figures indicate a total quantity release on- and off-site of 7,345 lbs (3,330 kg) PAA in 1997 (US-EPA, 1999a). These release figures represent a worst-case estimate, because they are based on conservative assumptions and do not take into consideration any breakdown on-site by biological or physical means such as waste-water treatment, incineration and flaring (US-EPA, 1999b).

1 lb = 1 pound = 0.4535924 kg

4.2 Envionmental Fate and Biotransformation

4.2.1 Distribution

The theoretical distribution of PAA has been estimated using the fugacity model of Mackay, Level 1 (Mackay *et al*, 1992). The calculations were conducted for the equilibrium grades of PAA in Table 10, using the partial vapour pressure of PAA in those solutions. According to the model, the majority of PAA (99.3 to 99.9%) released into the environment enters the water phase, while the remainder is found in air. No partitioning into soil, suspended matter or biota is expected (Table 10).

Table 10: Distribution of PAA, for Different Grades of PAA, between Environmental Compartments at 25°C *(Jacobi, 1997)*

Grade (%):	**5**	**15**	**35**
Compartment / Distribution:	**(%)**	**(%)**	**(%)**
Air	0.08	0.29	0.70
Water	99.92	99.71	99.29
Soil	0.00	0.00	0.00
Sediment	0.00	0.00	0.00
Suspended matter (aquatic)	0.00	0.00	0.00
Biota	0.00	0.00	0.00

4.2.2 Atmospheric fate

Henry's Law constant of PAA, measured in the concentration range of 1 x 10^{-6} 1 x 10^{-4} mol/l at 25°C, is 0.22 Pa·m^3/mol (Lind and Kok, 1986) (Table 1). This value is 2-3 orders of magnitude lower than the value determined for H_2O_2 (Gunz and Hoffmann, 1990). So PAA may be washed out by rain but less easily than H_2O_2.

As stated in Section 2.6.2, PAA is quickly decomposed by 50% in the vapour phase within 22 minutes (Ancker and Zetterberg, 1997). This value may be taken as the atmospheric half-life, assuming first-order kinetics. Based on its chemical reactivity and short half-life, PAA is not expected to persist in the atmosphere.

4.2.3 Aquatic fate

The Henry's Law constant for PAA is measured as 0.22 Pa·m^3/mol at 25°C (Table 1). This value indicates that PAA will volatilise slowly from water surfaces.

Table 10 above shows that PAA will not partition into sediment, suspended matter or biota and for this reason the aquatic fate of PAA is mainly determined by degradation in the water phase. Degradation could be due to abiotic decomposition, hydrolysis, biodegradation or reaction with organic compounds, following the general reaction:

$$2\ CH_3C(O)OOH \longrightarrow 2\ CH_3C(O)OH + O_2 \quad \text{(Eq. 2)}$$

Decomposition can be spontaneous or initiated by metal catalysts such as copper, iron and chromium. Enzyme-calalysed degradation by catalase and peroxidase is also possible (Kirk *et al*, 1994) (Section 7.2.1). Decomposition results in a decrease of the active oxygen content of the solution.

Hydrolysis
Hydrolysis of PAA is based on the following reaction:

$$CH_3C(O)OOH + H_2O \longrightarrow CH_3C(O)OH + H_2O_2 \quad \text{(Eq. 4)}$$

When hydrolysis takes place the active oxygen content of the solution remains the same, which is in contrast to decomposition.

Yuan *et al* (1977a,b) calculated theoretical half-lives of PAA in water using a kinetic equation. The results revealed extensive half-lives which are not supported by experimental data. Both Yuan *et al* (1977a,b) and Mücke (1977) reported that the rate of hydrolysis is accelerated by increasing temperature, and more so by increasing pH. Mücke (1977) suggests that hydrolysis occurs almost exclusively by hydrolytic cleavage. He showed hydrolysis half-lives at 20°C, for a 2% PAA solution, of about 1 week at pH 4.4 and less than 1 day at pH 7.

Bioxal (1999) showed that the loss of PAA by hydrolysis of a 5% commercial grade of equilibrium PAA diluted to 1,000 mg PAA/l and 100 mg/l at 15°C, pH 3.4, was about 34% to 36% in 8 days.

Dychdala (1988) showed a 50% loss of PAA from a solution containing 170 mg PAA/l, at 21°C, pH 3.4, within 12 days (half-life). Teral and Gouges (1997) determined the rate of hydrolysis for a 19.7% distilled (non-equilibrium) PAA solution at various temperatures. Results at 20°C showed the half-life to be about 12 days. The pH was not stated, but a low pH may be assumed.

These data suggest that at acidic pH, the half-life of PAA will be around 7 to 12 days, while at neutral or alkaline pH, the rates will be more rapid, with half-lives of 1 day or less.

Degradation Studies
Abiotic degradation tests with diluted PAA solutions studies were performed according to EEC method C7 of Directive 92/69/EEC. Buffered solutions were prepared according to document L 383A (appendix to Directive 92/69 EEC). High PAA concentrations were measured by cerimetric titration, low concentrations by Merckoquant or Reflectoquant colorimetry (Table 7). Both decomposition and hydrolysis were expected to occur in these PAA degradation tests. The results (Table 11) show that the degradation was more rapid at a high temperature and increased with increasing pH. Decomposition half-lives seemed to be shorter when diluted solutions were used.

Table 11: Abiotic degradation of equilibrium PAA at different temperatures, pH and concentrations in buffered solution

Concentration (mg/l)	Temperature (°C)	pH	Half-life (h)	Reference
20	25	4	31[a]	Chemoxal, 1995a,b
20	50	4	3.3	
10	50	4	3.1	
20	50	7	1.6	
20	50	9	< 0.25	
20	60	4	1.7	
20	70	4	0.7	
748	25	4	62	Pierre *et al*, 2000
748	25	7	63	
748	25	9	< 64[b]	
95	25	4	48	
95	25	7	48	
95	25	9	< 3.6[c]	

[a] Obtained by calculation

[b] Based on the results the half-life was 64 hours. However, the pH at the end of the test was 5.3 and therefore the half-life is reported as < 64 hours

[c] Based on the results the half-life was 3.6 hours. However, the pH at the end of the test was not measured and it could have decreased. Therefore the half-life is reported as < 3.6 hours

In another test, Pierre *et al* (2000) studied the abiotic degradation of PAA in distilled water (pH 2) at 25°C and at concentrations of 95 and 748 mg/l. In this case the half-life was 18 and 19 days, respectively.

Solutions containing approximately 100 mg PAA/l in fresh water from a pond or a stream were found to degrade for 66% in 96 hours and completely (99%) in 3 weeks. The same solution in demineralised water was found to degrade for 80% within 3 weeks. H_2O_2 decomposition in the same period was comparatively small with a maximum loss of 8% in 96 hours. The overall breakdown of a 0.2% PAA solution (2,000 mg/l) was 45% in 120 hours. In drinking water and pond water, PAA degraded more rapidly than in demineralised water or lake or stream water. The tests were conducted under laboratory conditions (Chalkley, 1991a,b).

Half-lives of diluted PAA solutions (prepared from equilibrium PAA 40%, 14% H_2O_2 and 27% HOAc dissolved in drinking water) containing up to 200 mg PAA/l were less than 24 hours (Krüger *et al*, 1977). PAA concentrations measured in drinking-water

bottles of rats were found to decrease rapidly within 1 day. Concentrations between 3.1 and 200 mg/l decreased up to one third and one half of the original concentration, respectively. After 4 days the concentration decreased slowly to one fourth of the original concentration (Juhr *et al*, 1978).

PAA concentrations have also been measured during ecotoxicity studies with PAA in fish and water fleas (Section 6.2). During a semi-static test with the fish *Brachydanio rerio*, the mean loss of a 1 mg/l PAA solution was 7.5% in 4 hours. The loss of a 10 mg/l PAA solution was 5.1% in 4 hours (Bazzon *et al*, 1997). During the test with water fleas (*Daphnia magna*) the loss at 0.1 mg/l was 21% in 4 hours (Lamy *et al*, 1997).

The degradation of PAA in demineralised water, drinking water and seawater has been compared (Table 12). The data show 97% and 96% degradation in seawater after 1 day when the initial nominal concentration was 20 and 10 mg PAA/l, respectively.

Table 12: Degradation of PAA in Water at 20°C *(Teral and Hamon, 1995)*

Type of water	pH	Nominal concentration (mg/l)	Measured concentration (mg/l) Day 0	Day 1	Day 2	Day 4
Demineralised water	5	20	19.1	16.7	16	13.7
Drinking water	6	20	18.8	1	0	NS
Seawater	7	20	18.5	0.5	0	NS
Demineralised water	5	10	12	8.3	7.9	6.4
Drinking water	6	10	10.3	0.5	0	NS
Seawater	7	10	12.1	0.5	0	NS

NS Not Stated

The degradation of PAA in synthetic seawater was studied using a 15% PAA solution. With an initial concentration of 52.5 mg PAA/l, the half-life was 2 minutes at 3.3% and 2% salinity. When the concentration was doubled to 105 mg PAA/l, the respective half-lives at 3.3% and 2% salinity were 7 and 20 minutes. Thus, increased salinity enhanced the degradation rate (Kuhn, 2000).

The degradation of PAA is seawater seems to be faster than the degradation in fresh water, which could be related to the high pH and salinity (ionic strength).

4.2.4 Terrestrial fate

Degradation of a 1.1% PAA solution (11,190 mg PAA/l) was tested on a sample of dried soil (not specified). Following extraction with demineralised water, 99.2% of the compound appeared to have been destroyed in about 20 minutes (Chalkley, 1991c).

The penetration of PAA into soil (John Innes compost) columns was investigated with a solution containing approximately 2,000 mg PAA/l, prepared from equilibrium PAA 5% (20% H_2O_2 and 27% HOAc). One ml of the test solution was added to the top of each soil column. After 5 minutes, each column was washed with 100 ml of demineralised water (sufficient to remove all PAA) and the eluate content determined. Of the PAA, 21.5% was recovered at a soil depth of 25 mm, while 42% H_2O_2 was found at the same depth. PAA recovery decreased to 3.2% at 50 mm, 0.3% at 100 mm and < 0.2% at 150 mm, where 10% of the H_2O_2 was still present. Similarly after 10 minutes only 8.7% PAA was recovered at 25 mm depth (Chalkley, 1991a).

4.2.5 Biodegradation

The biodegradability of PAA was evaluated in various experimental test systems.

PAA appeared to be not readily biodegradable in the OECD Closed Bottle Test. However, when inoculum of adapted bacteria derived from a Zahn-Wellens Test with the same compound was added, PAA (initial concentration of 2 - 5 mg/l) proved to be highly (> 79%) degradable (Gerike and Gode, 1990).

In a Coupled Units Test with PAA, where the organic carbon is measured to estimate ultimate biodegradability, 56% carbon removal was found. In another test using detection of recalcitrant metabolites 98% carbon removal was measured (Gerike and Jasiak, 1983; Gerike and Gode, 1990).

Inhibition of the microbial degradation by PAA was measured with an oxygen consumption inhibition test. PAA was shown to have inhibitory activity at 90 mg/l (Gerike and Gode, 1990).

In a Modified OECD Screening Test (OECD 301 E) which determines ultimate biodegradation by measurement of removal of dissolved organic carbon (DOC), PAA was added once at a concentration of 5 mg DOC/l. A bactericidal effect was found and a biodegradable reference substance was not degraded. Therefore, the test procedure was modified and PAA doses were increased stepwise over 2 weeks until the nominal concentration of 5 mg DOC/l was reached. Thus, a very high DOC removal of 98% was achieved within the 28-day test period (Richterich and Gode, 1986), supporting the view of the ready biodegradability of the compound. Based on a simple distribution (PAA is very soluble in water and the volume of bacterial cells is very low compared to the volume of the medium), no significant uptake of PAA is expected to have taken place. Active uptake is very unlikely.

The hydrolysis products HOAc and H_2O_2 are both readily biodegradable (Verschueren, 1983; Groeneveld and De Groot, 1999).

4.2.6 Bioaccumulation

The octanol-water partition coefficient was measured for PAA and H_2O_2 using the US Environmental Protection Agency (EPA) shake flask method (Byers, 1998). The values were 0.30 ± 0.13 and 0.40 ± 0.07 for PAA and H_2O_2, respectively. Compounds with such

a low octanol-water partition coefficient are not considered to be bioaccumulable.

4.2.7 Evaluation

PAA released in the environment will partition almost exclusively (> 99%) to the water compartment. Only a minor part (< 1%) will remain in the atmosphere, where it is expected to undergo rapid decomposition with a half-life of 22 minutes. The fate of PAA in the environment is mainly determined by its degradation.

The fate of PAA in water will be influenced by abiotic degradation, which yields HOAc and oxygen and hydrolysis which forms HOAc and H_2O_2, both of which are easily (bio)degradable compounds. The abiotic degradation increases with temperature and pH. At acidic pH, the half-life of PAA will be around 7 to 12 days, while at neutral or alkaline pH, half-lives may be 1 day or less. In seawater degradation is expected to be rapid (half-life < 1 h). Most abiotic degradation studies of PAA in water were done at concentrations that resulted in acute effects on aquatic organisms. In these situations, abiotic degradation is the single degradation pathway of PAA. However, these concentrations are not realistic environmental concentrations during normal use of PAA products. At low PAA levels (< 1 mg/l), the biotic degradation by algae, and micro-organisms could significantly increase the degradation in aquatic ecosystems.

In the soil, a diluted PAA solution is rapidly and easily degraded by hydrolysis and transition metal decomposition, which is an instantaneous reaction. At low concentrations biodegradation could contribute to the degradation in soils.

Biodegradation studies with PAA show a rapid degradation of PAA if the biocidal effect is not too strong. Sewage treatment plants with adapted activated sludge, would easily degrade PAA. The biodegradation is also enhanced when the biomass is high (as in the case of sewage treatment plant).

Based on the low octanol-water partition coefficient and the rapid degradation in the environment, PAA is not bioaccumulable.

In conclusion PAA should be easily degraded in air, water and soil and does not persist or accumulate in the environment.

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

5.1 Environmental Levels

5.1.1 Air

No specific measurement data are available.

Based on atmospheric model calculations, trace levels (4 ppbv[a]) of PAA were predicted by Calvert *et al* (1985) and Gaffney *et al* (1987).

Hellpointer and Gäb (1989) could not demonstrate PAA (detection limit 0.07 µmol/l) in 32 rainwater samples collected at Freising near Munich in Germany (April and May 1988).

Junkermann *et al* (1993), using the sensitive (detection limit 0.06 ppb) enzyme fluorometric method developed by Lazrus *et al* (1986) (Section 2.8), found PAA to be present among other hydroperoxides and H_2O_2 in mountain air at two different altitudes at sites in Germany (Schafberg 1,175 m and Wank summit 1,780 m). A pronounced seasonal and daily variation in the total concentration and composition of the hydroperoxides was seen (Junkermann *et al*, 1993).

Heikes *et al* (1991) measured soluble organic peroxides, including PAA, in remote marine air over the South Pacific ocean (Australia and Fiji). The total concentration was 0.4 ppbv near the sea surface (< 91.4 m) and 0.6 ppbv between the marine layer and the free troposphere (914.4 m to 3,352 m). At high altitude (5,638 m), the level was 0.2 ppbv. No specific concentrations for PAA were given.

Tanner and Schorran (1995) reported total gaseous peroxide levels near the Grand Canyon (USA) in the range of 1.0 - 5 ppbv. The results varied, depending on the daylight and the season.

Peroxide measurements of cloud and rainwater collected (48 samples) in the eastern USA indicated the presence of organic hydroperoxides in only some of samples (Kelly *et al*, 1985).

5.1.2 Water, soil and biota

No data are available on concentrations of PAA in water, soil and biota.

5.2 Human Exposure Levels and Hygiene Standards

5.2.1 Non-occupational exposure

No data are available.

[a] Parts per billion by volume

5.2.2 Simulated occupational exposure studies

A number of measurements of atmospheric concentrations were performed in an experimental setting to obtain an indication of possible occupational exposures levels during certain operations (Table 13).

Table 13: Simulated Occupational Exposure Studies

Description	Results (mg PAA/m^3)	Reference
Fogging of 0.2% PAA in closed shed, measured at different distances	0.7 - 7 H_2O_2[a]	Fraser and
Fogging of 0.2% PAA in closed shed, measured 5 - 60 minutes	ND - 3 H_2O_2[b]	Thorbinson, 1986
Pulp mill A, refrigeration room, doors closed	1.8	Cerne *et al*, 1999
Pulp mill A, refrigeration room, doors open	0.45	
Pulp mill B, refrigeration room, doors closed	0.45	
Pulp mill B, refrigeration room, doors open	< 0.15 (ND)	
Distillation, spill of 20 litres cold PAA (intentional), doors closed	1.5	Ancker and
Container filling above manhole outdoors	0.5	Zetterberg,1997
Laboratory, beakers w/o lid	0.15 - 0.5	
Laboratory, beakers w/o lid in vented hood	0.3-3	
Bath with 0.35% PAA, measured at 0.4 meter above bath	0.8 - 1.0[c]	Simms, 1995
Bath with 0.35% PAA, measured at 0.1 meter above bath	3.3[d]	
Bath with 0.35% PAA, measured at 2.7 meter from bath	< 0.3[e]	
Ten litre 0.35% PAA in water bath (50 x 29 x 19 cm) at 28°C in room without ventilation or air changes	< 0.7	Harvey, 1992
Filling of 1,000 kg IBC[f] with 15% PAA, measured at 0.6 m from top of container	0.3 - 0.5[g]	Rowbottom, 1996a
Filling of 1,000 kg IBC with 5% PAA, measured at 0.6 m from top of container	< 0.5[h]	
Distillation house A of PAA, near ground floor, small leak in pump	0.9 - 1.2[i]	McDonagh, 1997;
Distillation house A and B of PAA, first floor	0.4 - 0.5[ij]	Rowbottom, 1996b
Ten litre 0.35% PAA in water bath, ambient temperature, closed room	< 0.02	Harvey, 1993
Ten litre 0.35% PAA in water bath, temperature of 32°C, sealed room	< 0.02	

a Reported as 0.5 - 5 ppm H_2O_2
b Reported as < 0.5 - 2.0 ppm H_2O_2
c Reported as 0.35 - 0.46 mg/m^3 H_2O_2
d Reported as 1.46 mg/m^3 H_2O_2
e Reported as < 0.15 mg/m^3 H_2O_2
f Intermediate bulk container
g Reported as 0.1 - 0.15 ppm PAA
h Reported as < 0.15 ppm PAA
i Reported as 0.3 - 0.4 ppm PAA
j Reported as 0.13 - 0.17 ppm PAA

During the studies of Fraser and Thorbinson (1986), Harvey (1992 and 1993), Simms (1995), Rowbottom (1996a,b) and McDonagh (1997), the air samples were drawn through an alkaline solution of phenolphthalein. Peracids and H_2O_2 produced a pink colour by the formation of phenolphthalein, which was detected spectrophotometrically, and the results were reported as total peroxygen concentrations.

Fraser and Thorbinson (1986) fogged a solution containing 0.2% PAA into a hen house, which means that an aerosol was present. The product which was used (4% equilibrium PAA) contained presumably also a relatively high content of H_2O_2 which meant that a significant quantity of the measured atmospheric peroxygen might have been H_2O_2 (assuming a constant composition). Therefore, the results of this experiment are expressed in Table 13 as H_2O_2 concentrations.

Also Harvey (1992, 1993), Simms (1995), Rowbottom (1996a,b) and McDonagh (1997) measured the total peroxygen concentrations but in this case a vapour was present. Because PAA has a higher vapour pressure than H_2O_2 (Section 2.5), the measured peroxygen was probably mainly PAA. The results of these studies are presented in Table 13 as PAA concentrations.

The analytical measurements reported by Ancker and Zetterberg (1997) and Cerne *et al* (1999) were based on FTIR spectroscopy (Table 8) . In this case the PAA concentration was measured directly.

5.2.3 Occupational exposure

Given the applications of PAA there is a possibility for occupational exposure to aerosols or vapours or dermal exposure to the liquid. Hygiene procedures are designed to minimise skin, eye and inhalation exposure by appropriate technical and personal protective equipment depending on the situation at the particular workplace. Recommended safe handling procedures are provided (Section 10.2).

Workplace (area) measurements at Akzo Nobel, Eka Chemicals were reported in 1997 using direct FTIR spectroscopy (Table 8). PAA could only be measured near the distillation reactor where short-term concentrations ranged from 0.15 mg PAA/m^3 (detection limit) to 0.30 mg PAA/m^3 (original data given in ppm). No PAA was detected near the storage tank or outside a laboratory hood (Ancker and Zetterberg, 1997). Using the same method, no PAA was detectable at the dosage area of two pulp mills in 1998 (Cerne *et al*, 1999). No further information is available.

Measurements carried out at Ausimont during 1999 indicate short-term workplace concentrations of PAA ranging from < 0.1 to 0.9 mg PAA/m^3 in different areas of the production plant, in particular the filling area. Sampling was performed 3 x 2 h and 14 x 1 h. The analytical method was not stated (Ausimont, 1999, 2000).

Degussa (1990a) reported levels of < 0.1 to 0.5 mg PAA/m^3 (20 - 30 min/area) during bottle disinfection at a pharmaceutical company in 1990. The analytical method was not detailed. PAA was calculated from the amount of active oxygen taking into account the measured H_2O_2 levels.

PAA exposure was determined in a university hospital where employees (150 workers) used 0.12 to 2% aqueous disinfection and sterilisation solutions prepared from an equilibrium PAA 40% (3.5% H_2O_2, 46% HOAc). There were 121 samples taken at 45 different areas (2 - 6 measurements at each workplace). PAA was determined by means of a spectrophotometric technique (oxidative formation of iodine from a potassium iodine solution) with a detection limit of 0.005 mg/m^3. Workplace, 8-hour concentrations ranged from below the detection limit to 1.84 mg PAA/m^3. The majority (60%) of employees had readings below 0.1 mg/m^3, 95% were below 1 mg/m^3 (Schaffernicht and Müller, 1998).

5.2.4 Hygiene standards

No country has adopted an Occupational Exposure Limit Value (OEL) for PAA.

An internal OEL of 0.15 ppm PAA (0.45 mg/m^3) for an 8-h time-weighted average (TWA) concentration has been developed by Solvay (2000).

The following table gives examples of national OEL values for the three principal components of PAA formulations (Table 14).

Table 14: Examples of OEL Values for Components of PAA Formulations

	TWA[a]		Ceiling Limit		STEL[b]		Reference
Country	**(ppm)**	**(mg/m^3)**	**(ppm)**	**(mg/m^3)**	**(ppm)**	**(mg/m^3)**	
PAA	-	-	-	-	-	-	
H_2O_2							
Germany	1	1.4	2[c]	2.8[c]	-	-	DFG, 1999a
UK	1	1.4			2	2.8	HSE, 2000
USA	1	1.4[d]	-	-	-	-	ACGIH, 2000
HOAc							
Germany	10	25	20[c]	50[c]	-	-	DFG, 1999a
UK	10	25			15	37	HSE, 2000
USA	10	25[d]	-	-	15	37[d]	ACGIH, 2000

[a] Time-weighted average concentration (8-h working period)
[b] Short-term exposure limit (15 min, unless specified otherwise)
[c] 5 min, maximum 8 times per shift
[d] Not reported as such

6. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

6.1 Micro-Organisms

PAA formulations are fast-acting oxidising biocides that are effective against a broad spectrum of micro-organisms including bacteria, yeasts and moulds, protozoa, algae and viruses. Spores, bacteriophages and enteroviruses are also susceptible.

PAA is effective against micro-organisms over a wide range of conditions (Block, 1991). PAA is most active at pH values below the pKa (8.2) and also displays biocidal activity under mildly alkaline conditions up to pH 9. PAA remains efficacious even at low temperatures (5°C) (Schliesser and Wiest, 1979; Baldry, 1983; Block, 1991). The activity of PAA is relatively unaffected by organic matter compared to other oxidising biocides (Block, 1991).

Concentrations of > 300 mg PAA/l (as diluted equilibrium products) were highly effective against vegetative bacteria and yeasts in suspension tests where a 99.999% reduction was achieved within 5 minutes. More diluted concentrations of 30 mg/l were still effective against vegetative bacteria. Higher concentrations and longer exposure times were needed to inactivate spores formed by bacteria and moulds (Baldry, 1983; Bloomfield *et al*, 1991; Setlow *et al*, 1997).

Lensing and Oei (1985) reported 2,500 mg PAA/l to be effective against *Bacillus subtilis* and *B. cereus* within 30 minutes. Krzywicka (1970) reported 2,000 mg/l being effective against *B. subtilis* in 10 minutes. For moulds, the PAA dose required was variable. Some mould spores were inactivated at 500 mg PAA/l in 5 minutes, while others were affected at > 1,000 mg PAA/l for longer exposure periods.

PAA is effective against bacteriophages and enteroviruses such as the poliovirus, rotavirus and Coxsackie virus. Concentrations in the range 400 - 2,250 mg PAA/l for a 5 or 10 minute contact period were reported. Lower concentrations were effective over longer contact times (Kline and Hull, 1960; Harakeh, 1984; Baldry *et al*, 1990).

The effect of PAA (2 mg/l) on the microbial respiration or sewage sludge, measured as conversion of ^{14}C-glucose to $^{14}CO_2$, has been studied at sludge concentrations of 2.5 to 50 mg (dry weight)/l (Thus *et al*, 1997). Independent of the sludge concentration, conversion of ^{14}C-glucose to $^{14}CO_2$ was reduced to 10% of expected in the first 24 hours. When after 24 hours fresh sludge was added the respiration was comparable to controls again, indicating that no PAA toxicity remained.

6.2 Aquatic Organims

The results of toxicity tests with aquatic organisms are summarised in Table 15.

Table 15: Toxicity of PAA to Aquatic Organisms

Species	Duration (h)	Composition (%) PAA	H_2O_2	HOAc	Endpoint, result EC_{50} or LC_{50} (mg PAA/l)	NOEC (mg PAA/l)	Reference	CoR[a]
Algae					**Growth inhibition** EC_{50}			
Selenastrum capricornutum[b]	120	5.2	20	NS	0.18	0.13	Hicks *et al*, 1996	2b
Selenastrum capricornutum	72	18.0	0.3	NS	< 1.0	< 1.0	Petit-Poulsen *et al*, 1997[c]	2b
Scenedesmus subspicatus	72	0.35	7	NS	0.035 - 0.35	0.035	Licata-Messana, 1995a	2b
Invertebrates					**Immobility** EC_{50}			
Daphnia magna	48	15	14	28	0.50	0.15	Douglas and Pell, 1986a	2b
Daphnia magna	48	4.5	27.5	NS	1.1	0.45	Burgess and Forbis, 1983	2b
Daphnia magna	48	15.5	22	15	0.69	0.16	Terrell, 1987a	2b
Daphnia magna	48	5.2	20	NS	0.73	0.56	Gardner and Bucksath, 1996a	2b
Daphnia magna	48	18.0	0.3	NS	< 1.0	< 1.0	Lamy *et al*, 1997	2b
Daphnia magna	48	0.35	7	NS	0.035 - 0.350	> 0.035	Licata-Messana, 1995b	2b
					Lethality LC_{50}			
Crangon crangon[d]	96	12	20	8	15	6.7	Tinsley and Sims, 1987a	2e
Mytilus edulis[d] *embryo*	48	12.5	19	18	0.27	0.13	Fairhurst, 1987	2e
Crassostrea gigas[d] *embryo*	48	12.5	19	18	0.28	0.13	Butler, 1987	2e

Table 15 continued

Species	Duration (h)	Composition (%) PAA	H_2O_2	HOAc	Endpoint, result EC_{50} or LC_{50} (mg PAA/l)	NOEC (mg PAA/l)	Reference	CoR[a]
Fish								
Oncorhynchus mykiss[e]	96	15	14	28	2.0	1.5	Douglas and Pell, 1986b	2b
Oncorhynchus mykiss	96	15.5	22	15	0.91	0.16	Terrell, 1987b	2b
Oncorhynchus mykiss	96	4.5	27.5	NS	1.0	0.45	Cohle and McAllister, 1983	2b
Oncorhynchus mykiss	96	5.2	20	NS	1.6	0.82	Gardner and Bucksath, 1996b	2b
Lepomis macrochirus	96	4.5	27.5	NS	1.2	0.45	McAllister and Cohle, 1983	2b
Lepomis macrochirus	96	15.5	22	15	3.3	2.7	Terrell, 1987b	2b
Lepomis macrochirus	96	5.2	20	NS	1.1	0.47	Gardner and Bucksath, 1996c	2b
Brachydanio rerio	96	18.0	0.3	NS	1.0	< 1.0	Bazzon *et al*, 1997[c]	2b
Brachydanio rerio	96	0.35	7	NS	≈ 0.35	> 0.035	Licata-Messana, 1995c	2b
Pleuronectes platessa[d]	96	12	20	8	11	6.7	Tinsley and Sims, 1987b	2e

a Code of reliability (Appendix B)
b Presently known as *Pseudokirchneriella subcapitata* or *Rhaphidocelis subcapitata*
c Analytical methods following Gouges and Teral, 1997
d Saltwater species
e Previous name: *Salmo gairdneri*
NS Not Stated

6.2.1 Algae

A study with a freshwater green alga (*Selenastrum capricornutum*) and equilibrium PAA (5.2%) has been reported. The study was performed to good laboratory practice (GLP) guidelines. The test concentrations were 0, 0.065, 0.13, 0.25, 0.50 and 1.0 mg PAA/l. Growth was determined by algal cell counts. The concentration of H_2O_2 was measured in the test solutions. At the start of the test, the H_2O_2 content of all test solutions was close to the nominal concentration. At the end of the test, the measured concentration was lower than the detection limit except for concentrations of 0.50 and 1.0 mg PAA/l where the remaining measured H_2O_2 concentrations were 84% and 110% of the nominal values, respectively. At a concentration of 0.13 mg PAA/l an initial, statistically significant, inhibition of growth was found between 0 and 72 hours. Growth had recovered at the end of the test probably due to decreased exposure. Based on the cell count at the end of the test, a concentration of 0.13 mg/l was considered to be an NOEC. At a concentration of 0.25 mg/l the cell count at the end of the test was 3% of the control value. The 120-hour EC_{50} value was estimated to be 0.18 mg/l (Hicks *et al*, 1996). This indicates a remarkably steep dose-response curve.

In another GLP study with the alga *Selenastrum capricornutum*, distilled PAA (18%) was used to prepare test solutions with concentrations of 0, 1.0 and 10 mg PAA/l (Petit-Poulsen *et al*, 1997). The solutions were renewed every 4 hours. The algal suspensions were centrifuged followed by re-suspension of the algae in freshly prepared test solutions. Concentrations of PAA were analytically determined before and after renewal of the test solutions without algae. The mean decrease in concentration in the 4-hour periods was 14.3 and 6.5% at concentrations of 1.0 and 10 mg/l, respectively. Although the algae were centrifuged and resuspended 17 times during the test, the control cell density of the algae increased 20-fold during the 72-hour test period, which was higher than the minimum value of 16-fold (validity criterion). The growth of the algae was completely inhibited at 1.0 and 10 mg PAA/l.

A GLP study with *Scenedesmus subspicatus* and diluted equilibrium PAA (0.35%) was performed at nominal, static test concentrations of 0.035, 0.35 and 0.88 mg PAA/l. No analytical concentration measurements were made. At the end of the test, at a concentration of 0.035 mg/l, the growth rate was inhibited by 3% and total biomass by 11% of controls, but the inhibition of biomass was not statistically significant. At concentrations of 0.35 and 0.88 mg/l the growth of the algae was completely inhibited (Licata-Messana, 1995a). A concentration of 0.035 mg PAA/l can be considered as a NOEC. The H_2O_2 content of the product was 20 times higher than the PAA content and therefore the effect on the algae could be due to H_2O_2.

The effect of diluted equilibrium PAA (5%, 20% H_2O_2, 10% HOAc) on cyanobacteria (*Anabaena variabilis* and *Synecococcus leopoliensis*) and green algae (*Chlamydomonas eugametos* and *Scenedesmus quadricauda*) was studied using microtitre plates. In many tests an initial effect on algal growth was found at various concentrations, but growth recovered, probably due to a decrease in PAA concentration during the tests. The results were strongly dependent on the initial density of algal cells. A high cell density resulted in a strong decrease of the PAA concentration and a small effect on algal growth.

Cyanobacteria appeared to be more sensitive to than green algae. NOEC and EC_{50} values were not reported (Rodgers, 1991). This study is not reliable due to the use of a non-standard test methodology and reporting of insufficient detail. It is not clear whether the concentrations are expressed on the basis of the product PAA or the component PAA.

Evaluation
Three well-designed algal tests were performed in accordance with GLP guidelines. The study reported by Petit-Poulsen *et al* (1997) did not include a full concentration range, but the concentration of PAA was measured and maintained due to regular renewal of the test solutions. The study by Hicks *et al* (1996) was performed with a representative product, including a full concentration range, but only the concentration of H_2O_2 was determined analytically, and the PAA concentration calculated. The study of Hicks *et al* showed a decrease of the H_2O_2 concentration and a recovery of algal growth at relatively low concentrations. If concentrations are sufficiently low, an initial effect on the algae is expected but the algae will be able to degrade the product and growth may fully recover. At high concentrations algal growth will be completely inhibited and the product not degraded. Therefore recovery of the growth does not occur.

A test with H_2O_2 in the green alga *Chlorella vulgaris* according to a modified OECD Guideline 201 revealed EC_{50} and NOEC values of 2.5 and 0.1 mg H_2O_2/l, respectively (Degussa, 1991). Based on these values and the relatively high H_2O_2 (compared to PAA) content of the tested solutions, H_2O_2 could have contributed significantly to the observed toxicity. In particular, Hicks *et al* (1996) used a product with a relatively high content of H_2O_2.

6.2.2 Invertebrates

Daphnia magna
Three toxicity tests with diluted equilibrium PAA (4.5-15.5%) in the fresh water flea *Daphnia magna* have been reported, without analysis of the PAA, active oxygen or H_2O_2 concentrations in the test solutions (Douglas and Pell, 1986a; Burgess and Forbis, 1983; Terrell, 1987a,b) (Table 15). A GLP toxicity test with equilibrium PAA (5.2%) in *Daphnia magna* and was reported. During this study the H_2O_2 content of the test solutions was determined spectrophotometrically, based on titration with potassium permanganate, and the PAA concentrations calculated accordingly. During the test the decrease in H_2O_2 concentration ranged between 19 and 35%. Nominal test concentrations were 0, 0.19, 0.32, 0.54, 0.90 and 1.5 mg PAA/l (Gardner and Bucksath, 1996a).

A test with distilled PAA (18%) in *Daphnia magna* was performed at test concentrations of 0, 1.0 and 10 mg PAA/l. At the highest concentration all daphnids were immobilised after 4 hours. At 1.0 mg/l the daphnids were transferred to fresh solutions each 4-hour period and PAA concentrations were measured spectrophotometrically, using titration with potassium iodide, before and after each renewal. The mean decrease in concentration over the 4-hour periods was 21%. At the end of the test the immobility of the daphnids was 75% at 1.0 mg/l (Lamy *et al*, 1997).

Exposure of *Daphnia magna* to concentrations of 0, 0.0035, 0.035 and 0.35 mg PAA/l (dilutions of equilibrium PAA 0.35%) for 48 hours resulted in immobilisation rates of 5%, 5%, 5% and 100%, respectively. The EC_{50} value was 0.035 - 0.35 mg PAA/l (Licata-Messana, 1995b). It should be noted that the H_2O_2 content of the product, and test solutions, was relatively high. At the highest concentration the H_2O_2 concentration was equivalent to 7 mg/l, while the 24-h EC_{50} is 2.3 mg H_2O_2 (reported as 7.7 mg/l for a 30% solution) (Bringmann and Kühn, 1982). Thus, the low EC_{50} value, expressed as PAA concentration, can be explained by the high concentration of H_2O_2. However, also during the studies of Burgess and Forbis (1983) and Gardner and Bucksath (1996a) an effect of H_2O_2 on the observed toxicity cannot be excluded if the results are compared with the 24-h EC_{50} value of 2.3 mg H_2O_2/l reported by Bringmann and Kühn (1982).

The EC_{50} values of four tests with *Daphnia magna* ranged between 0.50 and 1.1 mg PAA/l, which shows a good reproducibility. In another test (Lamy *et al*, 1997) the immobility was 75% at 1.0 mg/l and, although only two concentrations were tested, the results of this test do not conflict with the previous four *Daphnia magna* test results. The test of Licata-Messana (1995b) is not so representative of PAA products because of the relatively high H_2O_2 content.

Other invertebrates

The study with equilibrium PAA (12%) in brown shrimp (*Crangon crangon*) revealed an 96-h LC_{50} value of 15 mg PAA/l. The medium was renewed daily during the study but analytical concentration measurements were not made. The mean weight of these saltwater crustaceans was 1.25 g (Tinsley and Sims, 1987a). The larger size of the organism compared to daphnids may explain the lower sensitivity of the shrimp. The high LC_{50} value could also be related to the rapid degradation of PAA in seawater (Section 4.2.3)

Two embryo-larval assays were carried out on marine oysters with nominal concentrations of equilibrium PAA (12.5%) dissolved in seawater, to determine any effects during their first 48 hours of their development from embryo to larva. In this period a protective D-shaped shell was formed. Without a shell the embryos were extremely sensitive to reduced water quality. Both tests were conducted under static conditions. In the first test with embryos of the pacific oyster (*Crassostrea gigas*), a 48-hour EC_{50} of 0.28 mg PAA/l was obtained (Butler, 1987). Another test with embryos of the common mussel (*Mytilus edulis*) resulted in an EC_{50} value of 0.27 mg PAA/l (Fairhurst, 1987).

The effect of PAA on the fertilisation rate of a marine tubeworm (*Pomatoceros triqueter*) was reported. Eggs and sperm were mixed with the test compound and then left for 3.5 hours. The reported EC_{50} value was 0.12 - 0.24 mg/l. Abnormal embryos were also recorded at concentrations of 0.06 and 0.13 mg/l, but further data, which could have enabled quantification of the effects at these concentrations, were not presented (Dixon,1988; CoR 2c). For this reason a reliable NOEC cannot be derived from this study. Ageing of the test solutions for 24 hours (as a 12 mg/l stock in seawater) resulted in a marked reduction of the toxicity, probably due to decomposition of the test solution.

In conclusion, the PAA toxicity studies with other aquatic invertebrates showed a relatively low toxicity for the large brown shrimp but consistent EC_{50} values of 0.1 to 0.3 mg/l were found when small and young organisms were used.

6.2.3 Fish

Four acute studies with rainbow trout (*Oncorhynchus mykiss*) have been reported (Table 15). The studies with this cold-water species were conducted at temperatures of 12-14°C. Only during the study of Douglas and Pell (1986b) were the test solutions renewed daily. Gardner and Bucksath (1996b) made analytical measurements of H_2O_2 in the test solutions. Between the start (0-hour) and the end of the test (96-hour) the decrease in the concentration of H_2O_2 ranged between 14 and 26%. The LC_{50} values of these toxicity tests show a good reproducibility.

Three acute studies with the warm-water bluegill sunfish (*Lepomis macrochirus*) have been performed (McAllister and Cohle, 1983; Terrell, 1987b; Gardner and Bucksath, 1996c). During the first two studies the test solutions were not renewed and chemical analysis were not conducted. Gardner and Bucksath (1996c), in a preliminary test using concentrations of 0.32; 0.54; 0.90; 1.5 and 2.5 mg PAA/l, measured concentrations of H_2O_2 after 96 hours to be less than 5% of the nominal concentrations. Therefore the test solutions were renewed daily during the final test. The mean decrease in the H_2O_2 concentration over a 24-hour period was 12% and the decrease ranged between 0 and 36%.

A semi-static acute toxicity test was conducted with distilled PAA (18%) in zebra fish (*Brachydanio rerio*); the tested concentrations were 0, 1.0 and 10 mg PAA/l. The zebra fish were exposed for 96 hours and they were transferred to fresh solutions each 4-hour period. The PAA concentrations were measured before and after each renewal using a titration with potassium iodide followed by a spectrophometry. In this case the mean decrease in concentration in the 4-hour period was 7.5% (Bazzon *et al*, 1997).

Another toxicity test in *Brachydanio rerio* was conducted with equilibrium PAA (0.35%) at concentrations of 0, 0.0035, 0.035 and 0.35 mg PAA/l. After 96 hours the percentage mortality was 0, 10, 0 and 60, respectively. This showed that the calculated LC_{50} was slightly lower than 0.35 mg/l (Licata-Messana, 1995c). The low LC_{50} value may have been partly due to the relatively high H_2O_2 concentration (7 mg/l) of the test solution, although LC_{50} values for fish are generally higher than 7 mg H_2O_2 (ECETOC 1993). For the other fish tests with PAA there is no indication of a contribution of H_2O_2 to the observed toxicity of PAA based on the LC_{50} of H_2O_2.

In the study of Tinsley and Sims (1987b), plaice (*Pleuronectes platessa*), a saltwater fish species, with a mean weight of 8.5 g was used. Test solutions were renewed daily during this semi-static test. The high LC_{50} could be due to the rapid degradation of PAA in seawater. The half-life in seawater is less than 1 hour and therefore the exposure during the fish test could have been low (Section 4.2.3).

6.2.4 Birds

When quails were given a commercial mash diet containing 750 ppm PAA for 5 days, no signs of toxicity were observed (Terrel, 1986b; CoR 4a). The diet was not analysed for PAA and because the substance was probably unstable in the diet the actual exposure to PAA is unknown.

6.3 Summary and Evaluation

PAA is an active bactericide, fungicide and sporicide. Spores are generally more resistant, as well as viruses. Many studies are available which describe the effect of PAA solutions on these target organisms, but these studies are in general conducted at relatively high concentrations and few concentrations per study, and are therefore not very useful for an environmental hazard assessment.

Toxicity tests with PAA and wildlife species, plants or other terrestrial organisms are not available.

Many different toxicity tests with aquatic organisms have been reviewed in the previous sections. Full reports were in general available allowing critical evaluation of the data. Although analytical measurements were conducted for only a few studies, those without analytical measurements provide useful information about the acute toxicity of PAA solutions.

For several standard species, e.g. *Selenastrum capricornutum*, *Daphnia magna*, *Oncorhynchus mykiss* and *Lepomis macrochirus*, more than one toxicity test was performed. The toxicity tests were reproducible if concentrations were expressed as PAA concentrations irrespective of the concentrations of H_2O_2 and HOAc. This indicates that the PAA concentration explains the toxicity of PAA formulations and therefore the concentration of H_2O_2 and HOAc are less relevant in this respect. However, for algae and daphnids the absolute concentrations of H_2O_2, at the effect concentrations of PAA, were close to the effect concentrations of studies with H_2O_2 alone. For fish the absolute concentrations of H_2O_2, at the effect concentrations of PAA, were not close to the effect concentrations of studies with H_2O_2 alone. In conclusion, it can be stated that for algae and daphnids there could be a contribution of H_2O_2 to the toxicity of the PAA formulations, while for fish there is not always evidence for an effect of H_2O_2 on the toxicity of PAA. If the product contains 0.35% PAA and 7% H_2O_2 then evidence for a contribution of H_2O_2 to the toxicity of the product for fish was found. Apart from this one example the data for fish did not evidence than effect of H_2O_2 content on the toxicity of the PAA formulation.

The results of the toxicity studies indicate a relationship between the size and sensitivity of the organisms. Small test organisms, like unicellular algae and mussel and oyster embryos, seemed to be relatively sensitive while larger test organisms such as brown shrimp and fish seemed to be less susceptible. This phenomenon could be related to the relatively unspecific mode of action of the compound. The mode of action of PAA is based on the oxidising properties that are relevant for all organisms. Small organisms are probably more sensitive because their body-surface to body-weight ratio is relatively high, which results in a relatively high uptake (per gram body weight).

The lowest endpoint was reported for an algal study with *Scenedesmus subspicatus* which revealed a NOEC of 0.035 mg PAA/l (Licata-Messana, 1995a). However, this study employed an atypical product composition (0.35% PAA, 7% H_2O_2). Based on the remaining standard toxicity tests, the lowest reported NOEC is 0.13 mg PAA/l.

A NOEC of 0.13 mg PAA/l was found for the algal study with *Selenastrum capricornutum* (Hicks *et al*, 1996). Although, an initial effect on growth was observed at this concentration a recovery of growth was found during the last part of the test. Probably the algae are able to degrade PAA if the initial concentration is sufficiently low. At higher initial concentrations the algae are killed and in this case PAA is more stable. No initial effect on the growth of *Selenastrum capricornutum* was found at a concentration of 0.061 mg PAA/l.

It can be concluded that small organisms are relatively sensitive to PAA. Taking account of the large number of standard toxicity test with algae, invertebrates and fish, the lowest NOEC was 0.13 mg PAA/l. At such a low concentration, the organisms were apparently able to promote the degradation of PAA.

7. KINETICS AND METABOLISM

7.1 Absorption and Distribution

An *in vitro* skin penetration test with freshly prepared pig skin was described by Krüger and Jancke (1976). A solution of 0.8% PAA (110 ml) (diluted from 40% PAA containing 5% H_2O_2 and 40% HOAc) was incubated with pig skin (5 cm surface area) in a diffusion cell at 37°C for 24 hours. The receptor fluid, physiological saline (110 ml) was analysed every 2 hours for active oxygen using photometric detection after reaction with potassium iodide solution with a detection limit of 2 µg. No PAA could be detected in the receptor fluid when intact skin was used (7 samples). Only in one experiment with a damaged skin sample in which the deeper layers were affected 2.6 mg active oxygen (calculated as PAA) was detected.

Phillips (1994a) studied the fate of ^{14}C-labelled PAA solution after dermal application to 4 male Sprague-Dawley rats. As the skin of the animals was severely damaged due to the corrosive effects of the applied solution, the results of this study cannot be used to assess absorption of PAA through intact skin.

Details of the preparation of the sample and test solution are given in Table 16.

Table 16: Protocol Used by Phillips (1994a)

	PAA test solution	**Control PAA-free solution**
Chemical composition	Distilled water 0.35 ml	None
	HOAc (glacial) 0.13 ml	HOAc (glacial) 0.1 ml
	[1-^{14}C]-HOAc, Na salt (≈ 130 µCi) 0.12 ml	[1-^{14}C]-HOAc, Na salt (≈ 130 µCi) 0.61 ml
	H_2O_2 solution 70% (v/v) 0.286 ml	H_2O_2 solution 70% (v/v) 0.28 ml
	Dequest 2010 (stabiliser) 10 µl	None
	Dipicolinic acid 2 µl	None
Preparation method	Heated to 50°C for 3 days in Sovirel tube	Mixed immediately before use
Final concentration	PAA 5.02%[a], H_2O_2 22.3%[a]	PAA < 0.04%[b]
Distribution of radioactivity	^{14}C: 14.39 µCi/100 µl attributable to HOAc (74%) and PAA (24%)[cd]	^{14}C: 13.10 µCi/100 µl[c] wholly attributable to HOAc[cd]

a Determined by cerimetric titration
b Determined by iodometric titration
c Determined by liquid scintillation counting
d Ratio determined by HPLC analysis and liquid scintillation of the appropriate fractions

A volume of 100 µl of the test and control solutions were applied to an area of 2.5 cm^2 of the clipped rat skin using a acrylic glass ring glued to the skin of the animals. Medical gauze was glued to the top surface of the plastic ring and the animals were then immediately placed in a metabolic cage for 72 hours. Water-soluble vapours (i.e. evaporating HOAc and PAA), exhaled CO_2, urine and faeces were collected and analysed at regular intervals. After 72 hours the animals were killed and the total radioactivity content was determined of the following organs: liver, kidneys, heart, lungs, testes, brain, stomach, small intestines, caecum/large intestines, muscle and perirenal fat samples, residual carcass. In a pre-experiment quantitative recovery of radioactivity due to volatilisation of HOAc and PAA from the test solution and of HOAc from the control solution in the metabolic cage had been demonstrated after placing samples of the solutions in the cage.

Body weight gain was not significantly different in the two groups. The skin of the test group animals was severely damaged after the 3-day exposure period and revealed substantial areas of scar tissue whereas that of the positive control animals appeared undamaged. The main results with regard to recovery of radioactivity are summarised in Tables 17 to 19.

Table 17: Percent[a] radioactivity recovered after 72 hours *(Phillips, 1994a)*

	PAA test solution	**Control solution**
Evaporated from skin	0.44 ± 0.1	19 ± 11.42
$^{14}CO_2$	35.68 ± 7.24	26.97 ± 5.33
Urine	10.47 ± 3.02	16.67 ± 3.85
Faeces	2.64 ± 1.2	3.37 ± 1.26
Cumulative total	49.24	66.01

[a] Values represent the mean % ± SD from 4 rats given a single dermal dose of 100 µl solution

Table 18: Distribution[a] of radioactivity recovered after 72 hours *(modified from Phillips, 1994a)*

	PAA test solution	**Control solution**
Evaporated from skin	0.71 ± 0.14	25.86 ± 15.73[b]
$^{14}CO_2$	57.82 ± 4.16	37.10 ± 7.63
Urine	17.16 ± 5.16	22.82 ± 4.76
Faeces	4.40 ± 2.31	4.68 ± 1.92
Tissues, carcass	19.91 ± 3.99	9.54 ± 2.79

[a] Values represent the mean % ± SD from 4 rats given a single dermal dose of 100 µl solution

[b] Includes one low value of 1 animal

Table 19: Distribution[a] of absorbed[b] radioactivity (%) recovered after 72 hours *(Phillips, 1994a)*

	PAA test solution	Control solution
$^{14}CO_2$	58.3 ± 4.2	50.2 ± 2.5
Urine	17.3 ± 5.2	30.8 ± 2.5
Faeces	4.4 ± 2.4	6.3 ± 2.4
Tissues, carcass	20.0 ± 4.0	12.8 ± 1.3

a Values represent the mean % ± SD from 4 rats given a single dermal dose of 100 µl solution

b Total recovered minus part that evaporated from skin

Total recovery of radioactivity in air evaporated from skin, expired air, urine and faeces was about 49% in the test group and 66% in the control group (Table 17). Evaporation of radioactivity from the rat skin during the treatment (captured in a water trap) was less than 1% of the applied radioactivity for the test group and 29 to 41% for 3 control group animals in the first 24 hours. In one control group animal only 2.5% of the total radioactivity was detected in the water trap within 24 hours.

When the recovered radioactivity is presented as a percentage of the absorbed dose (dose minus part that evaporated) significant differences between the test and control animals were obtained, in particular with regard to the amount eliminated in urine (31% in controls versus 17% in test group animals) and exhaled as $^{14}CO_2$ (50% in controls, 58% in test group animals). Recovery in the tissues and carcass was 13% in controls and 20% in test group animals.

In the test group $^{14}CO_2$ exhalation was rapid up to 8 hours following administration (including initial lag phase of 1 - 2 h), and then continued at a lower rate up to 72 hours. In the first 24 hours, 5 to 10% of the total recovered radioactivity was excreted in urine. On day 2 and 3, 1 to 3% was recovered in urine. Excretion of radioactivity in the faeces of the test group animals varied between 0.4 and 3% of the total recovered radioactivity per day. About 20% of the total recovered radioactivity was found in the tissues and carcass of the test animals. Highest tissue levels of radioactivity were observed in the residual carcass, the liver, the gastro-intestinal tract and the skin. Recovery of radioactivity was significantly higher than in controls in a number of tissues including kidney, liver, testes and gastro-intestinal tract.

In 3 of the control animals, $^{14}CO_2$ exhalation started immediately after application of the control solution and a substantial proportion of the radioactivity was recovered after the first 3 hours, thereafter the rate was much lower. Urine recovery of radioactivity was approximately 5% of the total recovered radioactivity after 24, 48 and 72 hours for all control animals. Excretion of radioactivity in the faeces of the control group animals varied between 0.4 and 3% of the total recovered radioactivity per day and was thus similar to that of the test group animals. In the controls about 9.5% of the total recovered radioactivity was found in tissues and the carcass. Highest tissue levels of radioactivity were observed in the residual carcass, the liver, the gastro-intestinal tract and the skin.

The authors concluded that the metabolic fate of the absorbed [1-^{14}C]acetic acid in the control animals was consistent with the known fate of HOAc in mammals. Free acetate is known to be metabolised by extra-hepatic tissues such as muscle and gut and is incorporated into carbohydrates, fatty acids, glycogen, cholesterol and protein. Acetate carbon atoms are mainly excreted as CO_2 and urea. An exhalation of 50% of the dose as CO_2 is consistent with literature data on acetate. The main differences observed between the PAA solution and the acetate control treatment were the lower amount evaporating from the skin within 24 hours and the apparent lag phase in exhalation of radioactive CO_2, the lower excretion in urine and a higher retention of radioactivity in tissues.

The higher dermal absorption could be due to the severe damage of the barrier of the skin observed after application of the PAA solution, resulting in an enhanced absorption rate. This would be consistent with the *in vitro* data of Krüger and Jancke (1976). The other differences observed could, according to the authors, suggest a different metabolic fate of the PAA/HOAc mixture compared to HOAc alone. However, the difference in absorption rate between intact and damaged skin could also explain these differences. It is possible that the lag phase is due to a lower blood flow in skin capillaries and a slower distribution due to the formation of micro-emboli from oxygen formation from H_2O_2 and/or PAA after a higher absorption rate through damaged skin.

No toxicokinetic data are available for other routes of exposure.

7.2 Evaluation

Although only limited experimental data are available on the absorption and distribution of PAA, some general assumptions can be derived from the physico-chemical data. All components of the equilibrium are of low molecular weight, high water solubility, low fat solubility and have no tendency to bioaccumulate (Section 4.2.5). For the PAA molecule itself an octanol/water partition coefficient of log P_{ow} = 0.3 was determined (Table 1). For H_2O_2, a log P_{ow} < 1 can also be estimated, while for HOAc a log P_{ow} of -0.31 to -0.17 has been reported (Verschueren, 1983). It can be assumed that absorption of PAA through skin and mucous membranes is possible, but limited by the high water solubility and low partition coefficients of the equilibrium compounds. Degradation of PAA itself and in particular H_2O_2 at the site of entry may further limit absorption due to capillary microembolism (Hauschild *et al*, 1958), detachment of epithelium and mechanical rupture of tissues close to the port of entry (Sheehan and Brynjolfson, 1960; Ludewig, 1965; Urschel, 1967). However, a considerable intake of radioactivity (from PAA and/or HOAc) was observed in damaged skin, once the skin barrier is destroyed by the corrosive effects of PAA solutions (Phillips, 1994a). In the stomach at pH 2 the undissociated acid is the predominant species (from the pKa-value of 8.2 a ratio acid/anion 10^7/1 can be calculated) which can penetrate into the cells. At a cellular pH 7.4 the ratio of the acid to the anion is smaller (6/1). It is possible that the diffusion into the cells may be enhanced by the concentration gradient for the undissociated acid. However, in the stomach fluid and inside the cells enzyme-catalysed degradation is to be expected. Once absorbed, PAA is expected to be distributed in the body fluid and metabolised; it can be anticipated that no accumulation in organs or body fat occurs.

The study of Phillips (1994a) seems to support those assumptions as it was shown that radioactivity of [1-^{14}C] labelled HOAc and PAA in a PAA solution was mainly exhaled as $^{14}CO_2$ and excreted in the urine. Radioactivity recovered in other organs and tissues is most probably due to the metabolism of HOAc in physiological pathways and synthesis of biomolecules.

7.3 Metabolism

7.3.1 Enzymatic reactions *in vitro*

In vitro experiments with a number of different enzymes and peroxo acids showed that there were no significant degradations of PAA by different lipases, proteases and butylcholinesterase. Rates of degradation were generally below 0.05 µmol/min/ml (concentration of the acid 0.02 mM, enzyme concentration 0.3 mM, phosphate buffer pH 8, 25oC, 15 min). A slightly higher rate of decomposition was observed with pig liver esterase (2.3 µmol/min/ml) and acetylcholinesterase 0.48 µmol/min/ml under the same experimental conditions. Generation of PAA was observed when 25 mM acetylcholine was incubated with acetylcholinesterase 25 U[a] /ml and 10 mM of H_2O_2 at pH 7. H_2O_2 was consumed within 5 minutes and PAA generated which was then degraded slowly with a half-life of about 25 min (Kirk *et al*, 1994).

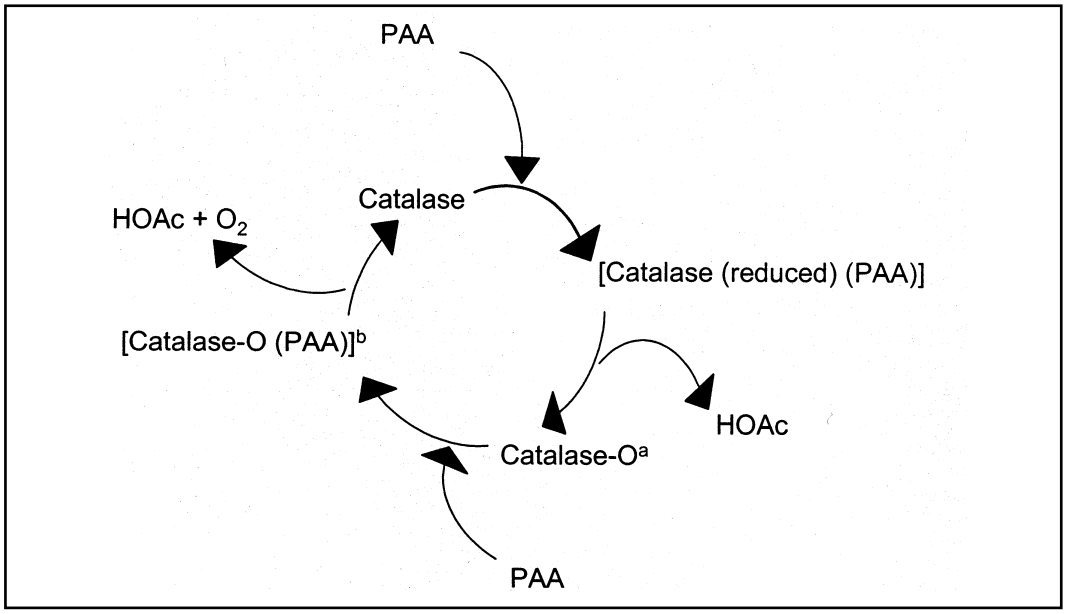
Several authors have shown that PAA is a substrate of catalases.

In vitro activity of beef liver catalase on PAA was evaluated by Ferri (1990). Beef liver catalase was dissolved in sodium phosphate buffer (70 mM, pH 7.0). Stock solutions of PAA (composition not stated) 5 mM in phosphate buffer were pre-treated with 8 nM catalase for 20 min at 20°C. Thereafter the stock solutions were diluted to the final concentrations. Spectrophotometry was performed using a double beamed spectrophotometer and thermostatically controlled cell. The difference in the molar absorption coefficients of the various oxidation states of the haem at 405 and 435 nm was used to quantify the kinetics of the inter-conversion of the different steps of the reaction. An amount of 1 nmol PAA corresponded to 5 x 10^{-3} absorbency units at 505 nm. Samples (70 µl) of the PAA solutions were added to a freshly prepared reaction mixture of phosphate buffer (0.1 M, pH 7.0), phenol (30 mM), 4-aminoantipyrine (6 mM), and horseradish peroxidase (2 U/ml). Under these conditions the peroxidase activity of catalase did not interfere with the assay. Catalase activity on H_2O_2 was assayed separately. The catalase reaction followed the summary equation:

$$2\ CH_3C(O)OOH \longrightarrow 2\ CH_3C(O)OH + O_2 \quad \text{(Eq. 2)}$$

[a] Activity Unit

Figure 1: Metabolism of PAA *(adapted from Ferri, 1990)*



[ ]	Theoretical intermediate
a	Compound I
b	Compound II
PAA	Peracetic acid
HOAc	Acetic acid
O_2	Oxygen

The first step is a first order reaction of catalase with substrate leading to immediate conversion of the enzyme-substrate complex to the oxidised state (Compound I) and the release of HOAc. Compound I is spectroscopically identifiable as a stable intermediate. The second step, first order with regard to Compound II and independent of the PAA concentration, regenerates the free catalase in a reduction reaction (kinetic constant $k_4 = 2 \times 10^{-4}$ s^{-1}). Oxygen and a second molecule of HOAc are released in that step which is the rate limiting reaction. The author showed that the catalytic cycle rate for PAA is independent of the substrate concentration and the rate determining step is the electron rearrangement inside the cycle rather than the adduct formation. This is different from the reaction of catalase with H_2O_2 or alkyl peroxide which is dependent on the substrate concentration.

Under steady-state conditions the PAA consumption was independent of the PAA concentration and the zero order rate constant was calculated to be 4×10^{-7} s^{-1}.

Another reaction was catalysed by catalase when the enzyme solution was supplemented with an excess of ethanol (10^3 to 10^4 times the enzyme concentration) prior to addition of PAA. Under these conditions ethanol was oxidised to acetaldehyde. In this reaction PAA was used as the source of oxygen for the oxidation reaction of ethanol. Because of the large excess of ethanol the reaction was only dependent on the PAA concentration

and the first order rate constant was determined to be 1.1 x 10^4 mol/l/s. During the reaction the enzyme spectrum was that of the resting state.

Jones and Middlemiss (1972) determined reaction rates of PAA (36 to 40%, no further data) with bacterial catalase (from *Micrococcus lysodeictikus*) or ox liver catalase. The PAA solutions used in the experiment were pre-treated with a small amount of catalase (2 nM) incubated for 30 min; the absence of H_2O_2 was assured by cerimetric titration. The PAA concentrations were determined iodometrically. The formation of Compound I was followed spectrophotometrically and was much slower than with H_2O_2. The reaction was more rapid with the ox catalase than with bacterial catalase. The pseudo first order rate constants were directly proportional to the PAA concentration, but the second order rate constants decreased with increasing pH. At pH 7 the first order rate constants for the formation of Compound I were respectively 1.44 x k_{HA}/mol/s with ox catalase and 5.72 x 10^{-2} x k_{HA}/mol/s with bacterial catalase. The rate constant apparently depended on the degree of dissociation and could be described as:

$$k_o = a\,(k_A^- - k_{HA}) + k_{HA} \quad \text{(Eq. 10)}$$

where A^- is the peroxoacetate ion, HA the undissociated PAA and a the degree of dissociation.

Different buffer systems showed similar results. From the results at different pH values the authors concluded that the reaction occurs predominantly with the undissociated acid. Compound I in this study was remarkably stable with the bacterial catalase, but less with the ox liver enzyme although a slow regeneration of free catalase eventually occurred. When ethanol or formate was added to a steady-state concentration of Compound I, the reaction rate with those substrates greatly exceeded the reformation of Compound I. The regeneration curves were first order and the pseudo first order rate constants were proportional to the substrate concentrations.

The reaction with human erythrocyte catalase *in vitro* confirmed that Compound I formation is a pH-dependent process. From pH 5.8 to 6.5 the rates were in the same range, but slowed down as PAA was deprotonated (pKa = 8.2). At pH 5.8 to 6.5 the apparent 2nd order rate constant for the formation of Compound I was 2.7x10^4/mol/s (Palcic and Dunford, 1980). Under the same conditions the rate constant is 6x10^6/mol/sec for H_2O_2 (Schonbaum and Chance, 1976). Below pH 5.8 Compound I was not stable and decomposed before steady state was achieved.

Addition of PAA to calf serum at a concentration of 0.05% at 4°C resulted in a degradation of PAA within 4 hours. Degradation is increased in whole blood owing to the presence of erythrocytes (Mücke, 1977).

One or 0.5 ml, respectively, of a 10% or 20% suspension of rat stomach fluid was added to 5 or 2.5 ml of aqueous solutions of PAA (5 to 200 mg/l) and PAA concentrations measured immediately after mixing. The PAA content was reduced by 28 to 76% depending on the concentrations. Addition of 100 µl of human saliva to 5 ml or 2.5 ml of PAA solutions containing 5 to 200 mg/l reduced the PAA content by 2 to 42 percent

immediately after addition of the saliva. These experiments indicate a catalytic degradation by catalases present in saliva and stomach fluid (Juhr *et al*, 1978).

The importance of the catalase reaction for the metabolism of PAA can be illustrated by looking at the distribution of catalases in the mammalian organism.

Catalases are present at a wide range of concentrations in nearly all mammalian cells; the enzymes are particularly efficient in metabolising large amounts of H_2O_2 (Chance *et al*, 1979). Catalases are located in sub-cellular compartments, mainly in peroxisomes (De Duve and Bauduin, 1966). Soluble catalases were found in erythrocytes (Saito *et al*, 1984).

The highest catalase content is observed in cells of the duodenum, liver, spleen, kidney, blood, mucous membranes and other highly vascularised tissues; the lowest catalase activity occurs in brain, thyroid, testes and connective tissue cells (Matkovics and Novak, 1977).

For a more detailed discussion of catalase activity, inter- and intra-species differences, the reader is referred to an ECETOC assessment of hydrogen peroxide (ECETOC, 1993, 1996).

7.3.2 Non-enzymatic degradation

In the absence of metal ions, diluted PAA solutions may undergo a pH-dependent hydrolysis yielding HOAc and H_2O_2. In the presence of metal ions, PAA may also decompose via the dismutation reaction to oxygen and HOAc (Mücke, 1977, see also Sections 2 and 3). While PAA is relatively stable at pH values around pH 2 it rapidly degrades to HOAc and oxygen at pH values at or above 7. PAA is stable at the pH of the stomach (pH 2) but will probably be degraded in the intestinal tract and locally after absorption in the cells. These reactions may play a role under physiological conditions. Reaction of PAA with reducing agents such as cysteine or gluthathione leads to a rapid reduction of PAA to HOAc (Mücke, 1977). This is likely to be important for the metabolic detoxification of PAA.

7.4 Elimination

Due to its rapid metabolism it can be assumed that PAA will not be excreted unchanged in urine, but will be degraded to oxygen and HOAc, the latter being further metabolised via normal physiologic pathways, ultimately to CO_2 and water. After dermal absorption of a PAA solution containing [1-^{14}C]-labelled PAA and HOAc it has been shown that the 58% of the absorbed radioactivity was exhaled as $^{14}CO_2$ and 17% was excreted in the urine (Philips, 1994a) (Section 7.1).

7.5 Summary and Conclusions

Only limited data are available on the kinetic properties of PAA. Due to the high water solubility and the low octanol water partition coefficients and possibly limited absorption by the formation of micro-bubbles of oxygen in the capillaries and tissues surrounding the exposed tissues, absorption into the circulation is assumed to be limited (ECETOC, 1993, 1996). However, skin damaged due to the corrosivity of PAA solutions can enhance the absorption of the components PAA and HOAc. In the stomach at pH 2 the undissociated acid is the predominant species (ratio acid/anion $10^7/1$) which can penetrate into the cells. At a cellular pH 7.4 the ratio of the acid to the anion is smaller (6/1). However, in the stomach fluid and inside the cells enzyme catalysed degradation is to be expected. Distribution is only likely in the body fluids and limited by the degradation of PAA. PAA may be degraded in the organism either non-enzymatically by hydrolysis, dismutation or reaction with reducing agents (cysteine, GSH), or enzymatically by the catalase reaction. The catalase reaction with PAA is independent of PAA concentration and may therefore be saturated. H_2O_2 is degraded rapidly by peroxidases, catalases and a number of other enzymes and antioxidants. As re-equilibration is probably slow, the influence of the withdrawal of H_2O_2 from the equilibrium on the degradation of PAA cannot be predicted from the available data.

8. EFFECTS ON EXPERIMENTAL ANIMALS AND *IN VITRO* TEST SYSTEMS

8.1 Acute Toxicity

8.1.1 Oral

A number of oral acute toxicity studies have been carried out in rats using aqueous solutions with different concentrations of PAA ranging from 0.89 to 40%. Details of these studies including the composition of the PAA solutions tested are shown in Table 20. Some studies were carried out keeping the volume constant and changing the PAA concentration according to the dose. Other studies were carried out using a constant concentration of PAA and changing the volume of administration according to the dose (indicated by a footnote in Table 20). In the older studies, the test concentrations were nominal, calculated from the basic PAA grade. In the most recent studies the PAA quality was analysed and the concentration of components measured. The more recent studies were carried out in accordance with standard OECD/EU/US-EPA and international GLP guidelines.

Table 20: Acute Oral Toxicity in Rats

Strain	Sex	Composition (%)			pH	LD_{50}[a] (mg/kgbw)	LD_{50}[a] (mg PAA/kgbw)	Effects observed	Reference	CoR
		PAA	H_2O_2	HOAc						
Sprague-Dawley	M+F	0.15	0.64[c]	NS	NS	> 5,000	> 7.5	None	Freeman, 1991a	1a
Wistar	M F M+F	0.89	7.27	10.85	NS	> 2,000 1,663 > 2,000	> 17.8 14.8 > 17.8	Severe inflammation of gastro-intestinal tract	Den Besten, 1994	1a
Wistar	M	2	7	19	< 0.7	1,175	23.5	No gross alterations at necropsy	Joakimson da Silva and Keiko s. Coimbra, 1990a	3a
Sprague-Dawley,	M F M+F	4.89	19.72	10[d]	NS	316 118 185	15.5 5.8 9.0	Local irritation in gastro-intestinal tract, nose, eyes and respiratory tract, diarrhoea	Kuhn, 1996a; Loera, 1996[e]	1a
Sprague-Dawley	M F M+F	5[f]	22[f]	10[f]	NS	1,993 1,859 1,922	99.7 93 96.1	Abdominal gripping and distension, loss of muscle control, gait disturbances, eye irritation, whitening of tissues and blood in gastro-intestinal tract	Freeman, 1998	1a
Sprague-Dawley	M F M+F	5.6	26.9	7.6	0.1	3,271 4,217 3,622	183.2 236.2 202.8	Soft faeces, reduced activity, irritation of gastro-intestinal tract	Haynes and Brightwell, 1998a[e]	1a
Sprague-Dawley	M F	10	NS	NS	NS	2,540[g] 2,390[g]	254 239	Sedation, local irritation of gastro-intestinal tract	Degussa, 1977a	1d
Sprague-Dawley	M+F	10.85	17.19	19	NS	200[h] - 1,000	21.7 - 325.5	Congestion of different organs, adherence of stomach, liver and gastro-intestinal tract	Gomond, 1998	2e
Sprague-Dawley	M F M+F	11.69	18.05	20[i]	NS	846 314 652	98.9 36.7 76.2		Kuhn, 1996b; Loera, 1996	1a
Wistar	M	14[i]	23[i]	16[i]	0.5	330[i]	23.1	No gross alterations at necropsy	Joakimson da Silva and Keiko s. Coimbra, 1990b	3a

Table 20 continued

Strain	Sex	Composition (%) PAA	H_2O_2	HOAc	pH	LD_{50}[a] (mg/kgbw)	LD_{50}[a] (mg PAA/kgbw)	Effects observed	Reference	CoR
Wistar	M F	15	21[k]	16[k]	< 2[k]	1,026 1,015	153.9 152.3	Local irritation of gastro-intestinal tract, respiratory tract and eyes	Degussa, 1982a[e]	1b
Sprague-Dawley	M F	17	22.9	NS	4	> 1,000 - < 1,260 < 397	> 170 - < 214.2 < 67.5		Cascieri and Freeman, 1983a	2b
Sprague-Dawley	M+F	35	7.3	NS	NS	50 - 500	17.5 - 175	Local irritation of respiratory tract and gastro intestinal tract (blood-filled stomach and intestines)	Freeman, 1987	1a
Albino	F	36 - 40	5	30	NS	263	95 - 105	Restlessness, increased respiration and cyanosis, hyperaemia and oedema of the gastro-intestinal tract, necrosis of kidney tubules	Busch and Werner, 1974[e]	2e
Albino	F	100	NA	NA	NS	314.8	314.8	Restlessness, increased respiration and cyanosis, hyperaemia and oedema of the gastro-intestinal tract,necrosis of kidney tubules	Busch and Werner, 1974[e]	2e

a Median dose expected to cause the death of 50% of the test animals after a 14 day observation period, except for the studies by Busch and Werner, who observed the rats for 3 days
b Code of reliability (Appendix B)
c Assumed value
d From Solvay, 1997a
e Dosage by constant volume
f Before dosing diluted to 1.25% PAA, 5.5% H_2O_2 and 2.5% HOAc
g Reported as 3.00, 3.00, 2.21 and 2.08 ml/kgbw; converted to mg/kgbw assuming a relative density of 1.15 (Table 2)
h Diluted to increase the dosed volume to 2.5 ml/kgbw
i From Solvay, 1997b
j Dispersed (1:1) in vegetable oil
k From Degussa, 1996b
F Female
M Male
NA Not applicable
NS Not stated

In the study of Den Besten (1994), 1 male rat and 4 females at the two highest dose groups were killed *in extremis* within 5 days of dosing. Clinical signs consisted of abnormal posture and gait, decreased locomotion, sniffeling, respiratory difficulties, ptosis and distended abdomen. Recovery became apparent from 2 days post dosing onwards, although surviving females at the highest dose level did not fully recover after 14 days of observation. Gross alteration in the female animals that were killed *in extremis* revealed severe inflammatory changes in the gastro-intestinal tract. No changes were seen in the survivors sacrificed at the end of the observation period.

Kuhn (1996a,b) administered two different concentrations of PAA (4.89 and 11.69%) to rats. Both concentrations caused overall the same clinical signs: decrease of activity as well as diarrhoea, nasal and ocular discharge, piloerection, gasping, polyuria, ptosis, staining of muzzle and back, salivation and respiratory chirp. In the vast majority of the animals, the signs were no longer evident at the end of the observation period of 14 days. The necropsy of the dead animals revealed gas in the gastro-intestinal tract and discoloured stomach, intestine, lungs, liver and spleen. The majority of the findings are indicative of the local irritant effect of the product; the authors did not explain the observed discoloration of the lungs and the spleen. No abnormalities were seen in survivors at the end of the observation period.

In the study of Freeman (1998), the most significant clinical signs observed were abdominal gripping and distension, loss of muscle control, squinting eyes, staggered gait, tremors, walking on toes, hypersensivity to touch, splayed hind limbs and hypothermia. Recovery was essentially complete after 7 days of dosing even if some signs persisted for up to 13 days. Examination of the animals that died revealed blanched stomachs and intestines, mottled and blanched livers, distended stomachs with thin linings, darkened red adrenals and white tracheas. Blood was found in the stomach and intestines. In the animals killed at the end of the observation period, only thinning of the stomach wall was seen at necropsy.

Haynes and Brightwell (1988a) reported general clinical signs, such as soft or mucoid faeces, reduced activity and piloerection, at all dose levels. Surviving animals generally recovered within 3 days. Macroscopic examination of the dead animals revealed abnormalities in the liver, stomach and regions of the gastro-intestinal tract. The stomach was commonly distended and white in colour. The intestines were dark red in colour. The liver either appeared dark or exhibited multiple pale areas. No significant abnormalities were found on necropsy of the survivors at the end of the observation period. The macroscopic findings in the dead animals are indicative of a local irritant effect of the product.

In the Degussa (1977a) study, clinical signs consisted of sedation, bloody discharge from the nose, ataxia and dyspnoea. Pathological findings were adhesion between the stomach and adjacent organs, perforation of the stomach in the animals found dead and haemorrhagic erosions of the stomach wall and oesophagus indicative of a severe irritation.

In the study of Gomond (1998), there were no deaths at the low dose level, while the mortality at the higher doses was between 60 to 100%, but without dose-response relationship. The autoptic examination of the descendants showed alterations to the stomach and congestion of different organs. The gross alteration of the survivors at the end of the observation revealed adhesion of different organs such as stomach, liver and gastro intestinal tract. No findings were see at the lowest dose level. The signs consisted of piloerection, abdominal constriction, hypoactivity and lessened muscular tone. These signs were evident a few hours after the administration and lasted up to 5 to 7 days following treatment. The method of administration of the low dose (dilution with distilled water) makes interpretation of the results difficult. This is also confirmed by the lack of a dose-response relationship at the higher dosages, supporting the hypothesis that all doses tested without dilution were severely irritant to the gastro-intestinal tract.

In the Degussa (1982a) study, signs indicative of irritation of the gastro-intestinal tract (writhing syndrome, stilted gait, and tremor), laboured breathing and bloody lachrymation were observed. Red coloured urine was also observed in females of the highest dose group. At necropsy adhesions were observed between the viscera and the peritoneum. The gastro-intestinal mucosa and parts of the liver close to the stomach appeared white or greyish in animals of the high dose group. In the lowest dose group no clinical signs indicating irritation were observed. This dose corresponded to a concentration of about 3% PAA, 4.5% H_2O_2 and 4% HOAc.

Cascieri and Freeman (1983a) observed mortality at all dose levels in males and in all but the 250 and 630 mg/kgbw doses in females. These data were not in accordance with the dose-response relationship and they were considered by the authors as indicative of the instability of the test material. The latter dose groups were tested at a later date than the preceding dose groups. The predominant clinical signs were decreased locomotion, rales, haematuria, abdominal distension, abdomino-genital staining, unthriftiness recumbacy, oral and nasal discharge. Gross necropsy of the decedents and the survivors included gross alteration of the stomach, liver and intestines.

Freeman (1987) reported that all animals died at 500 mg PAA/kgbw and one animal at 50 mg/kgbw. Predominant clinical signs were dyspnoea, oral discharge, chromorhinorrea and decreased locomotion. Gross lesions among descendants included mainly blood-filled stomachs and intestines. There were no gross internal alterations in any surviving rats.

A preliminary test with undiluted 40% PAA in Sprague-Dawley rats was aborted since all animals died from perforating ulcerations in the oesophagus and stomach at 0.5 ml/kgbw (226 mg/kgbw), the lowest dose tested (Degussa, 1977b; CoR 3a).

Several other studies are reported in the literature. Different values of LD_{50} (median dose expected to cause the death of 50% of the test animals) are cited but with a poor level of detail regarding the concentration and formulation of PAA used and the design of the study. This reduces their value for the toxicological evaluation of PAA (Tichácek 1972; Busch and Werner 1974; Merka and Urban, 1976; Reagan *et al*, 1983; all CoR 3a).

Evaluation

The acute oral toxicity data on the different PAA solutions tested do not show a consistent pattern that can be related to PAA dose or concentration, even when the composition appears to be similar. The test results also seem not related to the H_2O_2 concentration, but rather to the total composition of the tested formulation. The fact that the volume of administration was fixed or variable did not help to explain the differences seen in the results of the studies. Symptoms and pathological findings were similar in all studies and are consistent with the irritant/corrosive properties of the test material. Formulations containing less than 10% PAA seem to possess a low oral toxicity.

8.1.2 Dermal

Several dermal toxicity studies have been carried out in rats and rabbits with aqueous solutions of PAA at concentrations ranging from 0.89 to 11.6%. The most reliable dermal toxicity studies are summarised in Table 21. When indicated by the protocol, the PAA solutions were administered undiluted, adjusting the volume of administration according to the dose. The test concentrations were nominal, calculated from the basic PAA grade. In the most recent studies, the PAA quality was analysed and the concentration of components measured. The more recent studies were carried out in accordance with standard OECD/EU/US-EPA and international GLP guidelines.

Table 21: Acute Dermal Toxicity

Species (strain)	Sex	Composition (%) PAA	H_2O_2	HOAc	pH	Exposure conditions	LD_{50}[a] (mg/kgbw)	LD_{50}[a] (mg PAA/kgbw)	Effects	Reference	CoR[b]
Rat											
Sprague-Dawley	M+F	0.15	0.64[c]	NS	NS	24 h, occluded	> 2,000	> 3	No signs of toxicity, no pathological organ findings, no changes at site of contact	Freeman, 1991b	1a
Wistar	F	0.89	7.27	10.85	NS	24 h, occluded	> 2,000	> 17.8	No signs of toxicity, no pathological findings, white and red spots at the application site, encrustation in some animals 1 week after administration	Koopman, 1994	1a
Wistar	M	2	7	19	0.7	NS, presumably non-occlusive patch	> 12,000	> 240	No signs of toxicity, no pathological changes	Joakimson da Silva and Keiko s. Coimbra, 1990d	3a
Wistar	M	14[d]	23[d]	16[d]	0.5		> 12,000	> 1,680	No signs of toxicity, no pathological changes	Joakimson da Silva and Keiko s. Coimbra, 1990c	3a
Rabbit											
New Zealand Albino	M F M+F	4.89	19.72	10[e]	NS	24 h, semi-occlusive	1,280 1,040 1,147	62.6 50.9 56.1	Decreased activity, diarrhoea, nasal discharge, ptosis, salivation andslow gazing. No pathological changes attributable to the test substance. Local effects: moderate to severe erythema, slight to severe oedema, eschar formation	Kuhn, 1996c; Loera, 1996	1a

Table 21 continued

Species (strain)	Sex	Composition (%) PAA	H_2O_2	HOAc	pH	Exposure conditions	LD_{50}[a] (mg/kgbw)	LD_{50}[a] (mg PAA/kgbw)	Effects	Reference	CoR[b]
Rabbit											
New Zealand Albino	M F M+F	11.69	18.05	20[f]	NS	24 h, occlusive	1,912 1,990 1,957	223.5 232.6 228.8	Decreased activity, diarrhoea, nasal discharge, ptosis, salivation, slow gazing. No pathological changes attributable to the test substance. Local effects: moderate to severe erythema, slight to severe oedema, eschar formation	Kuhn, 1996d; Loera, 1996	1a
New Zealand White	M+F	17	22.9	NS	24 h, occlusive		> 200	> 34	No signs of toxicity. No pathological changes attributable to the test substance. Local effects: severe erythema, blanching of skin, eschar formation, exfoliation in 3 animals	Cascieri and Freeman, 1983b	1b

a Observation period: 14 days
b Code of reliability (Appendix B)
c Assumed value
d Dispersed (1:1) in vegetable oil
e From Solvay, 1997a
f From Solvay, 1997b
F Female
M Male
NS Not stated

Several other studies carried out in rats and mice are reported in the literature. Different values of LD_{50} are cited but with a poor level of details regarding the concentration and formulation of the PAA solution tested and the study design. The toxicological relevance of these studies is therefore questionable (Reagan and Becci, 1983; CoR 3a; Benes *et al*, 1966; CoR 4d; Kramer *et al*, 1987a; CoR 3a).

Evaluation

Overall, the dermal toxicity depends on the degree of skin damage caused by the different PAA solutions. Only Kuhn (1996c) reported signs of toxicity (nasal discharge) that could be attributed to systemic effects at the high dose levels. However, it is likely that these signs were caused by additional inhalation exposure in this particular study.

8.1.3 Inhalation

Various inhalation toxicity studies have been carried out in rats and mice with solutions containing up to 40% PAA. Details of the studies and the composition of the PAA solution are shown in Table 22. PAA was tested as vapour or aerosol. In most studies, no morbidity or mortality was seen.

Table 22: Acute Inhalation Toxicity

Species (strain)	Sex	Composition (%) PAA	H_2O_2	HOAc	pH	Duration (h)	LC_{50} (mg/m³)	LC_{50} (mg PAA/m³)	Reference	CoR[a]
Rat							**Aerosol**			
Wistar	M+F	15	NS	NS	NS	4	505 - 1,263	76 - 189	Terrell, 1986a	4a
Wistar	M	5.4	≥ 19	10	NS	4	NS	213[b]	Janssen and Van Doorn, 1994	1a
	F						NS	186[b]		
	M+F						4,080	204[b]		
Sprague-Dawley	M+F	4.5	27	16.7	NS	4	> 5,350	> 241	Dudek, 1984	1a
Sprague-Dawley	M+F	0.15[c]	0.67[c]	0.30[c]	NS	4	> 7,669	> 117[d]	Whitman, 1991	1d
Rat							**Vapour**			
Sprague-Dawley	M	35.5	6.8	39.3	NS	4		≈ 490[def]	Hutt and Kinney, 1985	1a
Wistar	M+F	5	20[g]	10[g]	NS	4	> 5,000	> 200[h]	Biffi, 1992a	2e
Wistar	M+F	5	20[g]	10[g]	NS	4	> 50,000	> 2,000[h]	Biffi, 1995	2e
Mouse										
CBA, NS		36-40[i]	NS[i]	NS[i]	NS	1	NS	1,334 - 5,404[f]	Krüger and Kruschinski, 1982	2a
						0.5	NS	4,171[f]		

a Code of reliability (Appendix B)
b Nominal concentrations calculated by the authors from aerosol composition, assuming 5% PAA content
c PAA 5%, diluted (1:33) in distilled water; H_2O_2 and HOAc concentrations from FMC, 1998a
d Measured concentrations
e Approximate Lethal Concentration
f Vapour/aerosol
g From Solvay, 1997a
h Calculated from partial vapour pressure of PAA in a 5% solution (Table 2)
i Inferred from other publications on the same compound
F Female
M Male
NS Not stated

Aerosol studies

Terrel (1986a) exposed rats to aerosol (or vapour, not clearly stated in the report) concentrations of PAA ranging from 18 to 2,138 mg/m^3. The animals were kept under observation for 14 days after the exposure. During the exposure the animals showed a range of clinical signs which consisted of blinking, foaming, gasping, nasal discharge, salivation, lachrymation, ptosis, laboured respiration, twitching, chewing motion, convulsions, staggering, cornea opacity or death depending on the concentration. Post-exposure clinical signs were laboured respiration, nasal discharge, gasping, lachrymation, haemorrhage from the eye, cornea opacity, blindness, staggering, loss of righting reflex, crusty appearance, piloerection or death depending on the dose. Gross necropsy of the animals that died during the observation period revealed alterations to the lungs and thymus, enteritis, swollen nose, congested nasal cavity and trachea, thickening of the oesophagus and larynx. Animals that were killed at the end of the observation period showed similar alterations. A more detailed evaluation of the study is not possible since only the summary is available.

Janssen and Van Doorn (1994) tested a 4.7 - 5.4% solution of PAA in rats exposed nose-only to aerosols containing measured concentrations of 87, 163, 185 and 267 mg PAA/m^3. The animals were observed for 14 days after exposure. Mortalities were observed only in the two highest dose groups. Clinical signs consisted of apathy, respiratory distress, reduced respiratory rates, decreased fear reaction, freezing and reduced locomotion activity. A number of clinical signs indicative of irritant effects of the product were noted. Surviving animals suffered from a temporary loss of body-weight. Animals that died during the observation period revealed increased lung weight and pulmonary oedema. No macroscopic alterations were seen at necropsy carried out at the end of the observation period.

In the study of Dudek (1984), none of the rats died during the study. All the animals showed irregular breathing and damp fur during the exposure. No macroscopic alterations were found at necropsy.

Whitman (1991) exposed rats whole-body to an aerosol / vapour (nominal concentration 66,171 mg/m^3, actually 7,669 mg/m^3) containing 117 mg PAA/m^3 and observed them for 14 days. A particle size analysis was attempted, but did not produce any valid results due to the extremely high (> 99%) water content of the test atmosphere and the volatility of the test material. No rats died during the study. Clinical signs observed during the exposure were decreased activity and closed eyes. After the exposure some animals showed ocular discharge that lasted for up to 8 days. At necropsy all animals appeared free from any test-related macroscopic alterations.

Janssen (1989a,b) exposed rats (Wistar, M and F) nose-only for 0.5, 1 and 1.5 hours to an aerosol nebulised from a solution containing 15% PAA (14% H_2O_2 and 28% HOAc). Two separate tests were carried out. In the first test, the animals were exposed for 15, 30 and 60 minutes (5 male rats per exposure period); in the second test another group was exposed for up to 90 minutes. The mean measured concentration of PAA in the first test ranged from 0.13 to 1.45 mg/l (130 - 1,450 mg/m^3), in the second test the measured concentration varied from 0.17 to 0.59 mg/l (170 - 590 mg/m^3). The animals were kept

under observation for 14 days after exposure. At necropsy, the organs of the respiratory tract as well as the head of the animal were removed and preserved for histopathological examination (the nasal cavities were also flushed with fixative). Two animals exposed to 590 mg/m^3 for 60 minutes were killed *in extremis* 24 hours after the exposure; mortality was also observed in the highest dose group exposed for 60 minutes in the first test. Clinical signs consisted of noisy breathing, sniffing, sneezing, nasal discharge and intensified grooming. The severity and time of disappearance of the clinical signs increased with the exposure level and duration. No clinical signs persisted until the end of the observation period. Macroscopic examination of animals that died or were killed *in extremis* during the observation period revealed alteration to the respiratory tract (red mucosa of internal nares and trachea, blood in trachea and red lungs), while gas was found in the gastro-intestinal tract; the latter was attributed to air swallowed during the exposure. Histopathology of the upper respiratory tract revealed tissue damage limited to the anterior parts of the nasal cavity in the area where the epithelial lining changes from respiratory to olfactory epithelium. Histopathology of the lungs revealed blood and alveolar macrophages in one animal and hyperplasia and metaplasia in two others. No alterations were found in the animals that were killed at the end of the observation period. No LC_{50} values were calculated in this study.

Benes *et al* (1966; CoR 4b as cited by Heinze et al, 1982) performed acute inhalation studies in rats (strain and sex not stated). Exposure to aerosols containing 7.2, 72, or 237.6 mg PAA /m^3 for 4 hours resulted in signs of restlessness in the low dose group. Additional signs in the mid-dose group consisted of lachrymation and laboured breathing. In the high dose group lung oedema was observed and one animal died (group size not reported).

Vapour / aerosol studies

Hutt and Kinney (1985) administered a vapour/aerosol atmosphere to groups of 6 male Sprague-Dawley rats. The animals were exposed nose-only for 4 hours to PAA concentrations varying from 260 to 670 mg/m^3. The test atmosphere was sampled and PAA concentrations analysed by iodometric titration. After the exposure the animals were kept under observation for 14 days. During the exposure the animals showed moderate red nasal discharge and did not exhibit a normal startle response. Rats exposed to 490 mg/m^3 had laboured breathing. Two rats exposed to 490 mg/m^3 and one rat exposed to 670 mg/m^3 died, 1 and 2 days respectively after the exposure. One to 4 days after cessation of exposure all animals showed lung noise, laboured breathing or gasping and nasal and ocular discharge. At lethal concentrations some rats had diarrhoea, hunched posture, wet or stained perineum and discoloured fur.

Biffi (1992a, 1995) carried out two different acute inhalation toxicity studies with a solution of 5% PAA containing 20% H_2O_2 and 10% HOAc. (Assuming the vapour phase contained 2% H_2O_2, 4% PAA and 9% HOAc, the respective partial pressures were 0.4, 0.3 and 0.8 hPa). Rats were exposed whole-body to a vapour with a nominal concentration of 5,000 mg/m^3 (limit test) and 50,000 mg/m^3. No mortality was seen. Clinical signs consisted of dyspnoea, piloerection and hyperaemia of nasal mucosa. Body weight gain was not affected. No alterations were found at necropsy after the 14-day observation period.

Krüger and Kruschinski (1982) studied the influence of fog density, i.e. the amount of liquid in 1 m^3 of air, on the concentration of PAA aerosol and vapour when aerosols were generated from solutions of different concentrations. Aerosols with droplet size ranging from 0.6 to 4 µm diameter, the majority between 1.5 and 2 µm (i.e. in the respirable range), were generated in a volume of 0.138 m^3. Groups of 10 CBA mice (sex not stated) were exposed to aerosols generated from diluted PAA solutions (1 to 23%; content of H_2O_2 and HOAc not stated) yielding fog densities of 7.25, 14.5, 29, 58 and 116 ml/m^3 for 1 hour. The post-exposure observation period lasted 47 hours. When the exposure time was held constant the lethal concentration was dependent on the fog density. A 50% death rate was reported for a 3.6% PAA solution (corresponding to a LC_{50} of 1,334 mg PAA/m^3) at a fog density of 116 ml/m^3 and an 18.5% PAA solution (corresponding to an LC_{50} of 5,404 mg PAA/m^3) at a fog density of 7.25 ml/m^3. In a second experiment, a 30-min LC_{50} of 4,171 mg/m^3 was obtained with aerosols created from 4, 5, and 8% PAA solutions with a fog density of 116 ml/m^3. According to the authors the LC_{50} was not related to the concentration of PAA expressed in mg/m^3. Furthermore, the aerosol was probably not stable over the experimental period and some PAA may have volatilised into the vapour phase, which would have complicated the determination of the actual concentration of PAA in the aerosols.

The same authors (Krüger and Kruschinski, 1982) exposed groups of 3 CBA mice (sex not stated) in closed chambers to atmospheres saturated with vapour/aerosol from PAA solutions of 5, 17, 20 and 40% PAA. The concentrations of PAA in the vapour phase were calculated using an equation derived from experimental determinations of PAA vapour equilibrium concentrations over open PAA solutions of different concentrations at different temperatures. Death of the animals occurred after inhalation of 3,800 mg PAA /m^3 for 1 hour or 260 mg/m^3 for 20 hours.

Other acute inhalation studies are reported in the literature. The lack of details regarding the study protocol and the experimental conditions prevents their use in a meaningful evaluation of the inhalation toxicity of PAA in experimental animals (Tichácek, 1972; Merka and Urban, 1976; Spiegelberger *et al*, 1984; all CoR 3a).

Evaluation

The available acute inhalation studies with aerosols and vapour derived from different PAA solutions suffered from the difficulty of generating and maintaining a stable atmosphere of PAA, and accurate measurement of the composition of the test atmosphere and particle size of the aerosol. The resulting LC_{50} values should therefore be treated with circumspection.

A common finding of those studies was local irritation of the respiratory tract, which seems more pronounced with PAA aerosols than vapours.

8.1.4 Intravenous

In mice, an intravenous LD_{50} of 17.86 mg/kgbw was reported (composition and concentration of PAA solution not specified) (Li *et al*, 1988; CoR 4). Gloxhuber and Kästner (1983; CoR 2c), testing a formulation containing 4.6% PAA, 29.4% H_2O_2 and 7.4% HOAc in CF1 mice, determined an LD_{50} value of 212 mg PAA/kgbw.

8.1.5 Summary and evaluation

The acute toxicity of PAA has been studied in experimental animals. The oral, dermal and inhalation routes are the most relevant routes of administration for health hazard assessment.

PAA is of moderate acute toxicity via the oral route. The acute oral toxicity of PAA formulations is dependent on the composition (i.e. the content of PAA, H_2O_2 and HOAc) and the concentration of the applied test solution. PAA formulations containing less than 10% of PAA are usually of low oral toxicity.

The acute dermal toxicity of PAA formulations is relatively low, depending on the applied concentration and presence of local irritation.

The available acute inhalation toxicity studies in rats and mice with aerosols and vapours derived from different PAA formulations suffer from difficulties in achieving and measuring constant concentrations due to the instability of the test substance itself and the aerosol droplets. Consequently LC_{50} values derived from such studies show a wide variation. The main effect in all studies was local irritation of the respiratory tract.

The predominant effect of PAA in all acute toxicity studies is local irritation at the site of contact, the extent of which depends on the concentration and the composition of the applied test solution.

8.2 Skin, Respiratory Tract and Eye Irritation, Sensitisation

8.2.1 Skin irritation

Rabbits

An overview of the available skin irritation studies in rabbits and composition of the PAA formulation tested is presented in Table 23.

Table 23: Skin Irritation Studies in Rabbits

Concentration applied[a] (% PAA)	Composition (%) PAA	H_2O_2	HOAc	Dilution	Exposure duration	Result	Reference	CoR[b]
40	36-40	< 5	45	None	4 h	Corrosive	Janssen and Pot, 1987	2b
17	17	23	16	None	4 h	Corrosive	Cascieri and Freeman, 1983c	1a
15	15	15	30	None	4 h	Corrosive	Janssen and Pot, 1987	2b
15	14-15	22-23	16	None	4 h	Corrosive	Degussa, 1982b	1b
15	14-15	22-23	16	None	3 min	Corrosive	Degussa, 1990b	1a
10	10	< 5	25	None	3 min	Corrosive	Degussa, 1988a	1a
5	20[c]	10[c]	NS	1:4	24 h	Corrosive	Biffi, 1992b	2b
5	5	20	10	None	4 h	Corrosive	Janssen and Pot, 1987	2b
5	5	24-25	4-5	None	45 min	Corrosive	Degussa, 1988b	1a
5	5	24-25	4-5	None	3 min	Moderate to severe irritant	Degussa, 1988b	1a
3.87	15.5	22	15	1:4	1 h	Corrosive	Van Beek, 1980	2e
3.87	15.5	22	15	1:4	3 min	Not irritant	Van Beek, 1980	2e
3.4	34	7.5	40	1:10	24 h	Corrosive	Duprat *et al*, 1974	2e
0.35	14	23	16	1:40	24 h	Not irritant (slight erythema)	Joakimson da Silva and Keiko s. Coimbra, 1990e	2e
0.34	34	7.5	40	1:100	24 h	Slight irritant	Duprat *et al*, 1974	2e
0.20	2	7	19	1:9	24 h	Not irritant (slight erythema)	Joakimson da Silva and Keiko s. Coimbra, 1990f	2e
0.17	34	7.5	40	1:200	24 h	Slight irritant	Duprat *et al*, 1974	1d
0.15	5-6	22-23	10-11	1:33	4 h	Not irritant	Freeman, 1991c	1a
0.034	34	7.5	40	1:1,000	24 h	Not irritant	Duprat *et al*, 1974	1d

a Sample volume for all tests: 0.5 ml
b Code of Reliability (Appendix B)
c From Solvay, 1997a
NS Not Stated

PAA solutions of 40% (Janssen and Pot, 1987), 17% (Cascieri and Freeman, 1983c), 15% (Degussa, 1982b; Janssen and Pot, 1987) and 5% (Janssen and Pot, 1987; Biffi, 1992b) were found to be corrosive to rabbit skin. The test solutions were applied at a volume of 0.5 ml for 4 hours using standard skin irritation protocols (Draize Test).

Exposure of the skin of one animal to 0.5 ml PAA 15% for 3 minutes under occlusive conditions resulted in white to yellowish discoloration of the application site and deepening of the treated skin area. Severe erythema was observed at the border of the application site and slight oedema was reported. Microscopic examination revealed

complete coagulation necrosis of the epidermis and upper third of the corium including skin adnexae. The damage developed within 1 hour. It was concluded that 15% PAA was corrosive after 3 minutes of occlusive exposure (Degussa, 1990b).

After exposure of 3 rabbits to 10% PAA for 3 minutes under occlusive conditions whitening of the skin was observed 1 hour after removal of the patch. After 24 hours severe damage of the skin developed with necrosis up to 5 mm in depth (Degussa, 1988a).

Groups of 6 male New Zealand white rabbits were exposed to PAA 5% for 24 hours under occlusive conditions. The patches were removed 24 hours after the application and the skin was washed using saline solution. The alterations were scored using the Draize method, from 1 to 7 days after exposure. The medium score was 4.00, i.e. PAA was extremely irritant (Biffi, 1992b).

Groups of 3 rabbits were exposed to PAA 5% for 3 or 45 minutes under occlusive conditions. After the 3 minutes exposure period, moderate to severe erythema and very slight to slight oedema (primary irritation index 3.3) were observed. The effects were completely reversible within 14 days. Exposure for 45 minutes resulted in corrosive effects. For humane reasons the animals were killed after two days (Degussa, 1988b). An *in vitro* skin corrosion study using Corrositex Continuous Time Monitor Assay was also conducted with 5% PAA. The results indicate that a 5% solution is corrosive according to the US Department of Transport (DOT) Packing Group II classification system (Nims, 1996a).

A 3.4% test solution (from 3.4% PAA, diluted 1: 10) was corrosive when applied to rabbit skin for 24 hours in a volume of 0.5 ml (Duprat *et al*, 1974). A 3.87% (diluted) PAA solution was placed in contact with the skin of rabbits for 3 minutes (4 animals) or 60 minutes (6 animals). There was no skin reaction other than slight erythema following the 3-min exposure. Severe skin reactions were noted in animals exposed for 60 minutes to the final concentration of 3.87% PAA, indicating a corrosive response (Van Beek, 1980).

Duprat *et al* (1974) reported slight irritation after exposure of rabbit skin to 0.34% or 0.17% test solutions for 24 hours. Joakimson da Silva and Keiko s. Coimbra (1990e,f) found no skin irritation after exposure to a 0.20% solution or 0.35% solution for 24 hours under an occlusive patch.

PAA was evaluated in rabbits in the Draize test. Solutions of 0.15% PAA were in contact with the skin for 4 hours under occlusive wrap. No irritation was noted at any site (Freeman, 1991c). Exposure of rabbits to 0.034% had no effect on the skin other than reversible enlargement of scars in scarified skin areas (Duprat *et al*, 1974).

Guinea pigs

Bulnes *et al* (1982a; CoR 3c) exposed the depilated skin of 20 guinea pigs to dressings impregnated with 1 or 3% PAA (further composition not stated) solutions for up to 5 hours. Animals exposed to 3% for 2 hours or more developed an acute dermatitis. No irritation was noted after exposure to 1% for up to 5 hours under the conditions of the experiment. In another study, Bulnes *et al* (1982b; CoR 3c) exposed guinea pigs via cage humidification to 1% or 3% PAA solution for a single exposure. Skin tissue was saved

24, 48 and 72 hours after exposure for histopathological evaluation. Animals exposed to 1% or 3% solutions had no changes to skin sections compared to untreated control animals. Neither of these studies (Bulnes *et al*, 1982a,b) are appropriate for evaluation of skin irritation because the study design is not a standard protocol for this end point.

Kramer *et al* (1987a; CoR 2c) attempted simulation of skin disinfection with PAA in surgical hand disinfection, using guinea pigs. They found no irritation in guinea pigs after 5 consecutive applications (presumably 5 minutes each time) of 0.5% PAA (diluted from equilibrium PAA 40%, 14% H_2O_2 and 27% HOAc). Moderate erythema was noted when 0.5% PAA was applied for 5 minutes after soaping, brushing and washing of the animal skin (3 x 3 min). Focal necrosis and eschar formation was observed after soaping, brushing and washing (2 x 3 min) and subsequent application of 0.5% PAA for 5 minutes. Soaping, brushing and washing alone led to mild erythema after 3 x 3 min and moderate to severe erythema after 2 x 3 min.

8.2.2 Eye irritation

An overview of the available eye irritation studies in rabbits and composition of the PAA formulation tested is presented in Table 24.

Table 24: Eye Irritation Studies in Rabbits

Concentration applied[a] (% PAA)	Composition (%) PAA	H_2O_2	HOAc	Dilution	Exposure duration (h)	Result	Reference	CoR[b]
17	17	23	16		4	Corrosive	Cascieri and Freeman, 1983d	1b
5	20[c]	10[c]	NS		24	Corrosive	Biffi, 1992c	2b
3.4	34	7.5	40	1:10	24	Corrosive	Duprat *et al*, 1974	2e
0.35	14	23	16	1:40	24	Corrosive	Joakimson da Silva and Keiko s. Coimbra, 1990g	2e
0.34	34	7.5	40	1:100	24	Severe irritation	Duprat *et al*, 1974	2e
0.22	2	7	19	1:9	24	Severe irritation	Joakimson da Silva and Keiko s. Coimbra, 1990h	2e
0.15	5-6	22-23	10-11	1:33	4	Mild irritation	Freeman, 1991d	1a
0.034	34	7.5	40	1:1,000	24	Very slight irritation	Duprat *et al*, 1974	2e

a Sample volume for all tests: 0.1 ml
b Code of reliability (Appendix B)
c From Solvay, 1997a
NS Not Stated

PAA was corrosive or severely irritant to the rabbit eye at concentrations of 0.2% and higher (Duprat *et al*, 1974; Joakimson da Silva and Keiko s. Coimbra, 1990g,h).

Cascieri and Freeman (1983d) tested 17% PAA in rabbit eyes and found that it was extremely irritant to washed and unwashed eyes. An *in vitro* test was performed with 5% PAA using the Bovine Corneal Opacity and Permeability test. A classification of severe irritant was determined (Nims, 1996b).

Groups of 6 male New Zealand white rabbits were exposed to PAA 5%. The product was instilled into the conjunctival sac at the dose of 0.1 ml/animal. The eyes were then observed from 1 hour to 7 days after exposure. The alterations to the cornea, iris and conjunctiva were scored using the Draize method. The index of ocular irritation was 75.00 at 1 hour and 90.00 from 24 hours up to 7 days. The alterations had not resolved after 7 days. Based on the Draize scale the author concluded that PAA was irritant (Biffi, 1992c). A more appropriate evaluation would be to consider this solution as corrosive. Duprat *et al* (1974) found maximal irritation at 3.4% PAA and extreme irritation at 0.34%, both with severe irreversible corneal opacity (at 0.34% only 2 of 6 animals) and severe conjunctivitis, ulceration and iritis. A diluted solution of 0.35% PAA was maximally irritant (Joakimson da Silva and Keiko s. Coimbra, 1990g). A diluted solution of 0.2% was severely irritant to rabbit eyes (Joakimson da Silva and Keiko s. Coimbra, 1990h). When a solution of 0.15% PAA was evaluated in rabbit eyes it was found to be mildly irritant (Freeman, 1991d; CoR 1a). Similarly, a 0.034% solution caused no effects other than slight conjunctivitis during the first 24 hours after exposure (Duprat *et al*, 1974).

8.2.3 Respiratory tract irritation

Janssen (1989c; CoR 1a) nebulised a 15% PAA (14% H_2O_2, 28% HOAc) solution into an exposure chamber for 25 minutes. Male Wistar rats were exposed (nose-only) to the aerosol at concentrations ranging from 9.5 to 40.3 mg PAA/m^3 (3.7 to 14.3 mg H_2O_2/m^3; HOAc not measured) and their respiration rate was monitored. The RD_{50}, referring to a concentration of PAA inducing a 50% reduction of respiratory rate, was calculated to be 21.5 to 24.1 mg/m^3. Reduction of respiratory rate occurred at levels from 5 to 10 mg PAA/m^3. After termination of exposure the respiratory rates returned to normal and the animals recovered fully within 3 days. No other clinical signs and no histopathological changes were observed.

The same author (Janssen, 1990; CoR 1a) exposed male Wistar rats to aerosol concentrations ranging from 221 to 487.5 mg PAA/m^3 (8.45 to 63.05 mg H_2O_2/m^3; HOAc not measured), generated from a 15% PAA (14% H_2O_2, 28% HOAc) formulation. Recovery was complete in the lowest dose group while respiratory rates were still depressed after 24 hours in one animal of the mid-dose (299 to 331.5 mg PAA/m^3) and 2 animals of the high dose group (435.5 to 487.5 mg PAA/m^3). Microscopic examination of the nose, trachea and lungs revealed necrosis in the anterior part of the nose while no treatment-related effects were observed in the trachea and lungs. The RD_{50} in this study was determined to be less than 299 mg PAA/m^3.

Guinea pigs exposed by inhalation to aerosol atmospheres (concentration not reported), generated from 1 to 3% PAA formulations (further composition not stated), for 3 days showed eye irritation and coughing. Histopathological examination of the animals 24, 48 or 72 hours after exposure to the 3% solution showed indications of irritation of the respiratory tract mucosa. No effects were noted following exposure to the 1% solution (Bulnes *et al*, 1982b; CoR 3a). This study did not include sufficient detail for further evaluation to be made.

Spraying cattle in closed stables with 0.4 - 1.6% PAA solutions induced coughing and moderate lachrymation and salivation (Zrunek, 1966; CoR 4c as cited in Kretzschmar *et al*, 1972).

8.2.4 Skin sensitisation

In skin sensitisation tests performed with diluted solutions of 14% PAA (23% H_2O_2 and 16% HOAc) and 2% PAA (containing 2% PAA, 7% H_2O_2 and 19% HOAc) administered intradermallly to guinea pigs, no evidence of sensitisation was found (Joakimson da Silva and Keiko s. Coimbra, 1990i,j; CoR 3a). However, PAA was diluted (1 : 1,000) in saline and probably degraded during the test.

A skin sensitisation study using the Bühler method was conducted on short-haired albino guinea pigs to determine if a 5% PAA (20% H_2O_2 and 10% HOAc) formulation could induce dermal sensitisation (Kuhn, 1996e; CoR 1a). The animals were treated (1 x /wk) with 0.4 ml of a 10% solution of the test compound in deionised water for 3 weeks. After a 2-wk rest period, the animals were challenged at a virgin test site with an application of 0.4 ml of a 7% solution of the test substance. After the challenge, a very faint erythema was observed in both the control and the treated group and, therefore, 5% PAA was not considered to have elicited a sensitising reaction in guinea pigs.
A similar study was conducted with 12% PAA (20% H_2O_2 and 20% HOAc) (Kuhn, 1996f; CoR 1a). In this case the animals were challenged with 0.4 ml of a 0.5% solution of the test substance in deionised water. The results showed that 12% PAA did not elicit a sensitising reaction in guinea pigs.

The Bühler method for skin sensitisation was also used with 0.15% PAA (5-6% PAA, 22-23% H_2O_2, 10-11% HOAc) (Freeman, 1991e; CoR 1a). Groups of 10 male and 10 female guinea pigs were treated with 0.3 ml of a diluted (1 : 33) test solution of PAA in contact with the skin for 6 hours. This treatment was repeated once a week for 3 weeks. Fourteen days after the third treatment the animals were challenged at a virgin site. No irritation or sensitisation reactions were noted.

A solution of 5% PAA (20% PAA, 10% H_2O_2, HOAc not stated; diluted with distilled water) was tested in guinea pigs (20 females) using the Magnusson and Kligman protocol to investigate the ability of the test material to produce skin sensitisation. The test solution (5% PAA) was administered during the induction phase by intradermal injection (0.1 ml/animal) and topical application (0.5 ml/animal). Twenty-one days after induction,

the test solution was administered by percutaneous injection (0.5 ml/animal) to challenge the animals. A second group of control animals was treated with the vehicle alone during the induction phase and then challenged with the test material by the same procedure above (Biffi, 1992d; CoR 3b). The authors considered the test material to be moderately sensitising. The study is, however, poorly reported and does not follow GLP guidelines. In particular, the results were not divided into control and treated animals. There were 3/10 animals responding with grade 1 reported in the first table and 5/10 responding with grade 1 reported in the second table. Not knowing which corresponds to the control and which to the treated animals makes it difficult to understand the author's conclusion of moderately sensitising. This study is deficient and does not allow a valid conclusion to be drawn on the sensitising potential of PAA.

8.2.5 Summary and evaluation

PAA should be considered as corrosive at concentrations of 10% and higher when applied to the skin of rabbits. PAA was also corrosive to rabbit skin at concentrations of 3-5% if contact lasted 1 hour or longer; contact for 3 minutes resulted in less severe responses. Concentrations of less than 1% PAA were only slightly irritant or not irritant, depending on the length of exposure of the skin.

PAA was corrosive at concentrations of 0.35% and greater when tested in the rabbit eye. Slight or no eye irritation was found at concentrations of 0.15% or less PAA. Evidence of respiratory irritation could be detected above 5 mg/m^3 in rats. The RD_{50} for respiratory irritation is 21-24 mg/m^3.

No skin sensitisation was observed in two Bühler tests in guinea pigs with different formulations of PAA. In one guinea pig maximisation test a positive result was claimed, but the report does not permit critical evaluation of the results.

8.3 Repeated Dose Toxicity

8.3.1 Oral

The available oral toxicity studies with PAA are summarised in Table 25. PAA was administered in the diet or drinking water of the animals.

Table 25: Toxicity following Repeated Oral Dosage

Route of administration, species, strain	Number of animals/ group, sex	Composition (%) PAA	H_2O_2	HOAc	Concentration	Dose (mg PAA/kgbw/d)	Duration (d)	Results LOAEL	NOAEL[a] (mg/kgbw/d)	Main effects	Remarks	Reference	CoR[b]
Diet					**(mg PAA/kg food)**								
Rat, Wistar	10 M	38	14[c]	27[c]	0, 429, 859, 1,718, 3,435 and 6,870	0, 60, 120, 240, 480, 960	5	NS	960	From 480 mg/kgbw, statistically non-significant reduction in food consumption and body-weight gain	Dose levels questionable because of gas formation in food, indicating instability of PAA in the diet	Krüger *et al*, 1977	3
Rat, Wistar	20 M	38	14[c]	27[c]	NS	0, 6, 21, 420	28	21	6	Decrease of serum alkaline phosphatase levels. Unclear if truly treatment related.	Dose levels questionable because of gas formation in food, indicating instability of PAA in the diet .No histopathology performe	Krüger *et al*, 1977	3
Pig, "Läufer"	NS	38	14[c]	27[c]	NS, presumably 1,400[d]	NS	5	NS	NS	No effects (behavioural, clinical signs)	Dose levels uncertain. No histopathology performed	Krüger *et al*, 1977	3
Drinking water					**(mg PAA/l water)**								
Rat, BD IX	10 M	40	14[c]	27[c]	0, 3.1, 6.2, 12.5, 25, 50, 100, 200	NS	7	NS	NS	Reduced water consumption, but no influence on body weight, growth, reproduction, histopathology of liver, lung, spleen, kidney and gastro-intestinal tract	Reportedly 200 mg/l was without effects, but due to instability of the test compound, concentrations were reduced by 50 - 60% after 1 day and 75% after 4 days	Juhr *et al*, 1978	2

Table 25 continued

Route of administration, species, strain	Number of animals/ group, sex	Composition (%) PAA	H_2O_2	HOAc	Concentration	Dose (mg PAA/kgbw/d)	Duration (d)	Results LOAEL	NOAEL[a] (mg/kgbw/d)	Main effects	Remarks	Reference	CoR[b]
Rat , BD IX	NS, M	40	14[c]	27[c]	200	NS	10 months	NS	NS	No influence on body weight, growth, reproduction, histopathology of liver, lung, spleen, kidney and gastro-intestinal tract.	Reportedly 200 mg/l was without effects, but due to instability of the test compound, concentrations were reduced by 50 - 60% after 1 day and 75% after 4 days	Juhr *et al*, 1977, 1978	3
Mouse, NMRI and C3Hf Gerbil Guinea pig, Pirbright white Golden hamster, Ha: AURA	NS, M, F	40	14[c]	27[c]	200	NS	10 months	NS	NS	No influence on body weight, growth, reproduction, histopathology of liver, lung, spleen, kidney and gastro-intestinal tract.	Reportedly 200 mg/l was without effects, but due to instability of the test compound, concentrations were reduced by 50 - 60% after 1 day and 75% after 4 days	Juhr *et al*, 1977, 1978	3
Rat, Wistar	12, M	36-40	NS	NS	0, 1, 10, 50	0.13 - 0.15, 1.3 - 1.5, 6.5 - 7.6[e]	28	0.13 - 0.15	NS	Elevated haemoglobin levels, increased spleen weights, increase in haemosiderin in spleen. At 0.13 - 0.15 mg/kgbw/d: cloudy swelling of liver, congestion of kidney medulla.		Veger *et al*, 1977	2

a No-observed adverse effect level
b Code of reliability (Appendix B)
c From other publications by the same authors
d Highest concentration in the diet was 10 x that used for disinfection of pigpens. Food changed daily
e Based on reported average body weight of 217 g and water consumption between 28 and 33 ml
F Female
M Male
NS Not Stated

Dietary studies

In none of the dietary studies of Krüger *et al* (1977) were details given concerning the stability of PAA in the diet, apart from the observation of an increased feed volume and oxygen formation indicating decomposition of the test substance. The authors performed some further testing in order to evaluate the degradation of PAA under specific conditions. When 1,400 mg PAA was added to 1 kg of feed, only 10% of the amount of PAA could be detected in the feed directly after mixing with PAA. The stability of PAA was dependent on the water content of the diet. The higher the water content in the food, the less rapid was PAA degradation. PAA stability was greater in water than in food. Based on this indication of decomposition, the doses that the rats or pigs received should be regarded as nominal only and the results should not be used for hazard assessment.

Drinking water

Rats received drinking water containing 3.1 to 200 mg PAA/l for one week. The concentration was determined daily by photometric analysis after reaction with potassium iodide. At higher dilutions yielding concentrations of 12.5 mg/l or lower, the PAA had almost disappeared within 2 days. Contamination by saliva to aqueous PAA solutions may have further reduced the PAA content. Animal water consumption was reduced by 12-19% at 200 mg/l and by 4% at 6.2 mg PAA/l. No effect on water consumption was found at 3.1 mg/l (Juhr *et al*, 1978).

The same authors briefly reported on the toxic effects of PAA administered in the drinking water of rats, mice, hamsters, gerbils and guinea pigs at a single concentration of 200 mg PAA/l for 10 months. The tests were designed to evaluate possible adverse effects of a concentration of PAA that would be used in disinfection of drinking water of farm animals. Water bottles were changed every week. The breeding capacity and health status of the animals were observed continuously. At regular intervals (not specified) interim kills were performed, the animals were autopsied and underwent pathological and histopathological examination. No changes were seen on growth, reproduction and histology of liver, kidney, spleen, lung and intestines. No further details were given (Juhr *et al*, 1977, 1978).

Drinking water containing 0.1% PAA administered to rats for 7 weeks did not results in any toxicological change (Benes *et al*, 1966; CoR 4b as cited in Kramer, 1982).

Rats received 1, 10 and 50 mg PAA/l in distilled water for 4 weeks (Veger *et al*, 1977). Three control groups were included in the study, one received distilled water only; the other two groups received distilled water with chlorine in concentrations of 1 and 10 mg/l respectively. Fresh test solutions were prepared daily and water consumption was recorded. Six animals per group were killed immediately after the end of the exposure period while the other half was kept for a recovery period of another 4 weeks. Clinical signs were recorded twice a week. Haematology and organ weight data (lungs, heart, liver, kidneys, adrenals, and stomach) were obtained from all animals after termination of the study. In the recovery group organ histopathology of the low- and mid-dose group animals was evaluated. Water consumption was significantly reduced in all dose groups compared to the water only control group. In the chlorinated water groups, water consumption was also lower than in the water only control group, but the difference

was not statistically significant. No differences in body weight and body-weight gain were observed between the groups. Haemoglobin levels were elevated in all dose groups compared to water only controls. An increase in haemoglobin levels was also reported in the high chlorine control group. In the lower-chlorinated water group a decrease in haemoglobin levels was observed. The number of leukocytes and differential blood counts were not different between the groups. In the PAA dose groups and the lower-chlorinated water rats, spleen weights were increased significantly compared to controls. All other organ weights (heart, liver, adrenals, stomach, and lungs) were not different from controls. Histopathology at week 8 did not reveal any significant differences from controls in the low dose group. In all dose groups treated with PAA an increase of haemosiderin in the red matter of the spleen was reported. In the 10 mg/l dose groups of both PAA and chlorine, changes in spleen (cloudy swelling of the white pulp), the liver (cloudy swelling) and congestion of the kidney medulla were observed in the majority of the treated animals. The increase in blood haemoglobin levels and haemosiderin in spleen of the animals treated with PAA (low doses only) were considered to be related to an increased absorption of iron due to acidic pH of the drinking water. (This conclusion is not supported by experience with other acids. As the iron uptake is receptor-regulated it seems doubtful that it could be substantially influenced by the pH. It is possible that the haematological changes could be related to the decreased drinking water consumption of the animals.) The LOAEL with regard to haematological changes was 1 mg PAA/l (0.13-0.15 mg/kgbw). Liver and kidney changes were observed in the 10 mg/l (1.3 to 1.5 mg/kgbw) and higher dose groups, thus a no-observed adverse effect level (NOAEL) for liver and kidney effects of 0.13 - 0.15 mg PAA/kgbw could be derived from this study. In the opinion of the Task Force the effects on liver and kidney could well be an artefact of the experimental procedures and hence should be viewed with caution.

8.3.2 Dermal

The available dermal toxicity studies on PAA are summarised in Table 26, including details of the study protocol and results.

Table 26: Toxicity following Repeated Open Dermal Application

Number of animals/ group, sex	Composition (%) PAA	H_2O_2	HOAc	Concentration (%)	(mg PAA/l)	Dose (mg PAA/kgbw)	Frequency, duration	Main Effects	Remarks	Reference	CoR[a]
Guinea pig											
20, M, F	40	14	27	0.3	1,200	0, 3.84[b]	2 x /d, 5 d/wk, 28 d	Skin: slight skin irritation reduced body-weight gain from day 20, slight evelvation of liver enzymes and LDH[c], slight decrease of liver weights, no histopathological findings.	Control and treated animals had pneumonia, more severe in treated	Kramer *et al*, 1982	2e
20, M, F	40	14	27	0.3	1,200	0, 3.84[b]	2 x /d, 5 d/wk, 90 d	Slight skin irritation and reduced body-weight gain from day 44, white blood cell count increased, slight elevation of liver enzymes and LDH, increased relative kidney and spleen weights, histopathological changes in liver and kidneys	Control and treated animals had pneumonia, more severe in treated	Kramer *et al*, 1982	2e
Rabbit											
28, F	40	14	27	0.5	2,000	1[d]	3 x /wk, 12 months	Skin: atrophy and vacuolar degeneration of hair follicles	Only skin was examined (1 animal after 1d, 1,2,3 wk, 2 animals every month from month 1 to 12)	Müller *et al*, 1988	2e
Pig											
5, F	40 NS[f]	14	27	NS	15,000 15,000[f]	113.6[e]	1 x / 2 d, 120 d	Skin: inflammation, hair loss, and hyper-parakeratosis. No systemic effects		Busch and Werner, 1974	4e

a Code of reliability (Appendix B)
b Applied as 0.16 ml/100 gbw = 1.92 mg/kgbw, assuming a density of 1 mg/ml
c Lactate dehydrogenase
d 1 ml of the test solution was applied; the dose was calculated assuming an adult rabbit of 2 kgbw and density of the test solution 1 mg/ml
e Reported as 250 ml/33 kgbw, assuming a density of the test solution of 1 mg/ml
f Pure (distilled) PAA
F Female
M Male
NS Not Stated

In the 28-day study of Kramer *et al* (1982) with dermal application of diluted PAA in guinea pigs, water consumption and clinical signs were recorded daily. Body weight and heart action were checked twice weekly at the beginning of the experiment and weekly thereafter. At the end of the study haematological and clinical chemistry parameters were determined and organ weights recorded. The following organs were examined macroscopically and microscopically: liver, lungs, kidneys, adrenals, pancreas, heart, brain, spleen and skin. Fourteen animals showed slight skin irritation with reduced intensity from day 25 of dosing. A number of animals of the control group also showed transient slight erythema. No differences in water intake were observed between treated and control animals. A reduction in body-weight gain was observed in the treated animals compared to controls from day 20. Body weight gain returned to normal in the post-exposure observation period (40 days) within 10 days. Heart rate was elevated in both control and exposed animals, but to a slightly greater extent in the exposure group. Relative liver weights were slightly decreased. Liver enzyme levels and lactate dehydrogenase (LDH) levels were slightly elevated in the treated animals. No macroscopic changes were seen. No characteristic histopathological findings were observed. Pneumonia was observed in all animals including controls with an increased severity in the treated animals. According to the authors this could be due to an infection that was possibly aggravated by inhalation of PAA vapours originating from the treated skin. As the animals in this study were suffering from infection, observed effects could have been secondary to the infectious disease. It follows that no reliable conclusions on possible systemic effects of PAA after dermal application can be drawn from this study.

Kramer *et al* (1982) performed a 90-day study in guinea pigs using an otherwise identical protocol to that described above. The clinical findings were identical to those of the 28-day study, except that the reduction in body-weight gain began later, from day 44. Relative liver weights were not reduced, but an increase in kidney and spleen weights relative to body weight was observed in treated animals compared to controls. Haematological effects were confined to an increase in white blood cells of the treated animals. Liver enzyme levels and LDH levels were slightly elevated in the treated animals. In 7 of 9 animals some greyish yellow areas were reported on the liver surface. A number of animals showed focal liver cell necrosis (periportal) and fatty hepatocytes in the liver. Cell infiltration was seen in the Glisson triangle and swelling and slight sectional proliferation of the Kupffer cells. Pneumonia was observed in all animals including controls with an increased severity in the treated animals. According to the authors this could be due to an infection that was possibly aggravated by inhalation of PAA vapours originating from the treated skin. In the kidneys of the test animals, but not of controls, interstitial lymphocyte infiltration were observed in the glomeruli (Kramer *et al*, 1982). As all the animals in this study were infected, the observed effects could have been secondary to the infectious disease. Accordingly, no reliable conclusions on possible systemic effects of PAA after dermal application can be drawn from this study.

Busch and Werner (1974) applied a 1.5% PAA solution to the skin of pigs. The solution was applied to the whole back of the animals using a sponge. Clinical signs were recorded daily. Body weight determinations and haematological examinations were performed every 20 days. The animals showed signs of salivation, lachrymation and increased respiratory rate within 10 to 15 min after application, probably due to inhalation of PAA

that evaporated from the skin. Transient skin irritation was observed immediately after application of the test substance but was reversible within 10 to 15 min. After 20 days the skin showed signs of hyperkeratosis, parakeratosis, hair loss and signs of inflammation (cellular infiltration up to the corium). Gains in body weight were comparable to controls throughout the observation period. Haematological and clinical chemistry examinations did not reveal any treatment-related effect. The kidney function of the treated animals (phenol red test) was similar to that of controls.

8.3.3 Inhalation

The available studies on possible toxic effects of repeated exposure to PAA by inhalation are summarised in Table 27. The test compounds was administered as a vapour or aerosol. No analytical determination of the concentration of PAA in the test atmosphere was performed in any of the studies. The nominal concentration of the test atmosphere was calculated from the amount of PAA used for aerosol or vapour generation and the chamber volume. In some cases aerosol droplet sizes were measured.

Table 27: Repeated Dose Studies in Mice and Guinea Pigs by Inhalation

Number of animals/ group, sex	Composition (%) PAA	H_2O_2	HOAc	Concentration Solution (%)	Atmosphere (mg PAA/m^3)	Vapour or aerosol, particle size	Frequency, duration	Results (mg/m^3) LOAEC	NOAEC[a]	Main effects	Remarks	Reference	CoR[b]
Mouse[c]													
40, F	40[d]	14[d]	27[d]	0.39, 1.56, 6.25	0, 70, 281, 1,125	Aerosol, 0.5-8 µm	5, 10, 15 min/d for 29 d	1,125	281	Acute effects during and immediately after exposure: respiratory distress, eye irritation. Decreased body-weight gain, increased mortality (15 min exposure group), increased red/white blood cell count, haemoglobin, haematocrit, lung inflammation (pneumonia)	No analytical determination of atmospheric concentration of PAA	Heinze *et al*, 1981	2e
40, NS	40[d]	14[d]	27[d]	2.06, 7.8, 16.1	0, 280, 1,125, 2,250	Vapour, NS	5, 10, 15 min/d for 29 d	2,250	1,125	Laboured breathing, eye irritation, increased mortality, decreased body-weight gain. Increased red/white blood cell count, haemoglobin, haematocrit, inflammation of the lung	No analytical determination of atmospheric concentration of PAA	Heinze *et al*, 1982	2e
40, NS	40[d]	14[d]	27[d]	0.39, 1.56, 6.25	0, 70, 280, 1,125	Aerosol, 0.5-8 µm	5, 10, 15 min/d for 29 d	1,125	280	Laboured breathing, eye irritation, increased mortality, decreased body-weight gain. Increased red/white blood cell count, haemoglobin, haematocrit, inflammation of the lung	No analytical determination of atmospheric concentration of PAA	Heinze *et al*, 1982	2e

Table 27 continued

Number of animals/ group, sex	Composition (%) PAA	H_2O_2	HOAc	Concentration Solution (%)	Atmosphere (mg PAA/m^3)	Vapour or aerosol, particle size	Frequency, duration	Results (mg/m^3) LOAEC	NOAEC[a]	Main effects	Remarks	Reference	CoR[b]
10, NS	36-40[d]	NS	NS	NS	0, 70, 140	Aerosol, 0.5 µm (MMAD[e] 1.6 µm)	3 x 1 h/wk for 28 d		70	Respiratory distress during exposure, small inflammatory foci in the lungs.	No data on analytical determination of PAA, limited reporting	Merka and Urban, 1976	3a
20 or 60, NS	40[d]	14[d]	27[d]	1, 1.5	0, 186, 280	Aerosol, NS	2 x 30 min/d for 90 d	186		Inflammatory changes in the lung, liver granuloma and lymphocyte infiltration.	No analytical determination of atmospheric concentration of PAA, liver granuloma could be related to infection	Heinze and Nattermann, 1984	2e
Guinea pig[c]													
20, NS	40[d]	14[d]	27[d]	1, 1.5	0, 186, 280	Aerosol, NS	2 x 30 min/d for 90 d	186		Decreased body-weight gain, increased ALAT[f] levels, inflammatory changes in the lung, granuloma, lymphocyte infiltration and increased amount of lipid droplets in the liver.	No analytical determination of atmospheric concentration of PAA, liver granuloma could be related to infection	Heinze and Nattermann, 1984	2e

a No observed adverse effect concentration
b Code of reliability (Appendix B)
c Strain not stated
d Inferred from other publications on the same product
e Mass median aerodynamic diameter
f Alanine aminotransferase
F Female
M Male
NS Not Stated

Heinze *et al* (1981) exposed mice to PAA aerosols by whole-body exposure; control groups received either no treatment or water aerosol for 10 min/d. Interim kills were performed on days 1, 2, 3, 4, 5, 8, 16, and 22. In all PAA-treated groups, excitement followed by lethargy was observed during exposure, an effect that was dose-related. After exposure, signs of respiratory distress were observed for several hours in the highest dose group. These effects were independent of the daily duration of exposure. Signs of eye irritation were also observed in some animals. Compared to both control groups, mortality and decreased body-weight gain was noted in the 1,125 mg/m^3 group exposed for 15 min/d. A significant decrease in body weight was also observed in the active (water aerosol) control group compared to the passive control (no treatment) group. Increased erythrocyte count, haematocrit, haemoglobin content and white blood cells were observed at the high dose group, but no exposure-duration relationship was evident. Changes in leukocyte and lymphocyte counts did not follow a consistent pattern and were not clearly attributable to treatment. Histopathological changes in the lungs (pneumonia) were noted mainly at the 1,125 mg PAA/m^3 dose and related to the duration of exposure. Other organs were not examined. The changes in blood parameters were attributed to the lung damage (compensatory changes). A NOAEL for inflammatory changes in the lung of 281 mg PAA/m^3 can be derived from this study.

In two other studies (Heinze *et al*, 1982) mice were exposed (with different frequency) to PAA vapours or aerosols by whole-body exposure; passive (no aerosol) and active (water aerosol) controls were also used. Deaths occurred in the high-dose groups at 2,250 mg PAA/m^3 as vapour and 1,125 mg PAA/m^3 as aerosol respectively. In all treated groups, there was excitement followed by lethargy during the inhalation period, while lethargy persisted after exposure in the high-dose groups (vapour and aerosol). Evidence of respiratory distress and marked inflammation of the eye were noted in many animals of the high-dose aerosol group. Decreased body-weight gain was noted in the high-dose vapour/aerosol groups for all treatment durations. The observed increases in erythrocyte count, haemoglobin content, haematocrit and white blood cell count were considered to be related to exposure at 1,125 mg PAA/m^3 aerosol and 2,250 mg/m^3 vapour, but in this latter group changes were less severe. In the high-dose aerosol exposure group the gastro-intestinal tract was found to be distended and had a foamy appearance. Inflammatory changes in the lungs were found to be significant at the high-dose vapour/aerosol groups; these changes increased with duration of exposure. No histopathological changes were observed in the liver and kidneys. The authors concluded that all effects observed were due to the irritant effect of PAA as similar findings were reported following exposure to lactic acid, HOAc aerosols or sulphur dioxide gas. The overall NOAEL based on irritant responses was 1,125 mg PAA/m^3 vapour or 280 mg PAA/m^3 aerosol, both for exposures of up to 15 min/d.

In the study of Merka and Urban (1976) in mice, signs of respiratory distress were observed in the animals during exposure; these effects disappeared after cessation of exposure. Gains in body weight of exposed animals were reduced compared to untreated controls. In mice killed after 14 days of exposure the only histopathological findings were mild morphological changes in the lung. No other organs (unspecified, but presumed to be heart, liver, spleen, kidneys as for an acute study reported in the same paper) were affected. Isolated small foci of inflammation in the lungs were seen after 4 weeks of exposure.

Heinze and Nattermann (1984) exposed mice to PAA aerosols and included additional groups of animals that were treated with different drugs in order to study their influence on PAA toxicity. Control groups received no treatment or water aerosol with and without drugs. Body-weight gain in all groups was similar to controls. Haematology and clinical serum chemistry parameters also did not differ significantly between the groups. Histopathological examination of the lungs revealed an increased incidence and severity of inflammatory changes (thickening of alveolar walls, epithelial cell proliferation, infiltration by eosinophils and neutrophils) in treated animals compared to controls. Epithelial cell tumours were observed in the lungs of 3 test animals of the low dose group only and one control mouse. Since these tumours were not observed in the higher dose group, they were not considered to be due to PAA treatment. In addition the number of control animals in which lungs were examined was less than the number of test animals examined. Examination of the livers of the test animals after 30 and 90 days of treatment revealed an increase in lymphocyte infiltration and granuloma compared to controls. The size of the granuloma increased after 90 days of treatment. Follow up studies of the livers of the animals indicated that bacterial infection could have been the reason for the observed changes. It is not clear from the report if the histopathology of organs other than lungs, liver and kidneys was examined.

In a similar study (Heinze and Nattermann, 1984) guinea pigs were exposed to PAA aerosols, as well as additional groups of animals treated with different drugs to study their influence on PAA toxicity. Control groups received no treatment or water aerosol with and without drugs. Body-weight gain in the treated groups was decreased compared with controls. Haematology studies revealed no significant treatment-related differences in white blood cell count, erythrocyte count, haemoglobin and serum proteins, except for a slight increase in γ-globulin in treated compared with control animals. Serum liver enzyme values of asparagine aminotransferase (ASAT) were not different from controls, but alanine aminotransferase (ALAT) levels were significantly higher in the treated animals compared to controls. Histopathological examination of the lungs revealed an increased incidence and severity of inflammatory changes (thickening of alveolar walls, epithelial cell proliferation, infiltration by eosinophils and neutrophils) in treated animals compared with controls. Examination of the livers of the test animals revealed a slight increase in lymphocyte infiltration and granuloma compared to controls from day 60 of treatment as well as an increase in lipid droplets. Changes in the liver and in γ-globulin were possibly related to bacterial infections in the animals. It is not clear from the report if the histopathology of organs other than lungs, liver and kidneys was examined.

One of 10 rats died after inhalation for 4 days of vapours from a 3% PAA solution (Polakova, 1968; CoR 4c as quoted in Krüger and Kruschinski, 1982). No deaths were observed after exposure of rats for 28 days to PAA vapours from a 1% solution. The only sign noted was transient restlessness at the beginning of the treatment (Benes *et al*, 1966; CoR 4b as cited in Krüger and Kruschinski, 1982).

Benes *et al* (1966; CoR 4b as cited in Heinze *et al*, 1982 and Krüger and Kruschinski, 1982) exposed rats to 0, 7.2 and 72 mg/m^3 PAA aerosol for 1 h/d, during 24 exposures in 28 days. Reduced body weight and clinical signs (restlessness, eye discharge and respiratory distress) were reported in the 72 mg/m^3 group. In the 7.2 mg/m^3 group signs of excitement, but not irritation or other clinical signs, were observed.

8.3.4 Other studies

Pigs (5) and calves (15) were exposed for 1 h/d to 0 and 50 mg PAA/m^3 aerosol for 14 days. The aerosol (droplet size 0.5 to 6 µm) consisted of 2 ml/m^3 of diluted (6.25%) equilibrium PAA 40% (14% H_2O_2 and 27% HOAc). Simultaneously, animals infected with *Chamydiae* were treated to study the effect of PAA aerosols on bacterial infections. In the context of this report, only the results for non-infected animals are of relevance. Clinical observations in pigs and calves consisted of increased lachrymation, salivation, nasal discharge and cough in the first 3 to 5 days. Additionally, pigs showed signs of laboured breathing and vomiting. The effects were less pronounced after further exposures. At the end of the 86-day test period, treated pigs had decreased body-weight gain compared to untreated controls. In calves no effect on body-weight gain was observed. An increased pulse and respiratory rate was observed in exposed calves. Haematological changes (decreased red blood cell counts and haemoglobin levels) were noted. These effects were transient and adaptation occurred during treatment. Acute lung inflammation was also reported to affect both control and treated calves (Heinze *et al*, 1979).

Groups of 5 mice were exposed (1 h/d) to 50 mg PAA/m^3 aerosol (droplet size 0.5 to 6 µm) for 14 days. Some animals were immunised, while others were infected with a virus. PAA exposure did not influence the immune reaction and generation of antibodies (Heinze *et al*, 1979).

8.3.5 Summary and evaluation

A number of publications on the toxicity of PAA after repeated oral, dermal or inhalation exposure in different animal species have been reviewed.

There are deficiencies in the reporting of the available repeat-dose toxicity studies, including uncertainties regarding the nature, concentration and the stability of the test substance, the limited amount of doses tested and limited reporting on histopathology. Furthermore in a number of studies the test animals suffered from infectious diseases and it remains unclear to what extent the reported effects can be attributed only to the administration of PAA. In spite of those limitations, a number of conclusions may be drawn from the studies.

The reduced food or water consumption observed in some of the oral studies may well be related to the unpalatability due to the odour and irritant properties of PAA. No treatment-related changes were observed in a drinking water study in rats, mice, golden hamsters, gerbils and guinea pigs receiving up to 200 mg PAA/l water for 10 months. However, the stability of PAA in drinking water varied and was not sufficient during these studies to inspire confidence in the lack of findings.

Only one study reported an increase in haemoglobin levels and haemosiderin deposition in the spleen of rats receiving PAA in drinking water for 28 days from 1 mg PAA/l corresponding to a dose of about 0.15 mg/kgbw. As these effects have not been reported in other studies even at higher dose levels and as the methodology was not sufficiently

described, these results may not be related to the test substance. In the same study, effects on kidney, liver and spleen were reported at doses from 10 mg PAA/l (1.5 mg/kgbw); these could well be an artefact of the experimental procedures and should thus be treated with circumspection.

Repeated dermal exposure of pigs to a 1.5% PAA solution for 120 days resulted in irritant effects to the skin including hair loss, hyper- and parakeratosis as well as signs of inflammation. No systemic effects were observed. In guinea pigs exposed to a 0.3% solution of PAA (corresponding to 3.84 mg/kgbw/d) twice daily for 90 days, transient slight skin erythema was observed. A reversible reduction of body-weight gain was also reported. A slight increase in numbers of white blood cells and of liver enzyme levels were reported in the treated group. An increase in relative kidney and spleen weights and changes in liver (focal liver cell necrosis) and kidneys (lymphocyte infiltration) were observed in the treated animals. As pneumonia was reported for both treated and control animals the effects observed could be a consequence of the infectious disease, rather than treatment with PAA.

Effects seen in repeated-dose inhalation studies are mostly attributable to the irritant properties of the test substance. The single exposure periods however, were relatively short (5 min to a maximum of 1 hour per exposure).

A NOAEL of 280 mg PAA/m^3 for aerosols or 1,125 mg/m^3 for PAA vapours was derived for mice exposed up to 15 min/d for 29 days.

Subchronic inhalation studies using PAA aerosols in different species (pigs, calves and mice exposed for 1 h/d) showed restlessness, irritation of the respiratory tract, lung damage and related transient blood parameter changes from 50 mg PAA/m^3. No effect or very slight irritation only was found at 7.2 mg PAA/m^3.

Inflammatory changes of the lung and the liver were reported in mice and guinea pigs exposed (2 x 30 min/d) to PAA aerosols of 186 or 280 mg/m^3 for 90 days. It remains unclear if these effects were treatment related or attributable to an infection in the animals. In all, the predominant effects arising from oral, dermal or inhalation exposure to PAA seem to be related to local irritation at the site of contact. However, systemic effects on liver, kidney and perhaps spleen cannot be ruled out from the limited studies available. Clear no-adverse effect levels cannot be derived from the available studies.

8.4 Genetic Toxicity

8.4.1 Gene mutation *in vitro*

The available studies on possible gene mutation activity of PAA *in vitro* are presented in Table 28.

Table 28: In Vitro Genetic Toxicity Assays

Test system	Test organism, strain	Composition (%) PAA	H_2O_2	HOAc	Dose (PAA)	Metabolic activation	Result[a]	Reference	CoR[b]
Spot-test	*Salmonella typhimurium* TA 1535, TA 1536, TA 1537,TA 1538	35-37	8-9	36-38	10 µg/plate	No	**-ve**[c]	Agnet *et al*, 1977	3a
	Wild strain LT-2	36	8.5	37	10 µg/plate	No	**+ve**[d]	Agnet *et al*, 1977	3a
	Wild strain LT-2	36	8.5	37	10 µg/plate	No	**-ve**[e]	Agnet *et al*, 1977	3a
	TA 1978	36[f]	8.5[f]	37[f]	6 µg/plate	No	**+ve**[d]	Dorange *et al*, 1974	3a
	TA 1978	36[f]	8.5[f]	37[f]	6 µg/plate	No	**-ve**[e]	Dorange *et al*, 1974	3a
Gene conversion/ mitotic recombination	*Saccharomyces cerevisiae* Strain D7	36[g]	8.5[g]	37[g]	0 - 40 µg/ml	No	**-ve**	Dorange *et al*, 1974	3a
Reversion-assay (Ames test)	*S. typhimurium* TA 1978	36	8.5	37	0 - 40 µg/ml	No	**+ve**[g]	Agnet *et al*, 1977	3a
	TA 98, TA 100	9	NS	NS	50 µg/plate	Yes	**-ve**[g]	Yamaguchi and Yamashita, 1980	4e
	TA 98, TA 100, TA 102, TA 1535, TA 1537, TA 1538	4.5	25.5	6.7	7 - 4,576 µg/plate	Yes / No	**-ve**[g]	Wallat, 1984a	1d
	TA 97, TA 98, TA 100, TA 1535	40	NS	NS	0.3 - 200 µg/plate	Yes / No	**-ve**[g]	Zeiger *et al*, 1988	2e
Unscheduled DNA[h] synthesis	Human lung fibroblasts, WI-38 CCL75	31[i] 42[i]	4.7 5.5	NS NS	0.2 - 32 mg/ml	No	**-ve**[g]	Coppinger *et al*, 1983	1d
DNA repair assay	Human lung fibroblasts, WI-38 CCL75				4 - 32 µg/ml	No	**-ve**[g]	Coppinger *et al*, 1983	1d
Chromosomal aberration	Human lymphocytes	5.17	20[i]	10[i]	0.25 - 5 mg/ml	Yes / No	**-ve** **+ve**[k]	Phillips, 1994b	1b

a **-ve**, negative; **+ve**, positive
b Code of reliability (Appendix B)
c His-reversion
d Resistance towards potassium chlorate (with LT-2 combined with resistance towards 2-desoxy-D-galactoside)
e Resistance towards ethionine
f Inferred from Agnet *et al*, 1977
g Test was conducted up to cytotoxic concentration
h Deoxyribonucleic acid
i Measured
j Inferred from Blowers, 1994a, 1995
k At highest, cytotoxic doses
NS Not Stated
ND Not Determined

In bacteria and yeast

Several studies on bacterial gene mutation tests in which PAA was assayed using the Ames method have been reported. In a number of tests possible toxic or detoxifying effects were investigated in the presence and absence of the so-called S9 metabolic activation system (supernatant of centrifuged 9,000 x g liver homogenate) containing the microsome and cytosol fractions usually derived from rats previously treated with microsomal enzyme inducing compounds such as phenobarbital or Aroclor.

A diluted equilibrium PAA solution was tested in the spot test using different strains of *Salmonella typhimurium* and different selection for mutants. No mutagenic effects were observed using the strains TA 1535, TA 1536, TA 1537, TA 1538. With strain TA 1978 and the wild strain LT-2, respectively, resistance towards ethionine was not found. When selecting the two strains for mutants resistant to potassium chlorate and 2-deoxy-D-galactose, the authors claimed to have observed an induction of mutants after treatment with PAA at 6-10 µg PAA/plate, compared to the untreated control (Dorange *et al*, 1974; Agnet *et al*, 1977). Judging from the limited data presented in the reports the effect is quite small (not quantified).

The same authors also tested PAA in the Ames test with *S. typhimurium* strain TA 1978 up to 40 µg PAA/ml without metabolic activation. An increase in mutation frequency above threefold appears to have been seen only in concentrations that reduced bacterial survival far below 50% (> 15 µg PAA/ml) (Agnet *et al*, 1977). Detailed information on the induced mutation frequencies of treated and untreated samples is not given.

Dorange *et al* (1974) also reported that treatment of the yeast *Saccharomyces cerevisiae* strain D7 with diluted equilibrium PAA, failed to stimulate mitotic recombination, gene conversion or homo-allelic reversion in yeast strain D7. No details of the results were reported.

When a solution of 9% PAA in HOAc (not further specified) was tested in *S. typhimurium* TA 98 and TA 100 in the presence of S9 mix, no mutagenic activity was found. Data on the results without S9 mix were not explicitly given (Yamaguchi and Yamashita, 1980). An evaluation of the concentration-activity relationship is not possible, as only one concentration, 50 µg/plate (probably of the formulation) was tested.

It is generally known that peroxides are highly toxic especially to repair-deficient *S. typhimurium* strains. *S. typhimurium* TA 102 that is not repair-deficient has been suggested as the strain of choice for this type of test substance (Berglin and Carlson, 1986). Therefore, strain TA 102 was included in another reversion-assay with PAA. In strain TA 102, PAA up to cytotoxic concentrations produced only a slight increase of reverted colonies (up to 30%) and the test substance was judged to be non-mutagenic. Total inhibition was achieved in concentrations exceeding 183 and 915 µg PAA/plate (depending on the strain and activation system). With regard to cytotoxicity no marked differences, i.e. reduced sensitivity, were observed in strain TA 102 (Wallat, 1984a). The concentrations that were reached in this assay were relatively high compared with the results presented by other authors.

Equilibrium PAA (40%) proved to be negative in the standard *S. typhimurium* reversion assay at concentrations of 0.3 to 200 µg PAA/plate. The highest concentration was chosen after toxicity testing prior to the actual test and represents the dose that elicited toxicity or a dose immediately below (half-log dose intervals). In addition to rat liver S9 mix, material from hamster tissues was also used as a metabolic system. With both protocols PAA was found to be devoid of mutagenic activity (Zeiger *et al*, 1988).

DNA repair in cultured mammalian cells

The possible induction of UDS by PAA (40% nominal) was investigated in human diploid foetal lung cells. Ethyl methane sulphonate, N-methyl-N'-nitro-N-nitrosoguanidine (MNNG), and 4-nitroquinoline-1-oxide were used in preliminary experiments to assure the appropriateness of the test system to show UDS and DNA repair. MNNG was used as positive control in both the UDS and DNA repair assay (Table 28). Cells incubated with PAA for 4 hours did not reveal a consistent dose-related increase of UDS using liquid scintillation counting (duplicate experiments). Slightly, but statistically significantly elevated rates of UDS were reported at 8 and 16 µg PAA/l in the first experiment and at 16 and 32 µg/l in the second experiment. The increase never exceeded 1.6 times the solvent control, which were reported to be within the variability of the test system. Therefore, the results did not meet the criteria for a positive response, i.e. 2-fold increase above controls. The authors explained the slight increase by a possible oxidation of hydroxyurea, which is used in this test system. No statistically significant increase of UDS compared to solvent (water) controls was detected in a second (triplicate) experimental series using autoradiography (a more sensitive technique that does not require hydroxyurea). In this assay 32 µg PAA/ml was clearly cytotoxic (50% survival). Conflicting results were obtained; the first experiment with PAA indicated a possible positive response. However, repeated testing with the same lot of PAA showed negative results (Coppinger *et al*, 1983).

Using the same test system and controls, a DNA repair assay (three independent experiments) was conducted. Cells incubated with PAA were assessed by equilibrium ultra-centrifugation of density-labelled DNA. The assay was negative at all dose levels. At the highest concentration normal DNA replication was considerably reduced (Coppinger *et al*, 1983).

In conclusion, PAA was negative in UDS and DNA repair assays in human lung fibroblasts when tested up to cytotoxic concentrations.

Chromosomal aberrations in cultured mammalian cells

Two independent experiments on the potential of PAA to induce structural chromosomal aberrations in human lymphocytes were conducted with equilibrium PAA (5.17%). Cells were treated at 0.25, 0.5, 1.0, 2.0 and 4.0 mg PAA/ml for 20 hours in the first experiment and with 0.25, 0.5, 0.75, 1.0 and 1.5 mg/ml in the second experiment. Treatment in the presence of S9 mix was carried out at 0.31, 0.63, 1.25, 2.5 and 5 mg/ml in both experiments and was limited to 3 hours. Cells were arrested in metaphase and harvested 20 and 44 hours after the start of treatment. Two hundred metaphases at each dose level were examined for structural chromosome aberrations. Cyclophosphamide (with activation) and Mitomycin C (without activation) served as positive controls (Table 28).

In the absence of S9 mix, 4 and 2 mg PAA/ml reduced the mitotic index of the cells to below 25% of the control in the test, chromosome analysis was conducted at the next three lowest concentrations and in the control. In the test with S9 mix, the highest concentration of PAA reduced the mitotic index to 69% and chromosome analysis was therefore conducted on the three highest concentrations and the controls. Without S9 mix there was a statistically significant and reproducible increase in the number of aberrant metaphases at 1.0 and 1.5 mg/ml. With metabolic activation, a concentration of 5 mg/ml was clastogenic. Effects observed were mainly deletions. Both in the 1.5 mg/ml (without S9) and 5 mg/ml (with S9) replicate, one single chromatid exchange was observed. Under the conditions employed, S9 mix reduced both cytotoxicity and mutagenicity. In summary, PAA revealed positive results only in the highest, moderately cytotoxic doses, which reduced the mitotic index to 44.5 - 63% without S9 mix and to 61 - 69% with S9 mix. The author concluded that PAA caused chromosomal damage in cultured human lymphocytes (Phillips, 1994b). It is speculated that the cytotoxicity and genotoxicity exerted by PAA is a result of the same mechanism at the cellular level, e.g. production of reactive oxygen species which are not detoxified at higher concentrations.

8.4.2 Gene mutation *in vivo*

The available *in vivo* studies on possible gene mutation of PAA are summarised in Table 29.

Table 29: In Vivo Genetic Toxicity Assays

Test	Route of application	Composition (%) PAA	H_2O_2	HOAc	Dose (mg PAA/kgbw)	Result[a]	Reference	CoR
Chromosomal aberration, mouse	Topical Intraperitoneal Intraperitoneal	40	5[b]	45[b]	0, 5[c] 0, 50[d] 0, 5[e]	**+ve**[b]	Paldy *et al*, 1984	3b
Micronucleus test, mouse	Oral, gavage	4.5	26.7	6.7	0, 400 -1,600	**-ve**	Wallat, 1984b	1b
Micronucleus test, mouse	Oral, gavage	5.17[f]	20	10	0, 8 - 150	**-ve**	Blowers, 1994a	1b
Unscheduled DNA synthesis, rat	Oral, gavage	5.17	20	0	0, 330, 1,000	**-ve**	Blowers, 1994b	1b

a **-ve**, negative; **+ve**, positive
b Assumed value
c 0.1 ml equilibrium PAA 40%
d 2 ml of 0.5% solution in distilled water
e 1 ml of 0.1% solution in distilled water
f Blowers (1995) confirmed that 15.17% was a typing error

Chromosomal aberration and micronucleus induction in mammals

In a bone marrow chromosome aberration test in mice (male and female, unspecified strain), PAA was found to cause chromosome mutations after topical or intraperitoneal (i.p.) application. The authors recommend further in-depth investigations (Paldy *et al*, 1984) (Table 29). Insufficient detail was reported in this study and the chromosome analysis conducted does not comply with the relevant OECD guideline 475. Only 200 mitoses/group were evaluated compared to the evaluation of at least 100 metaphases per animal required by the OECD guideline and the data are not specified separately for each animal. No information is given on cytotoxicity to the bone marrow. Given the small number of analysed metaphases per animal and dose group, the numbers of aberrations recorded do not show a convincing dose dependency in the i.p. treated groups. Only one dose was applied epicutaneously and only two by i.p. administration. The results obtained are surprisingly similar, independent of the treatment regime and dose.

In a micronucleus test conducted with equilibrium PAA (4.5%), the test solution was administered by gavage to groups of 7 male and 7 female CF21/W68 mice. The animals received two doses of 200, 400, and 800 mg PAA/kgbw/d at 0 and 24 hours. Six hours after the second administration the animals were killed. Cyclophosphamide served as a positive control. The femoral bone marrow was removed and examined for the incidence of micronuclei in polychromatic erythrocytes, the proportion of polychromatic erythrocytes in the erythrocyte population and the incidence of micronuclei in normochromatic erythrocytes. Dose-dependent clinical signs of toxicity were observed in all groups. No mortalities were recorded within the time frame of the investigation and no increased incidences of micronuclei were found. General bone marrow toxicity was detected as the inhibition of proliferation in the erythropoiesis since the ratio of normochromatic versus polychromatic erythrocytes was increased in the highest dose group (Wallat, 1984b). The samples were collected 6 hours after the last or 30 hours after the first administration, whereas current standard guidelines require the samples to be collected once within time interval of 18 to 24 hours.

In a mouse micronucleus test with equilibrium PAA (5.17%), groups of 15 male and 15 female CD-1 mice were given single oral doses by gavage. Positive control groups of males and females were given a single oral dose of 100 mg/kgbw cyclophosphamide to confirm that the system was capable of detecting the effects of a known genotoxin. Five males and 5 females from each group were killed at 24, 48 or 72 hours after treatment and bone-marrow smears prepared for each time point. There were no significant differences in the frequency of micronuclei in polychromatic or normochromatic erythrocytes between mice treated with PAA and the untreated controls. This was true for all doses of PAA tested, all three sampling times and both sexes of mice. PAA did not induce a dose-related decrease in the proportion of polychromatic erythrocytes, indicating a lack of toxicity to the bone marrow. No clinical signs were reported (Blowers, 1994a, 1995). It is not clear from this study whether PAA actually reached the target organ. In the light of this, the significance of the negative results obtained are questionable. In preliminary studies the highest dose tested (150 mg/kgbw) had been found to be the maximum tolerated dose in both sexes of mice. In the main study the highest dose of PAA had no effect on body-weight gain.

Primary DNA repair after in vivo treatment

An *in vivo / ex vivo* UDS assay (Table 29) was conducted in groups of 6 male F344 rats receiving doses of equilibrium PAA (5.17%) at 330 or 1,000 mg PAA/kgbw by gavage, the maximum dose causing no observable toxicity as determined in a preliminary toxicity study. A positive response with controls receiving 2-acetylaminofluorene and nitrosodimethylamine confirmed the validity of the assay. From each treatment group, 2 animals were killed after 2 hours and 4 animals were killed after 16 hours, and hepatocytes were isolated. No significant increases in UDS (measured as net grain increase) were observed in both treated groups at either time. It was concluded that the tested PAA formulation was not genotoxic under the conditions of the study (Blowers, 1994b). Information on the type of toxicity observed at higher doses, which could confirm bioavailability, is not given in the report.

8.4.3 Summary and evaluation

Limited information is available on effects of PAA on DNA and its potential to induce gene and chromosome mutations both *in vitro* and *in vivo*. Considering the paucity of reliable data, a final reliable evaluation of the mutagenic potential of PAA can hardly be achieved (DFG, 1999b). Several bacterial tests are available, but these are of limited value because PAA is a biocide and exerts its cytotoxic effects in these systems at low concentrations. Cytotoxicity in most cases was diminished by the addition of an exogenous metabolic system. In the strain TA 102, considered to be most sensitive with regard to mutagenicity, only a slight response was detected, that was not statistically significant.

The results of two DNA repair tests in human foetal lung cells did not indicate that PAA had a genotoxic potential. In the *in vitro* chromosome aberration test, positive findings were obtained only in concentrations that produced cytotoxicity. A common mechanism for cytotoxicity and genotoxicity could be at play, e.g. relating to insufficient detoxification of developing reactive oxygen species at high doses.

In one adequate *in vivo* study, PAA did not produce micronuclei. Another study failed to prove that PAA had actually reached the target organ. In this study the doses may have been too low to produce clinical signs of toxicity and cytotoxicity in the target organ.

In an *in vivo / ex vivo* UDS assay in rats, PAA did not show genotoxic potential. The highest dose was chosen to produce no toxicity and, as in the micronucleus tests, bioavailability of PAA at the target organ was not verified. However, after oral treatment it is more likely that a considerable amount of PAA reaches the liver after absorption in the gastro-intestinal tract via the portal vein.

8.5 Chronic Toxicity and Carcinogenicity

8.5.1 Chronic toxicity

No data are available.

8.5.2 Carcinogenicity

No data are available.

8.5.3 Tumour initiation-promotion

Bock *et al* (1975) reported diluted equilibrium PAA 40% (5% H_2O_2, 40% HOAc) to be a skin tumour promoter and a weak initiator in mice. The results of the experiments are summarised in Table 30.

Table 30: Initiation- Promotion Study with PAA (40%) on the Skin of Mice
(Bock et al, 1975)

Initiation with DMBA[a]	Concentration[b]	Solvent	Duration of treatment (wk)	Incidence	
				Skin tumour (non-invasive)	Skin cancer (invasive)
Yes	3%	Water	66	24/30	5/30
Yes	1%	Water	66	8/30	1/30
Yes	0.3%	Water	66	2/30	0/30
Yes	0%	None	66	0/30	0/30
Yes	2%[c]	Water	56	2/30	0/30
Yes	1%[c]	Acetone	56	2/30	0/30
No	2%	Water	52	3/30[d]	0/30[d]
No	2%	Acetone	52	NA[e]	NA[e]
No	1%	Acetone	52	0/30	0/30
No	0%	None	66	0/30	0/30

a 7,12-Dimethylbenz[*a*]anthracene, 1 x 125 µg in 0.25 ml acetone, 3 weeks prior to treatment
b Related to formulation or active substance (not stated)
c "Decomposed"
d After first 26 weeks of treatment
e Not applicable, because all animals died early in the experiment

The clipped dorsal skin of 3 groups of 30 female ICR Swiss mice was painted once with 7,12-dimethylbenz[*a*]anthracene (DMBA) in acetone. After 3 weeks, the mice were treated (5 x 0.2 ml/wk) with 0.3%, 1% or 3% PAA solutions for 66 weeks. The authors reported that a pilot study had indicated that 4% "aqueous PAA" would be excessively lethal. (It is not clearly stated in the paper if the given concentrations relate to the formulation or active substance. If the latter were so, the test solutions contained 1,200, 4,000 or 12,000 mg PAA/l). Two other groups of 30 mice pre-treated with DMBA were painted (5 x 0.2 ml/wk) with "decomposed PAA" solutions (2% in water and 1% in acetone) for 56 weeks. PAA was "decomposed" by passing the product through a screen made of a precious metal acting as catalyst. After this procedure, peroxy compounds could not be detected iodometrically in the solution (detection limit not specified). Three additional groups of 30 mice each were not treated with DMBA, but received (5 x 0.2 ml/wk) 2% PAA in water or 1-2% PAA in acetone for 52 weeks. The mice were examined weekly and the number and distribution of tumours were noted. A lesion was classified as a skin tumour if it was at least 1 mm in diameter and if it persisted on the skin for at least 3 successive weeks.

After initiation with DMBA, a solution of PAA in water exhibited a dose-dependent tumour-promoting activity at concentrations of 3% and 1%, respectively, but not at 0.3% (Table 30). After DMBA pre-treatment both the 2% "decomposed PAA" in water and the 1% "decomposed PAA" in acetone produced 2/30 tumours (7%) after 56 weeks. Without DMBA pre-treatment, application of 2% PAA in water produced tumours in 3/30 (10%) of the animals after 26 weeks. Subsequent treatment for another 26 weeks failed to increase the tumour rate. No tumours were recorded after treatment with PAA in acetone. With regard to toxicity of PAA in acetone, an extraordinarily steep dose-response curve was obtained. At 2% PAA all animals died early in the experiment, whereas 1% was reported to be well-tolerated, as were PAA solutions of up to 3% in water. Skin irritation resulting from the treatment with PAA was mentioned but not specified as to the extent and expected differences between the dose and control groups.

The observed tumours were further classified by the authors as "skin cancers" if they were capable of invading tissues below the *panniculus carnosus*. The tumours induced by PAA in water alone were classified as non-invasive, but not explicitly specified as benign. It should be noted that the applied tumour classification does not correspond to current standards of tumour classification (Greaves and Barsoum, 1990).

This initiation-promotion study suffers from deficiencies in experimental design and reporting of results. An irritation threshold was not determined and the concentration of PAA used was apparently irritant. As only one dose of PAA in water was used, no dose-response analysis can be made. Furthermore, the negative control mice do not appear to have been treated in the same manner as the other groups. In particular, in the negative controls, the two solvents (water and acetone) do not seem to have been applied and it is not clear whether the hair was clipped.

Tumour generation ceased in the second phase of the experiment with PAA in water only; after the first 26 weeks 3/30 (10%) tumours were found, but this number did not increase over the next 26 weeks of treatment. With regard to historical data on tumour

incidence in Swiss mice, Bock *et al* claim that only one skin tumour was found in thousands of negative controls painted with acetone for up to 1.5 years. After treatment with DMBA followed by acetone or water only, the authors reported a historical incidence of 5.4% tumours in this strain. According to Ingram and Grasso (1991) the general scientific consensus is that up to an incidence of 10%, there is no carcinogenic activity induced in mouse skin by irritant substances. The effect is thought to be due to an enhancement of spontaneous tumour incidence. In this context it is difficult to evaluate the relevance of the observed 10% incidence of skin tumours with vehicle alone in a single dose group.

8.5.4 Summary and evaluation

No chronic toxicity or carcinogenicity studies have been conducted with PAA.

In one study, PAA acted as a tumour promoter in mouse skin after DMBA initiation. It is likely that this is due to chronic irritation caused by PAA treatment. The data are insufficient to identify PAA as an initiator, i.e. a complete carcinogen.

The German MAK Commission[a] has classified PAA in category 3 for its carcinogenicity (i.e. substances which give rise to concern because of possible carcinogenic effects in humans, but which cannot be finally evaluated because of insufficient information), and states that a 40% PAA solution causes very severe inflammation and corrosion of the skin (DFG, 1999b). However, the "Ausschuß für Gefahrstoffe (AGS)", the official OEL setting committee in Germany, concluded that the available data on PAA do not allow for a final conclusion to be made with regard to its carcinogenicity, mutagenicity or toxicity to reproduction. Therefore, the AGS considered classification of PAA for those endpoints inappropriate; an OEL was not established (TRGS, 1997).

In conclusion, in the only available initiation-promotion study, which suffers from a number of experimental and reporting deficiencies, the observed effects represent an effect secondary to local irritation, rather than indicating a carcinogenic potential for PAA.

8.6 Reproductive Toxicity and Teratogenicity

8.6.1 Fertility

The breeding data from a specific-pathogen-free BD IX rat colony (77 animals, 67 controls) receiving PAA in their drinking water (200 PAA mg/l) over several generations (not specified) did not differ from those of the control group. Litter sizes and weights at weaning were similar to controls. No further details are given in the publication (Juhr *et al*, 1978) (CoR 4e).

Breeding pairs of NMRI and C3Hf mice, gerbils and Pirbright white guinea pigs were given drinking water containing 200 mg PAA/l *ad libitum* for 10 months. Drinking water

[a] Sentatskomission zur Prüfung gesundheitsschädlicher Arbeitsstoffe

was renewed every week. Breeding capacity was observed continuously. Growth and outcome of breeding was similar to known historical stock data. No further details are given (Juhr *et al*, 1978; CoR 4e).

Sperm head morphology

The sperm head morphology test is an *in vivo* test for evaluating the potential of a chemical to induce abnormalities to the heads of sperm. The test has the potential to identify chemicals that induce spermatogenic dysfunction and, possibly, heritable mutations. The relationship of positive results in this test to carcinogenic or mutagenic potential is not clear. No clear evidence is obtained from the test model whether alterations in sperm morphology are due to cytotoxicity or to a clastogenic effect. In addition, the validity of this test in assessing reproductive toxicity has not been established. The genetic consequences of fertilisation by sperm affected by chemical treatment during spermatogenesis remain unclear; embryonic death or transmission of genetic aberrations to live-born progeny are possibilities (Wyrobek *et al*, 1983). These authors found that all murine germ-cell mutagens tested also induce sperm-shape abnormalities in mice. Therefore, it is critical that the sperm head morphology test be stringently conducted so that the results can be properly interpreted.

A sperm head morphology test was conducted with PAA (40%, 14% H_2O_2, 27% HOAc), applied as a 0.1% solution of the formulation in distilled water. ICR mice (10 animals/group) were administered (0.2 ml i.p.) a dose of 2.6 mg PAA/kgbw/d for 5 days. Positive and negative controls were included in the study. Animals were killed 36 days after the first treatment, and spermatozoa were collected from the left and right epididymis of each animal. Spermatozoa (200/animal) were examined for abnormalities. The results showed that a dose of 2.6 mg PAA/kgbw doubled the incidence of sperm head abnormalities. When the dose was reduced to 1.3 mg/kgbw, no increase in anomalies was seen (Koch *et al*, 1989; CoR 3b). This study is deficient with regard to the proper conduct of the test in that a pure, colony bred mice strain was used, whereas hybrid strains are recommended (Wyrobek *et al*, 1983). Hybrid strains have a lower and more stable spontaneous incidence of abnormal sperm than pure inbred strains. The paper does not state that the epidydimes were minced, washed and filtered before sperm smears were prepared, steps necessary to ensure good quality sperm for evaluation. It is also not stated whether the smears were read "blind" to ensure lack of bias. The results of the test do not meet the criteria for a positive response of PAA because statistically significant results were not found at two consecutive dose levels. Thus, insufficient evidence was provided to conclude that PAA caused abnormal sperm heads. In addition, the i.p. route of exposure is not a route relevant to human exposure of PAA.

Subsequent to the i.p. study, the same group of investigators conducted a sperm head test following dermal exposure to PAA, a route more relevant to human exposure. Groups of ICR mice received twice daily dermal applications of 0.1 ml of 0.5% or 5.0% PAA (formulation above) dissolved in distilled water, for 28 days. Controls received water only. (The corresponding doses are estimated to be 0, 11.8 and 118 mg/kgbw/d). The backs of the mice were depilated prior to application. The mice were killed 36 days after the first application, the epididymides removed and smears of sperm prepared. The skin of animals exposed to 5.0% PAA had marked necrosis after 3 days. The results of

this test were positive, i.e. PAA caused abnormalities at both doses (Kramer *et al*, 1991; CoR 3b). The study has the same deficiencies as that of Koch *et al* (1989) in using inbred mice and in preparation and reading of sperm samples. In addition, a positive control was omitted.

The relevance of the findings in the two sperm head anomaly tests (Koch *et al*, 1989; Kramer *et al*, 1991) to the potential mutagenicity and clastogenicity of PAA is not clear. The two tests did not meet the scientific criteria for valid assays (Wyrobek *et al*, 1983).

8.6.2 Developmental toxicity

In a teratogenicity study with ICR mice, the animals (5-10/group) were exposed (2 x/d) by inhalation to nominal concentrations of 20 and 100 mg PAA/m^3 throughout gestation. The atmospheres were generated from a 1% or 5% dilution of PAA (40%, H_2O_2 14%, HOAc 27%). The authors reported a statistically significant retardation of foetal growth (body length and weight) at 100 mg PAA/m^3, but no retardation at 20 mg/m^3. No exposure related skeletal anomalies were observed. The health status of the dams was not reported (Kramer *et al* 1990; CoR 3a,b). Exposure to a level of 100 mg PAA/m^3 would have been expected also to produce maternal toxicity. Because of uncertainty about the exposure levels and limited reporting, a reliable conclusion cannot be drawn from this study.

8.6.3 Evaluation

No reliable conclusion can be drawn from the data regarding reproductive and developmental toxicity of PAA because the available studies are inadequate, poorly conducted or not relevant to these endpoints.

8.7 Other Studies

Laub *et al* (1990) studied the effects of PAA-containing disinfectants on Langerhans cells of the epidermis of guinea pigs. Equilibrium PAA (formulation presumably 40% PAA, 14% H_2O_2 and 27% HOAc) and a mixture of 10% PAA and 75% glyceroltriacetate were diluted with water yielding test solutions of 0.2% (2,000 mg PAA/l) of the formulation and 0.1% (1,000 mg PAA/l) of the mixture. The pH (5.6) was adjusted with acetate buffer. The test solutions were applied (1 x 50 µl/d) to the right ears of groups of 3 white guinea pigs (inbred strain) for 1, 7 or 14 days. The animals were killed and the epidermis of both ears (the left one was untreated and served as control) was isolated, fixed and cut into ultra-fine slices and mounted on slides. Langerhans cells were counted after staining with adenosine-triphosphatase (ATPase) stain. A time-dependent decrease in Langerhans cells was observed in the treated ears compared to the control ears for both preparations. When acetate buffered solutions were used the reduction of Langerhans cells was less pronounced. The authors speculated that the reduction of Langerhans cells in the epidermis after topical application of PAA solutions could alter the immunological defence capacity of the treated skin.

The effect on oral mucosa of long-term exposure to PAA was studied in a group of 8 rabbits exposed (1 - 8 h/d, 4 d/wk) via an "oral tank" to a 0.2% PAA solution (2,000 mg PAA/l) prepared from 40% PAA (formulation above) for 11 months. The oral tanks, made of Piacryl, were modelled to fit the oral cavity of the individual animals and slowly released the test substance into the animal's mouth (see Müller *et al*, 1978 for details). One control group of 16 animals received water via the oral tank, while another group of 10 rabbits remained untreated. The animals were regularly monitored for alterations of the oral mucosa over the whole test period. Histopathological evaluation of the oral mucosa was performed at the end of the study. Results indicated only epithelial thickening (free from dysplasia and reversible at the end of the exposure period) and inflammation of the oral mucosa. This effect was more pronounced in the PAA treated group compared with the water treated group (Müller *et al*, 1980). The test conditions are highly artificial and could have resulted in mechanical irritation of the mucous membranes of the mouth and in forced drinking.

One ml of a 0.2% PAA solution (2,000 mg PAA/l), freshly prepared from 40% PAA (formulation above) was applied (3 x/wk) to the oral or vaginal mucosa of groups of 1 or 2 rabbits for up to 12 months. Histology of the oral mucosa revealed isolated nuclear oedema in the mucosal epithelium and increased epithelial desquamation of the superficial layers of the epithelium beginning with the eighth month. No increase in mitotic rate or dysplasia was observed in animals treated for up to 12 months. In the vaginal mucosa slight focal oedema with circumscribed nuclear oedema and slight sub-epithelial fibrosis was observed after 12 months. The mucosal epithelium was unaffected (Müller *et al*, 1988).

8.7.1 Neurotoxicity

Possible neurotoxic effects of PAA vapours (nominal concentration 10 mg PAA/m^3) were studied in two behavioural tests (open field and maze trials) with mice and rats. In the first test, male and female ICR mice (10 animals/group) were exposed (10 min/d, whole-body) for 28 days to vapours evolving from 1 ml of equilibrium PAA 36-40% (containing 14% H_2O_2 and 27% HOAc) in a 23 litres desiccator. Water served as the control substance. The open field test was conducted for 10 minutes at the same time of day prior to the first exposure and after 18 and 28 days of exposure. The test was conducted immediately after exposure to the test substance. At day 18, an increase in activity was observed in the treated mice compared to controls with regard to field changeover, erect posture and jumping. No increase in tail drumming or grooming was observed. After 28 days of exposure, activity was significantly depressed compared with controls in respect of field changeover, erect posture and jumping, but there was increased grooming, probably to remove PAA from the fur. Body-weight gain was initially retarded, but subsequently recovered fully (Kramer *et al*, 1993; CoR 3b). It is likely that the observed effects were secondary to irritation.

In the second test, following a 5-day training phase in a maze, Wistar rats (number and sex not stated) were exposed using the same test conditions as for mice above. Four separate test series were conducted. The maze trial was conducted on days 7, 14, 21, and

28 with exposure taking place after passage through the maze on these days. For the control animals the arrival time was shortened and the number of errors reduced proportional to the length of the experiment. This was considered an expression of the learning capacity of the animals. In the animals exposed to PAA, arrival times were extended and did not get shorter with time. The number of errors did not decrease significantly in the tests. (No individual data were given in the paper.) The authors concluded that the effects observed in the animals were indicative of a possible neurotoxic effect of PAA (Kramer *et al*, 1993; CoR 3b). However, as the exposures were scheduled after the behavioural test it is possible that the delay of the animals was due to a learning effect associated with avoidance of the discomfort of exposure to an irritant vapour.

Evaluation

The protocols do not meet the standards for neurotoxicity evaluation by various regulatory authorities and hence the two experiments are not sufficiently standardised to enable firm conclusions to be drawn. The behavioural effects reported in the publication are likely to be secondary to the irritant properties of PAA. Clarification of the findings could only be obtained from studies which included appropriate control exposures with another known irritant using standard methods.

9. EFFECTS ON HUMANS

9.1 Acute and Subchronic Toxicity

No data are available.

9.2 Irritation

9.2.1 Skin irritation

The available data on skin irritation in humans related to PAA are presented below (Table 31).

Table 31: Skin Tolerance Testing in Humans with PAA Solutions

Concentration (% PAA)	Composition PAA	H_2O_2	HOAc	Dilution (%)	Effects	Reference
0.5	40	14	27	1.25	Dermatosis when used with soap and water for 7 days	Kramer *et al*, 1987a
0.5	40	14	27	1.25	Irritation	Mücke, 1970
< 0.5	40	14	27	1.25	No effects	Kretzschmar *et al*, 1972
0.4	NS	NS	NS	NS	No effects	Schröder, 1982
0.35					Irritation[a]	French, 1993
0.2	40	14	27	0.5	No effects	Mücke, 1970
0.2					No effects	Pazdiora and Kubiček, 1967
0.2	40	14	27	0.5	Rough skin and slippery feel for 1-2 days	Kretzschmar *et al*, 1972
0.1	1	7	10	10	No effects[a]	Baldry, 1992

[a] In eczema-prone patients

Kramer *et al* (1987a) reported immediate erythema formation in 3 of 15 surgeons using 0.5% PAA solution for hand disinfection repeatedly over a day. The procedure involved soaping, brushing, washing for 3 minutes followed by hand disinfection for 5 minutes and approximately 5 further hand disinfections of 5 minutes during the working day between different operations. In 6 of 15 surgeons, hand dermatosis developed after 7 days of using PAA disinfecting solutions.

Subjects using a wash solution of 0.5% PAA to disinfect hands reported irritation to the skin, whereas those using a more dilute solution (0.2% PAA) did not. Long-term use of 0.2% PAA solution for disinfection of hands did not result in any adverse effects on skin (Mücke, 1970).

Tolerance to 0.4% PAA was found in humans. This article provides no further information (Schröder, 1982).

Surgeons using 0.2% PAA for 3 minutes, followed by washing with soap, did not experience intolerance. A burning sensation was experienced only when small wounds were present. Concentrations of up to 0.5% PAA did not damage the skin of the hand (Pazdiora and Kubiček, 1967).

Skin desquamation was noted for 1 to 2 days after hand disinfection with 0.2% PAA. Rough skin was reported the day after treatment in 2 of 10 subjects. The roughness disappeared during continued treatment. Subjects also reported a slightly slippery feeling for 1 to 2 days when hands were washed with 0.2% PAA (Kretzschmar *et al*, 1972).

At concentrations of 0.35% PAA, 7 out of 56 eczema-prone patients showed irritation responses (French, 1993). Use of lower concentrations (0.1% PAA and less) under occlusive wrap was not associated with significant irritation in 122 eczema-prone patients in a clinical skin irritation study (Baldry, 1992). Higher concentration levels were not tested. A double-blind primary skin irritation study was conducted with various concentrations of PAA in petrolatum on 10 subjects. The test material was prepared in petrolatum and 0.2 ml applied under a band aid for 24 hours. The goal of the study was to determine the concentration of PAA that could be tolerated for 4 days (continuous exposure) without causing substantial skin damage. The criteria for a positive finding was a grade of less than 2 on a scale of 0 to 5 (highest) in 5 of 10 subjects. A grade 2 response corresponded to "intense redness/erythema". A concentration of 2% PAA in petrolatum was found to be the maximum concentration tested which met these criteria (Robinson, 1984).

9.2.2 Eye irritation

A solution of 0.1% PAA was applied with compresses to the eyelids for 5 to 10 minutes in 4 subjects. A slight burning sensation was felt which disappeared during the application (Kretzschmar, 1972). Ocular irritation was not reported, probably because PAA was applied to the eyelid.

9.2.3 Respiratory irritation

Respiratory effects or symptoms reported at different atmospheric concentrations of PAA are given in Table 32.

Table 32: Atmospheric PAA Concentrations and Reported Effects or Symptoms

Concentration (mg/m^3)	Effects or symptoms	Reference
7.0 H_2O_2[a]	Lachrymation, extreme discomfort and irritation of nasal membranes	Fraser and Thorbinson, 1986
2.8 - 4.2 H_2O_2[b]	Extreme discomfort	
1.4 - 2.8 H_2O_2[c]	Tolerable discomfort	
0.7 H_2O_2[d]	No discomfort	
0.9 - 1.2[e]	Not immediately irritant, but unpleasant for an extended period.	McDonagh, 1997
0.4 - 0.5[f]	Tolerable and not unpleasant	
< 0.7 PAA	No appreciable odour was detected	Harvey, 1992
< 0.3 PAA[g]	No symptoms of runny eyes or nose	Simms, 1995
< 0.15 PAA	Odour threshold lower than, but probably not much lower than, 0.15 mg/m^3	Ancker and Zetterberg, 1997

[a] Reported as 5 ppm H_2O_2 (Section 5.2.2)
[b] Reported as 2.0 - 3.0 ppm H_2O_2
[c] Reported as 1.0 - 2.0 ppm H_2O_2
[d] Reported as 0.5 ppm H_2O_2
[e] Reported as 0.3 - 0.4 ppm
[f] Reported as 0.13 - 0.17 ppm
[g] Reported as < 0.15 mg/m^3 H_2O_2

Fraser and Thorbinson (1986) reported lachrymation and extreme discomfort following exposure to 7.0 mg/m^3 total active oxygen compounds in an aerosol consisting of PAA and H_2O_2 (Section 5.2.2) for only 3 minutes. Extreme discomfort, but no lachrymation was reported for exposures of 3.5 - 4.2 mg/m^3 for about 5 minutes and for 2.8 mg/m^3 for up to 10 minutes. Exposure to 2.8 mg/m^3 for 4 minutes caused unbearable irritation, but was tolerated for 2 minutes of a 5-minute exposure.

McDonagh (1997) reported that exposure to PAA vapour at 0.9 - 1.2 mg/m^3 (0.28 - 0.38 ppm) was not immediately irritant, but would have been considered "unpleasant" for an extended time period. A vapour concentration of 0.4 - 0.5 mg PAA/m^3 (0.13 - 0.16 ppm) was tolerable and not unpleasant for up to 3 hours.

Exposure to PAA aerosols at a concentration of 1.5 ppm (4.74 mg/m^3) for 15 to 20 minutes caused discomfort to mucous membranes. Lower respiratory effects were not reported even after exposure to 5 ppm PAA, although upper respiratory effects were reported (Fraser and Thorbinson, 1986).

Schaffernicht and Müller (1998) conducted an investigation of 45 workplaces (150 workers) at a university hospital (Section 5.2.2). For an 8-hour time period the concentrations ranged from less than 0.005 mg PAA/m^3 (detection limit) up to 1.84 mg/m^3. Of the measured values recorded, 60% were less than 0.1 mg/m^3 and 5% exceeded 1.0 mg/m^3. The employees reported irritation around the eyes and of the nasal and pharyngeal mucous membranes, as well as reddening and itching of the skin on the hands and face.

In the same study, Müller and Schaffernicht (1998) investigated whether the concentrations observed in the 45 workplaces in the university hospital were likely to result in damage of the teeth and gingivae. The dental status of the persons exposed to a workplace concentration of > 0.4 mg PAA/m^3 was examined. The study included a test group and a control group of 26 females of the same age group with approximately the same oral hygiene status. The findings were based on three criteria: oral hygiene, condition of the gingivae, and the condition of the dental enamel. The only significant difference between the test and control groups was in the sulcus bleeding index according to Mühlemann and Son, indicating gingivitis in the front teeth area. Otherwise, no significant differences were found between the test and the control groups. The authors concluded that a damaging effect of PAA fumes on the gingivae probably could arise from low levels of exposure.

A concentration of 4.6 mg PAA/m^3 was used in intensive care rooms for short-term disinfection purposes. No symptoms were reported by clinical staff or patients other than a slight acidic odour (Dworschak and Linde, 1976).

Tichácek (1966 as cited in Kretzschmar, 1972) described irritant effects in humans exposed to aerosol application of 0.8% PAA solution in a closed room. Effects included lachrymation, increased nasal secretions, mucous membrane irritation and temporary loss of smell. No further details were provided.

9.3 Sensitisation

There are no cases of skin sensitisation reported by the German network of dermatological clinics (Informationsverbund Dermatologischer Kliniken) (IVDK, 1999).

9.4 Evaluation

When used as a hand wash solution, concentrations of 0.5% PAA caused skin irritation in humans, but not if the concentration of the wash solution was 0.2% PAA or lower. A solution of 0.1% PAA applied to the eyelids caused only a slight burning sensation.

Data from topical skin applications or ocular exposure in humans are in agreement with the information from animal studies (Section 8.2). Although the concentrations tested were not identical, both humans and rabbits showed similar sensitivity in that < 0.2% PAA was not irritant to skin and < 0.1% was not irritant to the eyes.

Exposure to atmospheric concentrations of 0.5 mg PAA/m^3 (0.16 ppm) or lower seem to be well tolerated by humans. Concentrations up to 1.2 mg/m^3 (0.38 ppm) were not immediately irritant but unpleasant after exposure for an extended time period.

10. FIRST AID AND SAFE HANDLING ADVICE

10.1 First Aid

Liquid and mist are corrosive and can cause burns, direct contact could cause irreversible damage to the eyes including blindness and/or irreversible destruction of skin tissue. Vapour / mist will irritate the nose, throat and lungs, but will usually subside when exposure ceases. The severity of the effects depends on the concentration and dose.

10.1.1 Skin and eye injuries

Eye contact: Immediately flush with water for at least 15 minutes, lifting the upper and lower eyelids intermittently. Continue flushing until further treatment. See medical doctor or ophthalmologist immediately.

Skin contact: Immediately flush with plenty of water while removing contaminated clothing and /or shoes. Thoroughly wash with water. See medical doctor if there is persistant irritation or if there are burns.

10.1.2 Inhalation

- The patient should be taken into fresh air and should rest in a seated posture.
- If breathing discomfort occurs and persists after cessation of exposure, see a medical doctor.
- If breathing has stopped, artificial respiration should be administered until qualified medical personnel are able to take over.

10.1.3 Ingestion

- Do not induce vomiting.
- If the subject is conscious, flush mouth with water, give 1 to 2 glasses of water to drink.
- Never give anything by mouth to an unconscious person but provide classical resuscitation measures.
- See a medical doctor immediately or take subject to a hospital.

10.2 Safe Handling

10.2.1 Handling and safety at work

- Operate in well ventilated area, do not breathe vapours
- Provide mechanical local exhaust ventilation
- No eating, drinking, smoking in work area
- Use adequate personal protective equipment (PPE) (below)
- Never return unused material to original container

- Avoid contamination of product
- Avoid contact with skin, eyes and clothing
- Wash face and hands after handling product
- Provide emergency showers and eye wash stations

Personal protective equipment

- Respiratory protection :
  - In case of emissions of vapours and aerosols, use suitable respiratory protection.
  - In case of large uncontrolled emissions, positive pressure self-contained breathing apparatus should be used.
- Hands - Wear suitable gloves made from materials with acceptable penetration times, e.g. butylrubber, polychloroprene, fluororubber
- Eyes - Use chemical proof goggles, full face shield or full face mask
- Body - Wear acid proof protective clothing., e.g. apron and boots made of butylrubber if risk of splashing.

10.2.2 Storage

- Store in vented containers in a clean, cool, dry, well-ventilated area
- Store away from reducing agents, fuels, non-compatible materials e.g., alkalis, reducing agents, metallic salts, combustibles and other oxidising agents.
- Keep away from direct sun light, heat sources and sources of ignition
- Keep in original package, keep closed, Use first in first out

10.3 Management of Spillage and Waste

10.3.1 Spills and waste

- Evacuate and isolate the hazard area, approach release from upwind
- Use adequate PPE (Section 10.2.1)
- Stop leak / contain spill (if this can be done safely)
- Dilute spilled material with large quantities of water or mix with an inert material such as sand or earth
- Do not seal waste material, do not use textiles, tissues, saw dust or combustible materials to clean spill
- Remove endangered containers to safe place, if this can be done safely
- Never return spilled material to original container
- Keep non-compatible materials away from spill
- Dispose of spilled material in accordance with all country, state and local regulations
- Immediately notify appropriate authorities

10.3.2 Fire-fighting measures

During a fire, PAA could begin to decompose releasing oxygen gas, which can support combustion of flammable materials. If decomposition occurs, a pressure burst may occur if the container is not properly vented. To fight the fire:

- Approach from upwind
- Use proper personal protective equipment such as an acid resistant over suit and a positive pressure self contained breathing apparatus
- Bring persons to safety, evacuate all non-essential personnel
- Use large quantities of water spray to fight the fire and to keep fire-exposed containers cool

Refer to the local authorities for disposal of PAA. For further and more detailed safety instructions, contact your PAA supplier.

For bulk storage spillage, an emergency plan should be worked out in conjunction with the supplier and the competent authority, if applicable.

11. BIBLIOGRAPHY

11.1 Databases Consulted

HSDB - Hazardous Substances Data Bank (CD Rom Search)
Chemical Abstracts Database
DIALOG
RTECS - Registry of Toxic Effects of Chemical Substances (CD Rom Search)
CA SEARCH 1998 American Chemical Society
Toxline format only 1998 The Dialog Corporation
BIOSIS PREVIEWS 1998 BIOSIS
AGRICOLA format only 1998 The Dialog Corporation
CAB Abstracts 1998 CAB International
Enviroline 1997 Congressional Information Service
Pollution Abs 1998 Cambridge Scientific Abstracts
Aquatic Sci&Fish Abs 1998 FAO (for ASFA Adv Brd)
Env.Bib. 1998 Internl Academy at Santa Barbara
SEDBASE
EMBASE
MEDLINE
TOXLINE
Chemical Safety News Base
NIOSH
Food Science and Technology Abstracts
International Pharmaceutical Abstracts
Life Sciences Collection
Drug Information Fulltext
Agrochemicals Handbook
Chemical Safety Newsbase
American Medical Association Journals Online
New England Journal of Medicine Online

11.2 References Quoted

ACGIH (American Conference of Governmental Industrial Hygienists). 2000. 2000 TLVs and BEIs, threshold limit values for chemical substances and physical agents and biological exposure indices. ACGIH, Cincinnati, OH, USA, pp 15, 42.

Agnet Y, Dorange JL, Dupuy P. 1977. Mutagenicity of peracetic acid on *Salmonella typhimurium*. Unpublished report, Annex 2. Institut National de la Recherche Agronomique, Station de Technologie des Produits Végétaux, Dijon, France.

AISE (Association Internationale de la Savonnerie, de la Détergence et des Produits d'Entretien). 2000. Peracetic acid, data for ECETOC JACC report [on peracetic acid from TAED]. Personal communication by Poelloth C, 28 March. AISE, Brussels, Belgium.

Akzo Nobel. 1998. SDS safety data sheet, peracetic acid (PAA) 38%, revised October 1998. Akzo Nobel, Eka Chemicals, Bohus, Sweden.

Ancker K, Zetterberg L. 1997. Mätning av perättiksyra vid Eka Chemicals AB i Bohus [Measurement of peracetic acid at Eka Chemicals AB, Bohus]. Unpublished report A97329, IVL (Institutet för Vatten- och Luftvårdsforskning), Stockholm, Sweden. Eka Chemicals, Bohus, Sweden [Swedish; English translation].

Ausimont. 1997a. Oxystrong 5%, scheda di sicurezza. Ausimont, Bollate, MI, Italy.

Ausimont. 1997b. Oxystrong 15%, scheda di sicurezza. Ausimont, Bollate MI, Italy.

Ausimont. 1999. Campagna de rilevamento igienico ambientale, risultati monitoraggio di area, reparto H_2O_2. Personal communication to Malinverno G, April 1999. Ausimont, Bussi, Italy.

Ausimont. 2000. Campagna de rilevamento igienico ambientale, risultati monitoraggio di area, reparto infusamento PAA. Personal communication to Malinverno G, March 2000. Ausimont, Bussi, Italy.

Bactria. 1995. Sicherheitsdatenblatt gemäß 91/155/EWG, Bactrozon 5/23, Austellungsdatum 30.03.95. Bactria, Kircheimbolanden, Germany.

Bactria. 1997. Sicherheitsdatenblatt gemäß 91/155/EWG, Bactrozon 15/23, Austellungsdatum 17.09.97. Bactria, Kircheimbolanden, Germany.

Baldry MGC. 1983. The bactericidal, fungicidal and sporicidal properties of hydrogen peroxide and peracetic acid. *J Appl Bact* 54:417-423.

Baldry MGC. 1992. Irritancy of peracetic acid to skin. Personal communication, memorandum MGCB/SB/M-4-92. Solvay Interox, Widnes, Cheshhire, UK.

Baldry MGC, Fraser JAL. 1988. Disinfection with peroxygens. In Payne KR, ed, *Industrial Biocides*, Wiley, Chichester, UK, pp 91-116.

Baldry MGC, French MS, Slater D, Desprez F. 1990. Désinfection par l'acide peracétique des effluents urbains, l'expérience anglaise. *L'eau, L'industrie, Les Nuisances* 137:42-44.

Baldry MGC, French MS, Slater DS. 1991. The activity of peracetic acid on sewage indicator bacteria and viruses. *Wat Sci Tech* 24:353-357.

Baldry MGC, Cavadore A, French MS, Massa G, Rodrigues LM, Schirch PFT, Threadgold TL. 1995. Effluent disinfection in warm climates with peracetic acid. *Wat Sci Tech* 13:161-164.

BAM (Bundesanstalt für Materialforschung und -prüfung). 1999. Verpackungen und IBC zur Beförderung von Salpetersäure, Ergebnisvermerks der Besprechung am 16. Dezember 1998 in der BAM, Berlin. Personal communication by Wieser KE. BAM, Berlin, Germany.

Basta J, Holtinger L, Ludgren P, Persson C. 1995. Emerging technologies in TCF bleaching. In TAPPI pulping conference. TAPPI, Technology Park, Atlanta GA, USA, pp 53-57.

Battelle. 1999. Personal communication of 14 December [on the consumption of TAED] by Dallé J to Leonhardt W, Degussa Hüls. Batelle, Darouge, Genève, Switzerland.

Bazzon M, Chauvire L, Giacalone J, Gondelle F, Lamy MH, Petit-Poulsen V, Bailleul S, Rose M. 1997. Toxicité aiguë vis-à-vis des poissons *Brachydanio rerio*. Substance d'essai: solution aqueuse d'acide peracétique. Unpublished report, study Ba567a, INERIS (Institut National de l'Environnement Industriel et des Risques), Verneuil-en-Halatte, France. Air Liquide, Chemoxal, Jouy en Josas, France.

Benes V, Tichácek B, Veger J. 1966. Toxicita kyseliny peroctové [Die Toxizität der Peressigsäure]. In Tichácek B *et al*, ed. *Kyselina peroctová a moznosti jejího využití v dežinfekci* [Peressigsäure und die Möglichkeiten ihrer Verwendung in der Desinfektion]. Zdrav. aktuality 163, Stát. Zdrav. Nakl. Praha [Staatsverlag für das Gesundheitswesen der CSSR, Prague, Czechoslovakia], pp 100-107 [Only title translated].

Berglin EH, Carlson J. 1986. Effect of hydrogen sulfide on the mutagenicity of hydogen peroxide in *Salmonella typhimurium* strain TA102. *Mutation Res* 175:5-9.

BG Chemie (Berufsgenossenschaft der chemischen Industrie). 1993. *Unfallverhütungsverschrift* 58, *Organische Peroxide*. BG Chemie, Heidelberg, Germany.

Biffi E. 1992a. Tossicita' inalatoria nel ratto (dose limite). Unpublished report 92/14445, Biolab SGS, Vimodrone, Milano, Italy. Solvay Interox, Milano. [Italian; English translation].

Biffi E. 1992b. Irritazione cutanea nel coniglio, acido peracetico 5 %. Unpublished report 92/14443, Biolab SGS, Vimodrone, Milano, Italy. Solvay Interox, Milano. [Italian; English translation].

Biffi E. 1992c. Irritazione oculare nel coniglio, acido peracetico 5 %. Unpublished report 92/14444, Biolab SGS, Vimodrone, Milano, Italy. Solvay Interox, Milano. [Italian; English translation].

Biffi E. 1992d. Sensibilizzazione allergica nella cavia, acido peracetico 5 %. Unpublished report 92/14446, Biolab SGS, Vimodrone, Milano, Italy. Solvay Interox, Milano. [Italian; English translation].

Biffi E. 1995. Tossicita' inalatoria acuta, acido peracetico 5 %. Unpublished report 95/01665, Biolab SGS, Vimodrone, Milano, Italy. Solvay Interox, Rosignano Solvay, Livorno, Italy. [Italian; English translation].

Bioxal. 1999. Bactipal 5/14, stabilité après dilution à 100 et 1000 ppm. Unpublished report. Bioxal, Chalon sur Saône, France.

Bioxal. 2000a. Produits chimiques à usage industriel, fiche de données de sécurité, Bactipal 5-14. Seppic-Air Liquide, Paris, France.

Bioxal. 2000b. Produits chimiques à usage industriel, fiche de données de sécurité, Bactipal 15-23. Seppic-Air Liquide, Paris, France.

Blakistone B, Chuyate R, Kautter D, Charbonneau J, Suit K. 1999. Efficacy of oxonia active against selected spore formers. *J Food Prot* 62:262-267.

Block SS. 1991. Peroxygen compounds. In Block SS, ed, *Disinfection, sterilization, and preservation*, 4th ed. Lea and Felbinger, Philadelphia PA, USA, pp 167-181.

Bloomfield SF, Arthur M, Looney E, Begun K, Patel H. 1991. Comparative testing of disinfectant and antispetic products using proposed European suspension testing methods. *Letters in Applied Biology* 13:233-237.

Blowers SD. 1994a. A micronucleus test with Proxitane-0510. Unpublished report 1324/1/2/94, BIBRA Toxicology International, Carshalton, Surrey, UK. Johnson & Johnson Medical, Skipton, N. Yorkshire, UK.

Blowers SD. 1994b. An *in vivo* unscheduled DNA synthesis assay with Proxitane-0510. Unpublished report 1334/1/2/94, BIBRA Toxicology International, Carshalton, Surrey, UK. Johnson & Johnson Medical, Skipton, N. Yorkshire, UK.

Blowers SD. 1995. A micronucleus test with Proxitane-0510. Unpublished report 1324/1/2/94, addendum 1, BIBRA Toxicology International, Carshalton, Surrey, UK. Johnson & Johnson Medical, Skipton, N. Yorkshire, UK.

Bock FG, Myers HK, Fox HW. 1975. Cocarcinogenic activity of peroxy compounds. *J Natl Cancer Inst* 55:1359-1361.

Bowler G, Malone J, Pehrsson R. 1996. Recent advances in the application of peracetic acid formulations in the European sugar beet industry. *Zuckerind* 121:414-416.

Bringmann G, Kühn R. 1982. Ergebnisse der Schadwirkung wassergefährdender Stoffe gegen *Daphnia magna* in einem weiterentwickelten standardisierten Testverfahren. *Z Wasser Abwasser Forsch* 15:1-6.

Bulnes C, Garcia MG, Tablada L. 1982a. Efectos toxicos del acido peracetico II, estudio morfopatologico en la piel de cobayos en condiciones de contacto directo. *Rev Salud Anim* 4:59-65.

Bulnes C, Garcia MG, Tablada L. 1982b. Efectos toxicos del acido peracetico I, estudio morfopatologico en la piel y las mucosas de cobayos sometidos a condiciones forzadas de inhalacion. *Rev Salud Anim* 4:75-84.

Bundesminister (für Umwelt, Naturschutz und Reaktorsicherheit). 1999. Allgemeine Verwaltungs-vorschrift zum Wasserhaushaltsgesetz über die Einstufung wassergefährdender Stoffe in Wassergefährdungsklassen (Verwaltungsvoschrift wassergefährndder Stoffe, VwVwS) vom 17.05.99. *Bundesanzeiger* 98a:1-31.

Burgess D, Forbis AD. 1983. Acute toxicity of Oxonia Active to *Daphnia magna*. Unpublished report report 30724, Analytical Bio-Chemistry Laboratories, Columbia MO, USA. Bonewitz Chemical Services, Burlington, Iowa, USA.

Busch A, Werner E. 1974. Zur Problematik der Tierverträglichkeit von Peressigsäure I. Mitt., Untersuchungsergebnisse nach Applikation von Peressigsäure. *Mh. Vet. Med.* 29:494-498.

Butler R. 1987. Determination of the 48 hour median effect concentration (EC_{50}) of Oxymaster to the pacific oyster (Crassostrea gigas) in terms of larval survival and development. Unpublished report CO1643-M/EV8687, WRc Environment. Interox Chemicals, Widnes, Cheshire, UK.

Byers L. 1998. Octanol-water partition coefficient for peracetic acid and hydrogen peroxide. Personal communication to Caropreso F, February 5. FMC, Princeton PA, USA.

Calvert JG, Lazrus A, Kok GL, Heikes BG, Walega JG, Lind J, Cantrell CA. 1985. Chemical mechanisms of acid generation in the troposphere. *Nature* 317:27-35.

Caropreso FE. 2000. Calculation of peracetic acid vapor compositions using ideal solutions. Personal communication, 25 April. FMC, Princeton PA, USA.

Cascieri T, Freeman C. 1983a. Acute oral toxicity of dilute peracetic acid in rats. Unpublished report, study I83-718. FMC Corporation, Somerville NJ, USA.

Cascieri T, Freeman C. 1983b. Acute dermal toxicity of dilute peracetic acid in rabbits. Unpublished report, study I83-721. FMC, Somerville NJ, USA.

Cascieri T, Freeman C. 1983c. Primary skin irritation and skin corrosion study of dilute peracetic acid in rabbits. Unpublished report, study I83-720. FMC, Somerville NJ, USA.

Cascieri T, Freeman C. 1983d. Primary eye irritation study of dilute peracetic acid in rabbits. Unpublished report, study I83-719. FMC, Somerville NJ, USA.

CEFIC (European Chemical Industry Council). 2000a. Peracetic acid production in Europe. Personal communication by Le Doré L, Peroxygens Sector Group, 10 April. CEFIC, Brussels, Belgium.

CEFIC (European Chemical Industry Council). 2000b. Peracetic acid production and consumption data. Personal communication by Le Doré L, Peroxygens Sector Group, 20 June. CEFIC, Brussels, Belgium.

Cerne O, Ancker K, Palokangas P. 1999. Arbetsmiljö och miljöeffekter av massaindustrins miljöanpassning, perättiksyra som blekkemikalie samt förstudie av slutning av processvattenströmmar [Occupational and environmental effects of the environmental approach in the pulp industry, and a pre-study of effluent closure]. Report B 1326. IVL (Institutet för Vatten- och Luftvårdsforskning), Stockholm, Sweden [English translation].

Chalkley NJ. 1991a. Degradation of peracetic acid, investigation of the depth of penetration of peracetic acid into soil. Personal communication 20th March 1991. Solvay Interox, Widnes, Cheshire, UK.

Chalkley NJ. 1991b. Degradation of peracetic acid in pond and stream waters. Personal communication 15th May 1991. Solvay Interox, Widnes, Cheshire, UK.

Chalkley NJ. 1991c. Degradation of peracetic acid in soil, potato and Brussels sprouts. Personal communication 6th February 1991. Solvay Interox, Widnes, Cheshire, UK.

Chalkley NJ. 1992. Degradation of peracetic acid in contact with coir and various samples of [tap] water. Personal communication 19th March 1992. Solvay Interox, Widnes, Cheshire, UK.

Chance B, Sies H, Boveris A. 1979. Hydroperoxide metabolism in mammalian organs. *Physiol Rev* 59:527-605.

Chemoxal. 1995a. Procès-verbal de la dégradation abiotique du APA 0.35%, hydrolyse en fonction du pH, protocole paru au JO des CE L383 A/229 du 29/12/92. Unpublished report. Air Liquide, Chemoxal, Paris, France.

Chemoxal. 1995b. Détermination de l'équation d'Arrhenius, At.Chem.95.05 suite. Unpublished report. Air Liquide, Chemoxal, Paris, France.

Chemoxal. 1997. Safety data sheet, Bactipal 15-14. Seppic-Air Liquide Group, Chalon-sur-Saône, France.

Chemoxal. 1999. Data about PAA 15% [Bactipal 15/23 and 15/14]. Personal communication by Gouges Y, 5 March. Chemoxal, Air Liquide Chimie, Paris, France.

Cohle P, McAllister WA. 1983. Acute toxicity of Oxonia Active to rainbow trout (*Salmo gairdneri*). Unpublished report 30723, Analytical Bio-Chemistry Laboratories, Columbia MO, USA. Bonewitz Chemical Services, Burlington, Iowa, USA. <Henkel>

Coppinger WJ, Wong TK, Thompson ED. 1983. Unscheduled DNA synthesis and DNA repair studies of peroxyacetic and monoperoxydecanoic acids. *Environmental Mutagenesis* 5:177-192.

Cords BR. 1994. New peroxyacetic acid sanitizer. In: *Proceedings of the twenty-third convention* [Reference details lacking].

Cords BR, Dychdala GR. 1993. Sanitizers, halogens, surface-active agents and peroxides. *Food Science and Technology* 57:469-537.

Crow S. 1992. Peracetic acid sterilization, a timely development for a busy healthcare industry. *Infection Control and Hospital Epidemiology* 13:111-113.

Dalin I. 1996. Framtida kemikalier i blekeriet [Future chemicals in the bleach plant]. Presented at: ÅF-IPK Fibre Line Conference, Stockholm, Sweden 27 November. Akzo Nobel, Eka Chemicals, Bohus, Sweden.

De Duve C, Bauduin P. 1966. Peroxisomes (microbodies and related particles). *Physiol. Rev.* 46:323-353.

Degussa. 1977a. Prüfung der akuten Toxizität von Peressigsäure 10%ig bei peroraler Applikation an Ratten. Unpublished report by Leuschner F, Laboratorium für Pharmakologie und Toxikologie, Hamburg, Germany. Degussa, Frankfurt am Main, Germany.

Degussa. 1977b. Orientierende Prüfung der akuten Toxizität von 40%iger Peressigsäure bei Sprague-Dawley Ratten. Unpublished report by Leuschner F, Laboratorium für Pharmakologie und Toxikologie, Hamburg, Germany. Degussa, Frankfurt am Main, Germany.

Degussa. 1982a. Bericht über die toxikologische Prüfung von Peressigsäure 15% nach einmaliger oraler Gabe an der Ratte. Ergänzende Mitteilung. Unpublished report Ind-Tox-86-81/82, 86/1-82/83 by Zechel HJ, Toxikologisches Institut Degussa-Asta, Bielefeld, Germany. Degussa, Frankfurt am Main, Germany.

Degussa. 1982b. Bericht über die Prüfung der lokalen Reizwirkung von Peressigsäure 15% nach einmaliger Applikation an der Haut des Kaninchens (Patch-Test). Unpublished report Ind-Tox-87-81/82 by Zechel HJ, Toxikologisches Institut Degussa-Asta, Bielefeld, Germany. Degussa, Frankfurt am Main, Germany.

Degussa. 1988a. Peroxyacetic acid 10%, acute toxicity, testing the primary irritancy after single application to the skin of the rabbit (patch test). Unpublished report study 864876 by Mayr W, Asta Pharma, Bielefeld, Germany. Degussa, Hanau, Germany.

Degussa. 1988b. Peroxyacetic acid 5%, acute toxicity, testing the primary irritancy after single application to the skin of the rabbit (patch test). Unpublished report study 864865 by Mayr W, Asta Pharma, Bielefeld, Germany. Degussa, Hanau, Germany.

Degussa. 1990a. Arbeitsplatzmessungen auf Peressigsäure in der Raumluft, Asta Pharma, Frankfurt am Main, Germany. Personal communication 12 December. Degussa, Hanau, Germany.

Degussa. 1990b. Peroxyacetic acid 15%, acute toxicity, testing the primary irritation/corrosion after single application to the skin of the rabbit (patch test). Unpublished report study 864870 by Zechel HJ, Asta Pharma, Bielefeld. Degussa, Hanau, Germany.

Degussa. 1991. Prüfbericht *Chlorella vulgaris*, Algenwachstumshemmtest mit Wasserstoffperoxid 35%G. Unpublished report 91/11/01 by Geschäftsbereich Industrie- und Feinchemikalien, Hanau, Germany. Degussa, Hanau, Germany.

Degussa. 1996a. Peracetic acid 15%, safety data sheet (93/112/EEC) valid from 06.09.1996. Degussa, Hanau, Germany.

Degussa. 1996b. Peracetic acid 35%, safety data sheet (93/112/EEC) valid from 19.2.1996. Degussa, Hanau, Germany.

Degussa. 1997. Peracetic acid 5%, safety data sheet (93/112/EEC) valid from 10.04.1997. Degussa, Hanau, Germany.

Den Besten C. 1994. Proxitane 0103, acute oral toxicity study in the rat. Unpublished report S.9406, Solvay Duphar, Weesp, Netherlands. Solvay Interox, Brussels, Belgium.

DFG (Deutsche Forschungsgemeinschaft). 1999a. MAK- und BAT-Werte-Liste 1999, Maximale Arbeitsplatzkonzentrationen und biologische Arbeitsstofftoleranzwerte. Mitteilung 35. Wiley-VCH, Weinheim, Germany, pp 12, 57, 108.

DFG (Deutsche Forschungsgemeinschaft). 1999b. MAK- und BAT-Werte-Liste 1999, Senatskommission zur Prüfung gesundheitsschädlicher Arbeitsstoffe. Mitteilung 35. Wiley-VCH, Weinheim, Germany, pp 90, 120-122, 166.

Dixon D. 1988. Comparative study of the toxicity and genotoxicity of Oxymaster and hypochlorite (on reproductive stages of the marine tubeworm *Pomatoceros triqueter L.*). Solvay Interox, Warrington, UK.

Dorange JL, Agnet Y, Dupuy P. 1974. Etude des propriétés mutagènes de l'acide peracétique. [The mutagenic acitivity of peracetic acid, Appendix 2-5]. Unpublished report, Aide DGRST 74-7-673 et 674, Annexe 2-5. Institut National de la Recherche Agronomique, Station de Technologie des Produits Végétaux, Dijon, France. Chemoxal, Paris, France. [French; English translation].

Douglas MT, Pell IB. 1986a. The acute toxicity of Proxitane 1507 to *Daphnia magna*. Unpublished report LPT44/851641. Huntingdon Research Centre, Huntingdon, Cambridgeshire, UK. Laporte Industries, Widnes, Cheshire, UK.

Douglas MT, Pell IB. 1986b. The acute toxicity of Proxitane 1507 to rainbow trout (*Salmo gairdneri*). Unpublished report LPT43/851643. Huntingdon Research Centre Huntingdon, Cambridgeshire, UK. Laporte Industries, Widnes, Cheshire, UK.

Drimus J, Matasa C. 1966. Sur la décomposition spontanée de l'acide peracétique [Spontaneous decomposition of peracetic acid]. *Bulletin de la Société Chimique de France* 12: 253-255 [French; English translation].

Dudek BD. 1984. Four hour acute aerosol inhalation toxicity study in rats of P3 Oxonia Active. Unpublished report, study 420-1467. ToxiGenics, Decatur, IL, USA. Bonewitz Chemical Services, Burlington, Iowa, USA. <Henkel>

Duprat P, Gradiski D, Delsaut L, Lepage M. 1974. Pouvoir irritant sur la peau et l'oeil du lapin de l'eau de Javel et de l'acide peracétique à différentes concentrations. *Revue Méd Vét* 125:879-895.

Dworschak D, Linde J. 1976. Raumluftdesinfektion mit Peressigsäure (PES)-Aerosolen auf Intensivtherapiestationen unf ihre Konsequenzen für die Behandlung des Hopitalismusproblems. *Dt. Gesundh.-Wesen* 31:1622.

Dychdala GR. 1988. New hydrogen peroxide-peroxyacetic acid disinfectant/sanitizer. In: Kutz SM *et al*, eds, 4th Conference on progress in chemical disinfection. Janauer G, Chairman. Dept. of Chemistry State University of New York NY, USA, pp 315-342.

EC (European Commission). 1996. Commission regulation (EC) No 1433/96 of 23 July 1996 amending annexes II and III to Council Regulation (EEC) No 2377/90 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin. *Official Journal of the European Communities L* 184:21-23.

EC (European Commission). 1998. Cas No 79-21-0, peracetic acid …%. In Annex to Commission directive 98/98/EEC of 15 December 1998 adapting to technical progress for the twenty-fifth time Council directive 67/548/EEC on the approximation of the laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances. *Official Journal of the European Communities L* 355:275.

ECE (Economic Commmission for Europe), Inland Transport Committee. 1996. European agreement concerning the international carrage of dangerous goods by road (ADR) and protocol of signature, done at Geneva on 30 september 1957, volume I. Agreement, protocol of signature, annex A and appendices to Annex A with amendments thereto up to 1 January 1997. ECE/Trans/115 (Vol.I). UN, Geneva, Switzerland.

ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals). 1993. Hydrogen peroxide, CAS 7722-84-1. Joint Assessment of Commodity Chemicals 22. ECETOC, Brussels, Belgium.

ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals). 1996. Hydrogen peroxide OEL criteria document, CAS 7722-84-1. Special report 10. ECETOC, Brussels, Belgium.

EEC (European Economic Community). 1990. Council regulation (EEC) 2377/90 of 26 June 1990 laying down a Community procedure for the establishment of maximum residue limits of veterinary medicinal products in foodstuffs of animal origin. *Official Journal of the European Communities L* 224:1-8.

Effkemann S, Karst U. 1998. Reagent for the high-performance liquid chromatography determination of peroxycarboxylic acids. *Analyst* 123:1761-1765.

Effkemann S, Brødsgaard S, Mortensen P, Linde SA, Karst U. 1999a. Determination of gas phase peroxyacetic acid using pre-column derivatization with organic sulfide and liquid chromatography. *J Chromatography* A 855:551-561.

Effkemann S, Pinkernell U, Harms D, Karst U. 1999b. Recent techniques for the determination of peroxycarboxylic acids. *International Laboratory* 29:14-19.

Effkemann S, Brødsgaard S, Mortensen P, Linde SA, Karst U. 2000. Spectrophotometric and direct-reading methods for the analysis of gas-phase peroxyacetic acid. *Fresenius J Anal Chem* 366:361-364.

EU (European Union). 1998. Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing of biocidal products on the market. *Official Journal of the European Communities L* 123:1-63.

EU (European Union). 1999. Directive 1999/45/EC of the European Parliament and of the Council of 31 May 1999 concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations. *Official Journal of the European Communities L* 200:1-68.

Europerox. 1997. New methods and instrumentation for selective peroxide monitoring in industrial processes, a standards, measurements and testing proposal (1994-1998). Theme 1, measurements for quality European products including written standards for industry, 1.3. Measurement and testing for the control of production, proposal description, part A. European Commission standards, measurements and testing programme project SMT4-CT97-2153. Europerox, University of Münster, Münster, Germany.

Fairhurst F. 1987. Determination of the 48 hour median effect concentration (EC_{50}) of Oxymaster to the common mussel (*Mytilus edulis*), in terms of larval survival and development. Unpublished report CO1644-M/EV8687, WRc Environment, Medmenham, Marlow, Bucks, UK. Interox Chemicals, Widnes, Cheshire, UK.

Feigenbaum H. 1997. The use of peracetic acid as a chemical oxidant in pharmaceutical synthesis. *Speciality Chemicals* 17:80-81.

Ferri A. 1990. Action of catalase on peroxoacetic acid. Kinetic studies. *Biochemistry. International* 21:623-631.

Fischbach LJ. 1985. Renalin, qualification as a dialyzer sterilant. *AAMI* 1985:15-19.

Fischer W, Arlt E, Brabäder B. 1989. Verfahren und Reagenz zur Bestimmung von Persäuren. Merck Patent, Darmstadt. Offenlegungsschrift DE 37 43 224 A1. Deutsches Patentamt, München, Germany.

FMC. 1998a. Material safety data sheet, peracetic acid 5%, version US/Canada. FMC, Princeton PA, USA.

FMC. 1998b. Material safety data sheet, peracetic acid 15%, version US/Canada. FMC, Princeton PA, USA.

FMC. 1998c. Material safety data sheet, peracetic acid 35%, version US/Canada. FMC, Princeton PA, USA.

Fraser JAL. 1986. Peroxygens in environmental protection. *Effluent and Water Treatment Journal* June 1986:186-199.

Fraser JAL, Thorbinson A. 1986. Fogging trials with Tenneco Organics Limited (30th June. 1986) at Collards Farm. Unpublished report. Solvay Interox, Warrington, UK.

Freeman C. 1987. 35% peracetic acid, preliminary oral toxicity study in rats. Unpublished report, study I86-0935. FMC, Princeton, NJ, USA.

Freeman C. 1991a. Peracetic acid 0.15% use dilution, acute oral toxicity study in rats, guideline 81-1. Unpublished report, study I91-1192. FMC, Princeton, NJ, USA.

Freeman C. 1991b. Peracetic acid 0.15% use dilution, acute dermal toxicity study in rats, guideline 81-2. Unpublished report, study I91-1193. FMC, Princeton, NJ, USA.

Freeman C. 1991c. Peracetic acid 0.15% use dilution, primary skin irritation study in rabbits, guideline 81-5. Unpublished report, study I91-1194. FMC, Princeton, NJ, USA.

Freeman C. 1991d. Peracetic acid 0.15% use dilution, primary eye irritation study in rabbits, guideline 81-4. Unpublished report, study I91-1194. FMC, Princeton, NJ, USA.

Freeman C. 1991e. Peracetic acid 0.15% use dilution, skin sensitisation study in guinea pigs, guideline 81-6. Unpublished report, study I91-1191. FMC, Princeton, NJ, USA.

Freeman C. 1998. Peracetic acid 5%, acute oral toxicity study in rats. Unpublished report, study I97-2236. FMC, Princeton, NJ, USA.

French M. 1993. Irritancy testing of peracetic acid to skin. Personal communication, 10 March. Solvay Interox, Widnes, Cheshire, UK.

Gaffney JS, Streit GE, Spall WD, Hall JH. 1987. Beyond acid rain. *Environ Sci Technol* 21:519-524.

Gardner C, Bucksath JD. 1996a. Static acute toxicity of 5 % peracetic acid (Vigor Ox) to *Daphnia magna*. Amended final report 42349, ABC Laboratories, Columbia, MO, USA. Unpublished report, study I95-2021. FMC, Princeton, NJ, USA.

Gardner C, Bucksath JD. 1996b. Static acute toxicity of 5 % peracetic acid (Vigor Ox) to rainbow trout (*Oncorhynchus mykiss*). Final report 42348, ABC Laboratories, Columbia, MO, USA. Unpublished report, study I95-2023. FMC, Princeton NJ, USA.

Gardner C, Bucksath JD. 1996c. Static renewal toxicity of 5 % peracetic acid (Vigor Ox) to bleugill (*Lepomis macrochirus*). Final report 42347, ABC Laboratories, Columbia, MO, USA. Unpublished report, study I95-2029. FMC, Princeton, NJ, USA.

Gerike P and Jasiak W, 1983. Biologische Abbaubarkeit der Peressigsäure. Unpublished report 1983/2179. Henkel, Düsseldorf, Germany.

Gerike P, Gode P. 1990. The biodegradability and inhibitory threshold concentration of some disinfectants. *Chemosphere* 21:799-812.

Gloxhuber C, Kästner W. 1983. Prüfung der akuten intravenösen Toxizität von P3-oxonia aktive im Vergleich zu Formalin (37,6 Gew.% Formaldehyd in Wasser). Unpublished report 1160, ZR-FE/Toxikologie. Henkel, Düsseldorf, Germany.

Gomond P. 1998. Toxicité orale aiguë chez le rat de la préparation Bactipal D. Unpublished report Te675/98-3904, Evic-Ceba, Bordeaux, France. Chemoxal, Chalon sur Saône, France.

Gouges Y, Teral G. 1997. Les méthodes d'analyses utilisées dans le cadre de l'étude d'écotoxicité de l'acide peracétique. Personal communication, 15 May. Chemoxal, Jouy en Josas, France.

Greaves P and Barsoum N. 1990. Pathology of tumours in laboratory animals, tumours of the rat, tumours of soft tissues. *IARC Sci Publ* 99:597-623 [Review].

Greenspan FP, MacKellar DG. 1948. Analysis of aliphatic peracids. *Anal Chem* 20:1061-1063.

Groeneveld AHC, De Groot WA. 1999. Activated sludge, respiration test with hydrogen peroxide. Unpublished report A.SOL.S.003, Solvay Pharmaceuticals, Weesp, NL. Solvay, Brussels, Belgium.

Gunz DW, Hoffmann MR. 1990. Atmospheric chemistry of peroxides, a review. *Atmospheric Environment* 24A:1601-1633.

Hanst PH, Gay BW. 1983. Atmospheric oxidation of hydrocarbons, formation of hydroperoxides and peroxyacids. *Atmospheric Environment* 17:2259-2265.

Harakeh MS. 1984. Inactivation of enteroviruses, rotaviruses and bacteriophages by peracetic acid in a municipal sewage effluent. *FEMS Microbiology Letters* 23:27-30.

Harvey AJ. 1992. Atmospheric test on Cidox formulation. Personal communication of 22 September 1992. Solvay Interox, Widnes, Cheshire, UK.

Harvey AJ. 1993. Atmospheric monitoring of peracetic acid. Personal communication of 25 August 1993. Solvay Interox, Widnes, Cheshire, UK.

Hauschild F, Ludewig R, Muelhberg H. 1958. Ueber die "aetzende" Wirkung von Wasserstoffperoxyd. *Naunyn-Schmiedeberg's Arch Exp Pathol Pharmak* 235:51-62.

Haynes G, Brightwell J. 1998a. Oxystrong 5, acute oral toxicity study in the rat, final report. Unpublished report 6018/T/192/97, Research Toxicology Centre (RTC), Pomezia-Roma, Italy. Ausimont, Bollate, Italy.

Haynes G, Brightwell J. 1998b. Oxystrong 5, acute dermal irritation study in the rabbit, final report. Unpublished report 6020/T/175/97, Research Toxicology Centre (RTC), Pomezia-Roma, Italy. Ausimont, Bollate, Italy.

Heikes BG, Miller WL, Lee M. 1991. Hydrogen peroxide and organic peroxides in the marine environment. In: Schiff HI, ed, *Measurement of atmospheric gases*. SPIE Proceedings 1433. SPIE International Society for Optical Engineering, Bellingham WA, USA, pp 253-260.

Heinze W, Nattermann H. 1984. Peressigsäure-Aerosol-Wirkung bei Langzeitanwendung niedriger keimwirksamer Konzentrationen auf Versuchstiere [The effect of peracetic acid in aerosol formed during long-term application in low antibacterial concentrations on test animals]. *Wissenschaftliche Zeitschrift der Humboldt-Universität zu Berlin, Math-Nat R* 18:513-517 [German; English translation].

Heinze W, Nattermann H. 1985. Zur Wirkung von Aerosolen, die aus verschieden konzentrierten Wolfasterillösungen hergestellt wurden, auf pathogene Bakterien. *Monatshefte Vet. Med.* 40:335-338.

Heinze W, Werner E, Krüger Von S, Wilsdorf G. 1979. Zur Tierverträglichkeit von Peressigsigsäure-Aerosolen unter besonderer Berücksichtigung der Beeinträchtigung der Abwehrleistung. *Monatshefte Vet. Med.* 34:212-217.

Heinze W, Werner E, Fischer AR. 1981. Wirkung und Wirkungsweise von Peressigsäure-Aerosolen auf den tierischen Organismus. *Monatshefte Vet. Med.* 36:343-49.

Heinze W, Hahn T, Wrensch G, Fischer AR. 1982. Wirkungsweise und Grenzen der Schadwirkung von Peressigsäure- (PES-), Milchsäure- und Essigsäure-Aerosolen sowie von Peressigsäure und Schwefeldioxid-Gasen bei Säugetieren. Wiss. *Z Humbolt.-Univ. Berlin, Math.-Nat. R.* 31:549-55.

Hellpointer E, Gäb S. 1989. Detection of methyl, hydroxymethyl and hydroxyethyl hydroperoxides in air and precipitation. *Nature* 337:631-634.

Henkel. 1995. P3-oxonia aktiv S [15%], material safety data sheet according to 91/155/EEC, ISO 11014-1, Classification and labelling according to GefStoffV. Henkel, Düsseldorf, Germany.

Henkel. 1997a. P3-oxonia aktiv [5%], material safety data sheet according to 91/155/EEC, ISO 11014-1, Classification and labelling according to GefStoffV. Henkel, Düsseldorf, Germany.

Henkel. 1997b. P3-oxonia aktiv S [30%], material safety data sheet according to 91/155/EEC, ISO 11014-1, Classification and labelling according to GefStoffV. Henkel, Düsseldorf, Germany.

Hicks L, Ziegler TA, Bucksath JD. 1996. Acute toxicity of 5% peracetic acid (Vigor Ox) to *Selenastrum capricornutum* Printz. Unpublished report 42866, ABC Laboratories, Columbia MO, USA. FMC, Princeton NJ, USA.

HSE (UK Health and Safety Executive). 2000. Occupational exposure limits 2000. EH40/98. HSE Books, Sudbury, Suffolk, UK, pp 12, 19.

Hutt CW, Kinney LA. 1985. Inhalation approximate lethal concentration (ALC) of peroxyacetic acid. Unpublished report 751-85, Haskell Laboratory, Newark DW, USA. Du Pont, Wilmington DW, USA.

Ingram AJ, Grasso P. 1991. Evidence for and possible mechanisms of non-genotoxic carcinogenesis in mouse skin. *Mutation Research* 248:333-340.

IVDK (Informationsverbund Dermatologischer Kliniken). 1999. Benzisothiazolinon (BIT), Peressigsäure. Schnuch A, personal communication to Sterzel W, 21 November. IVDK, University of Göttingen, Göttingen, Germany. Henkel, Düsseldorf, Germany.

Jacobi S. 1997. Mackay level I calculations for peracetic acid. Personal communication of 25 February. Degussa-Hüls, Hanau, Germany.

Jäger P, Püspok J. 1980. Peressigsäure als Desinfektionsmittel in Brauereien un Betrieben der alkoholfreien Getränkeindustrie. *Mitteilungen der Versuchsstation für das Gärungsgewerbe in Wien* 3/4:32-35.

Jäkärä J, Parén A, Nyman J. 1998. Production and use of different peracids in chemical pulp bleaching. *Paperi ja Puu - Paper and Timber* 80:281-287.

Jakobi G, Löhr A. 1991. Detergent ingredients, bleaches, householl detergents, references. In Gerhartz W, Yamamoto YS, Kaudy L, Pfefferkorn R, Rousaville JF, eds, *Ullmann's Encyclopedia of Industrial Chemistry*, 5th ed, Vol A8. VCH, Weinheim, Germany, pp 357-362, 373-375, 438-448.

Janssen PJM. 1989a. Acute inhalation toxicity studies of Proxitane 1507 in male rats I. Unpublished report S.8906, Duphar, Weesp, Netherlands. Solvay, Brussels, Belgium.

Janssen PJM. 1989b. Acute inhalation toxicity studies of Proxitane 1507 in male rats II. Unpublished report S.8908, Duphar, Weesp, Netherlands. Solvay, Brussels, Belgium.

Janssen PJM. 1989c. Acute inhalation study to investigate the respiratory irritating properties of Proxitane 1507 in male rats. Unpublished report S.8912, Duphar, Weesp, Netherlands. Solvay, Brussels, Belgium.

Janssen PJM. 1990. Preliminary acute inhalation study to investigate the respiratory irritating properties of Proxitane 1507 in male rats. Unpublished report S.9003, Duphar, Weesp, Netherlands. Solvay, Brussels, Belgium.

Janssen PJM, Pot TE. 1987. Primary irritation study of Proxitane 0512, Proxitane 1507 and Proxitane 4002 to the skin of the male rabbit. Unpublished report S.8706, Duphar, Weesp, Netherlands. Solvay, Brussels, Belgium.

Janssen PJM, Van Doorn WM. 1994. Acute inhalation toxicity study with Proxitane AHC in male and female rats. Unpublished report S.9408, Duphar, Weesp, Netherlands. Solvay, Brussels, Belgium.

Joakimson da Silva E, Keiko s Coimbra I. 1990a. Determinação da DL_{50}, por via oral, Proxitane RFA. Unpublished report 97976, Instituto de Tecnologia do Paraná, Curitiba, Parana, Brasil. Peroxidos do Brasil LTDA, Sao Paulo, Brazil.

Joakimson da Silva E, Keiko s Coimbra I. 1990b. Determinação da DL_{50}, por via oral, Proxitane 1512. Unpublished report 97975, Instituto de Tecnologia do Paraná, Curitiba, Parana, Brazil. Peroxidos do Brasil LTDA, Sao Paulo, Brazil.

Joakimson da Silva E, Keiko s Coimbra I. 1990c. Determinação da DL_{50}, por via dérmica, Proxitane RFA. Unpublished report 43041-A, Instituto de Tecnologia do Paraná, Curitiba, Parana, Brazil. Peroxidos do Brasil LTDA, Sao Paulo, Brazil.

Joakimson da Silva E, Keiko s Coimbra I. 1990d. Determinação da DL_{50}, por via dérmica, Proxitane 1512. Unpublished report 43040-A, Instituto de Tecnologia do Paraná, Curitiba, Parana, Brazil. Peroxidos do Brasil LTDA, Sao Paulo, Brazil.

Joakimson da Silva E, Keiko s Coimbra I. 1990e. Teste de irritabilidade dérmica, Proxitane 1512. Unpublished report 46552-A, Instituto de Tecnologia do Paraná, Curitiba, Parana, Brazil. Peroxidos do Brasil LTDA, Sao Paulo, Brazil.

Joakimson da Silva E, Keiko s Coimbra I. 1990f. Teste de irritabilidade dérmica, Proxitane RFA. Unpublished report 46553-A, Instituto de Tecnologia do Paraná, Curitiba, Parana, Brazil. Peroxidos do Brasil LTDA, Sao Paulo, Brazil.

Joakimson da Silva E, Keiko s Coimbra I. 1990g. Teste de irritabilidade ocular, Proxitane 1512. Unpublished report 48397-A, Instituto de Tecnologia do Paraná, Curitiba, Parana, Brazil. Peroxidos do Brasil LTDA, Sao Paulo, Brazil.

Joakimson da Silva E, Keiko s Coimbra I. 1990h. Teste de irritabilidade ocular, Proxitane RFA. Unpublished report 48398-A, Instituto de Tecnologia do Paraná, Curitiba, Parana, Brazil. Peroxidos do Brasil LTDA, Sao Paulo, Brazil.

Joakimson da Silva E, Keiko s Coimbra I. 1990i. Teste de sensibilização dérmica, Proxitane 1512. Unpublished report 44119-A, Instituto de Tecnologia do Paraná, Curitiba, Parana, Brazil. Peroxidos do Brasil LTDA, Sao Paulo, Brazil.

Joakimson da Silva E, Keiko s Coimbra I. 1990j. Teste de sensibilização dérmica, Proxitane RFA. Unpublished report 44121-A. Peroxidos do Brasil LTDA, Sao Paulo, Brazil.

Johnson WK. 1995. CEH product review, acetaldehyde. In SRI International, ed, *Chemicals Economic Handbook* 601.5000A. SRI International, Menlo Park, CA, USA.

Jones P, Middlemiss DN. 1972. Formation of compound I by the reaction of catalase with peroxoacetic acid. *Biochem* J 130:411-415.

Juhr NC, Spranger A, Haas A. 1977. Erhaltung der Tränkwasserqualität beim Verbrauch, Versuche zur Tränkwasserkonservierung. *Z Versuchstierk* 19, 147-154.

Juhr NC, Klomburg S, Haas A. 1978. Tränkwassersterilisation mit Peressigsäure [Drinking water sterilization with peracetic acid]. *Z Versuchstierk* 20:65-72 [German; English translation].

Junkermann W, Fels M, Pietruk P, Slemr F, Hahn J. 1993. Peroxide measurements at remote mountain field sites (Wank - 1780 m. and 1175 m.), seasonal and diurnal variations of hydrogen peroxide and organic peroxides. In: Borell PM *et al*, eds, *Proceedings of EUROTRAC Symposium '92. SPB Academic*, The Hague, Netherlands, pp 180-184.

Kelly TJ, Daum PH, Schwartz SE. 1985. Measurements of peroxides in cloudwater and rain. *Journal of Geophysical Research* 90:7861-7871.

Kirk O, Damhus T, Christensen MW. 1992. Determination of peroxycarboxylic acids by high-performance liquid chromatography with electrochemical detection. *J Chromatogr* 606:49-53.

Kirk O, Christensen MW, Damhus T, Godtfredsen SE. 1994. Enzyme catalyzed degradation and formation of peroxycarboxylic acids. *Biocatalysis* 11:65-77.

Klahre J, Lustenberger M, Fleming HC. 1996a. Microbielle Probleme in der Papierfabrikation, Teil 1, Schäden, Ursachen, Kosten, Grundlagen. *Das Papier* 2:47-53.

Klahre J, Heim T, Flemming HC. 1996b. Environmental compatibility of peracetic acid and conventional biocides in paper industry applications. *DECHEMA Monographs* 133:501-506.

Klenk H, Götz PH, Siegmeier R, Mayr W. 1991. Peroxy compounds, organic. In Gerhartz W, Yamamoto YS, Kaudy L, Pfefferkorn R, Rousaville JF, eds, *Ullmann's Encyclopedia of Industrial Chemistry*. 5th ed, Vol A19. VCH, Weinheim, Germany, pp 206-211:224-233.

Kline LB, Hull RN. 1960. The virucidal properties of peracetic acid. *American Journal of Clinical pathology* 33:30-33.

Koch S, Kramer A, Stein J, Adrian V, Weuffen W. 1989. Mutagenitätsprüfung im Spermakopf-Test/Maus und mutagene Potenz von 2 Desinfektionsmitteln auf Basis von Peressigsäure bzw Phenolen [Investigation into the mutagenicity in the sperm head test on mice and the mutagenic potency of two disinfectants based on peracetic acid and phenols]. *Zbl Hyg* 188:391-403 [German; English translation].

Koopman TSM. 1994. Proxitane 0103, acute dermal toxicity study in the rat. Unpublished report S.9405, Solvay Duphar, Weesp, Netherlands. Solvay Interox, Brussels, Belgium.

Kramer A. 1989. Hinweise / Empfehlungen zur Herabsetzung einer Gesundheitsgefährdung durch peressigsäurehaltige Desinfektionsmittel im Gesundheits- und Sozialwesen. *Zent. Bl. Chir.* 114:619-625.

Kramer JF. 1997. Peracetic acid, a new biocide for industrial water applications. *MP (Materials Performance)* 36:42-50.

Kramer A, Weuffen W, Bauer M, Heinze W, Werner E, Lorenz G, Grimm U, Brachmann K, Schroeder H, Spiegelberger E, Fehrmann P, Wegner H. 1982. Subakute und subchronische percutane Verträglichkeitsprüfung im 28- und 90-Tage-Test von Desinfektionsmitteln bei epicutaner Applikation, dargestellt am Beispiel von Peroxyethansäure [Investigation into subacute and subchronic percutaneous tolerance of disinfectants in the 28 and 90 day test following epicutaneous application using the example of peroxyethanoic acid]. *Pharmazie* 37:41 [German; English translation].

Kramer A, Weuffen W, Merka V, Tichácek B. 1983. Toxizität von Peroxyethansäure (Peressigsäure). In Weuffen W, ed, *Handbuch der Antiseptik.*Vol II/2. Volk und Gesundheit, Berlin, Germany, pp 177-187.

Kramer A, Weuffen W, Adrian V. 1987. Toxische Risiken bei der Anwendung von Desinfektionsmitteln auf der Haut. *Hyg Med* 12:134-142 [German; English translation].

Kramer A, Koch S, Adrian V. 1990. Teratogene Potenz von Wofasteril® bei der ICR-Maus. *Hyg Med* 15:371-372.

Kramer A, Koch S, Adrian V, Stein J, Weuffen W. 1991. Mutagenitätsprüfung ausgewählter Desinfektionsmittel im Spermakopftest and der Maus. Investigation of mutagenicity of selected disinfectants in sperm head test in mice. *Hyg Med* 16:279-286 [German and English].

Kramer A, Zwinger B, Adrian V, Jülich WD. 1993. Tierexperimentelle Untersuchungen und Fragebogenerhebung zu neurotoxischen Risiken durch Peressigsäure. Animal studies and results of a survey on the neurotoxic hazards of peracetic acid. *Hyg Med* 18:377-385.

Kretzschmar Ch, Agerth R, Bauch R, Friedrich D. 1972. Peressigsäure, nur ein neues Desinfektionsmittel? [Peracetic acid, only a new disinfectant?]. *Monatshefte Vet Med* 27:324-332 [German; English translation].

Krüger S, Jancke S. 1976. Zur Problematik der Tierverträglichkeit von Peressigsäure, 2. Mitt., Qualitäts- und Rückstandsuntersuchungen an Fleish nach Applikation von peressigsäurehaltigen Lösungen auf die Haut von Schweinen. *Monatshefte Vet Med* 31:65-68.

Krüger S, Kruschinski D. 1982. Zur akuten Inhalationstoxizität von Peressigsäure-Aerosolen bei Mäusen. *Wiss Z Humboldt-Univ. Berlin*, Math-Nat 31:543-548.

Krüger S, Wilsdorf G, Bebenroth M. 1977. Toxikologische Aspekte der Zwischendesinfektion am Beispiel der Peressigsäure. *Monatshefte Vet Med* 32:785.

Krzywicka H. 1970. The effect of peracetic acid on the spores of bacteria. *Roczniki PZH* 21:595-599 [Polish; English translation]. <ECETOC*translation only>

Kuhn JO. 1996a. Proxitane AHC, acute oral toxicity study in rats. EPA guidelines 81-1. Unpublished report 2811-96, Stillmeadow, Sugar Land, TX, USA. Solvay Interox, Deer Park, TX, USA.

Kuhn JO. 1996b. Proxitane WW12, acute oral toxicity study in rats, EPA guideline 81-1. Unpublished report 2817-96, Stillmeadow, Sugar Land, TX, USA. Solvay interox, Deer Park, TX, USA.

Kuhn JO. 1996c. Proxitane AHC, acute dermal toxicity study in rabbits, EPA guideline 81-2. Unpublished report 2812-96, Stillmeadow, Sugar Land TX, USA. Solvay Interox, Deer Park TX, USA.

Kuhn JO. 1996d. Proxitane WW12, acute dermal toxicity study in rabbits, EPA guideline 81-2. Unpublished report 2818-96, Stillmeadow, Sugar Land, TX, USA. Solvay Interox, Deer Park, TX, USA.

Kuhn JO. 1996e. Proxitane AHC, dermal sensitization study in guinea pigs, EPA guideline 81-6. Unpublished report 2815-96, Stillmeadow, Sugar Land, TX, USA. Solvay Interox, Deer Park, TX, USA.

Kuhn JO. 1996f. Proxitane WW12, dermal sensitization study in guinea pigs, EPA guideline 81-6. Unpublished report 2821-96, Stillmeadow, Sugar Land, TX, USA. Solvay Interox, Deer Park, TX, USA.

Kuhn F. 2000. Decomposition of peracetic acid in synthetic seawater. Unpublished report 69/00. Degussa-Hüls, Hanau, Germany.

Kurzweg W, Steiger A, Profé D. 1988. Ökologische Aspekte des Desinfektionsmitteleinsatzes in der Tierproduktion [Ecological aspects of the use of disinfectants in livestock production]. *Arch Exp Vet Med* 42:518-527 [German; English translation].

Lamy MH, Lamy MH, Chauvire L, Gondelle F, Bazzon M, Giacalone J, Bailleul S, Rose M. 1997. Toxicité aiguë vis-à-vis des daphnies, substance d'essai: solution aqueuse d'acide péracétique. Unpublished report, study Ba567b, INERIS (Institut National de l'Environnement Industriel et des Risques), Verneuil-en-Halatte, France. Air Liquide, Chemoxal, Jouy en Josas, France.

Laub R, Möhring M, Beyer C, Welsch N. 1990. Einfluß von Desinfektionsmitteln auf epidermale Langerhanszellen, Möglichkeiten zur Verbesserung der Hautverträglichkeit. *Z gesamte Hyg* 36:559-560 [German; English translation].

LaZonby J. 1997. Dramatic improvements in microbiological control using the synergistic acivity between select organic biocides and a new non-halogenated oxidant. In TAPPI, ed, 1997 *Engineering and Papermakers conference proceedings*. TAPPI, Atlanta, GA, USA, pp 1107-1113 [Abstract]

Lazrus AL, Kok GL, Lind JA, Gitlin SN, Heikes BG, Shetter RE. 1986. Automated fluorometric method for hydrogen peroxide in air. *Anal Chem* 58:594-597.

Lefevre F, Audic JM, Ferrand F. 1992. Peracetic acid disinfection of secondary effluents discharged off coastal seawater. *Wat Sci Tech* 25:155-164.

Lenahan RJ. 1992. Peroxyacetic acid: the new generation sanitizer. *MBAA Technical Quarterly* 29:53-56.

Lensing HH, Oei HL. 1985. Investigations on the sporicidal and fungicidal activity of disinfectants. *Zbl Bakt Hyg I. Abt Orig B* 181:487-495.

Lever Industrial (Development and Application Centre). 1987. Reiniging en desinfectie, SU 338, CIP-desinfectie met perazijnzuur. *VMT (Voedingsmiddelentechnologie)* 10:22-26.

Li C, Ye Y, Deng J. 1988. Pharmacological actions of peracetic acid. *Yaoxue Tongbao* 23:345-348 [Chinese; English abstract].

Liberti L, Notarnicola M. 1999. Advanced treatment and disinfection for municipal wastewater reuse in agriculture. *Wat Sci Technol* 40:235-245.

Liberti L, Lopez A, Notarnicola M. 1998. Disinfection with peracetic acid for municipal wastewater reuse in agriculture. In *Proceedings of Innovations 2000*, joint conference of the European Water Pollution Control Association (EWPCA), the Water Environment Federation (WEF), 7-10 July 1998, Cambridge, UK. EWPCA Hennef, Germany and WEF, Alexandria, VA, USA.

Licata-Messana L. 1995a. Inhibition test (72 hours) in freshwater unicellular algae, semi-static system (1, 10 and 100 mg/l), test substance Dialox. Unpublished report F227, SEPC, Sarcey, France. SEPPIC, Paris, France.

Licata-Messana L. 1995b. Test to evaluate acute toxicity (48 hours) in *Daphnia*, semi-static system (1, 10 and 100 mg/l), test substance Dialox. Unpublished report F237, SEPC, Sarcey, France. SEPPIC, Paris, France.

Licata-Messana L. 1995c. Test to evaluate acute toxicity (96 hours) in freshwater fish (*Brachydanio rerio*), semi-static system (1, 10 and 100 mg/l), test substance Dialox. Unpublished report F236, SEPC, Sarcey, France. SEPPIC, Paris, France.

Lind JA, Kok JL. 1986. Henry's Law deteminations for aqueous solutions of hydrogen peroxide, methylhydroperoxide, and peroxyacetic acid. *Journal of Geophysical Research* 91:7889-7895.

Loera BS. 1996. Chemical characterization of test sample to determine amount of active ingredient. Unpublished report, study 2816-96, Stillmeadow, Sugar Land, TX, USA. Solvay Interox, Deer Park, TX, USA.

Ludewig R. 1965. Nachweis von $^{18}0$ in Exspirationsluft und Blut waehrend sublingualer Einwirkung $^{18}0$-markierten Wasserstoffperoxids. *Abhandl. Deutsch Akad Wiss Berlin, Kl Chem Geol Biol* 7:549-552.

McAllister WA, Cohle P. 1983. Acute toxicity of Oxonia Active to bluegill sunfish (*Lepomis macrochirus*). Unpublished report 30722, Analytical Bio-Chemistry Laboratories, Columbia, MO, USA. Bonewitz Chemical Services, Burlington, IO, USA.

McDonagh J. 1997. Atmospheric monitoring of peracetic acid on the existing caprolactone plant distillation houses A & B, assessment of results. Personal communication. Solvay Interox, Warrington.

Mackay D, Paterson S, Shiu WY. 1992. Generic models for evaluating the regional fate of chemicals. *Chemosphere* 24:695-717.

Malchesky PS. 1993. Peracetic acid and its application to medical intrument sterilization. *Artificial Organs* 17:147-152.

Matkovics B, Novák R. 1977. The effects of chronic peroxide intake on the peroxide metabolism enzyme activities of rat organs. *Experientia* 33:1574-1575.

Merck. 1994. Réflectomètre RQflex Merck. Laboratoires Merck-Clévenot, Nogent-sur Marne, France.

Merck. 1995. Peracetic acid. In: *Merckoquant, chemical microchips for analysis you take in your stride*. Merck, Darmstadt, Germany, p 27.

Merck. 1998. Merckoquant, peracetic acid test 1.10084.0001, RQ-flex en Reflectoquant, analytical test kit 115975. Merck, Darmstadt, Germany.

Merka V, Urban R. 1976. Study of inhalation toxicity of performic, peracetic and perpropionic acid in mice. *Journal of Hygiene, Epidemiology, Microbiology and Immunologynm* 20:54-60.

Meyer E. 1976. Abwasserdesinfektion in Tierkörperbeseitigungsanstalten mit Hifle der Peressigsäure. *Journal of Hygiene, Epidemiology, Microbiology and Immunology* 20:266-273.

Mielke H, Hopp H. 1982. Untersuchungen über den Einfluß der Peressigsäure auf Fußkrankheiten des Getreides. *Zeitschrift für Pflanzenkrankheiten und Pflanzenschutz* 89:282-290.

Mrazek H. 1996. Desinfektionsmittel. In Wildbrett G, ed, *Reinigung und Desinfektion in der Lebensmittelindustrie*, 1st ed. Behr, Hamburg, Germany, pp 65-67.

Mücke H. 1970. Die Eigenschaften der Peressigsäure [The properties of peracetic acid, excerpts relating to the bactericidal, sporicidal, viricidal and fungicidal effect of peracetic acid]. *Zeitschrift der Universität Rostock* 3:267-270 [German; English translation].

Mücke H. 1977. Untersuchungen über Einflüsse auf die Zersetzung von verdünnter Peressigsäure [Studies on effects on the decomposition of dilute peracetic acid]. *Pharmazie* 32:32:613-9 [German; English translation].

Mücke H, Sprössig M. 1967. Über die antimikrobielle Wirkung der Peressigsäure, 2. Mitteiliun: unetersuchingen zur Stabilität der Peressigsäure. *Pharmazie* 22:446-447 [Evaluates stability of PAA solutions; covered by Mücke, 1977].

Mücke H, Sprössig M. 1969. Die Eigenschaften der Peressigsäure. *Wissenschaftliche Zeitschrift der Humboldt-Universität zu Berlin*, Math-Nat Reihe B 18:1167-1170 [Reviews properties of PAA solutions; covered by Mücke, 1977].

Müller U, Schaffernicht H. 1998. Schädigung der Zähne und des Zahnfleisches durch Peressigsäuredämpfe [Damage of teeth and gingiva caused by fumes of peracetic acid]. *Zbl Arbeitsmed* 48:109-111 [German; English translation].

Müller P, Raabe G, Schumann D. 1978. Leukoplakia induced by repeated deposition of formalin in rabbit oral mucosa. *Exp Path* 16:36-42.

Müller P, Raabe G, Schumann D, Müller R, Schwabe L. 1980. Action of chronic peracetic acid (Wofasteril) administration on the rabbit oral mucosa. *Exp Path* 18:80-85.

Müller P, Raabe G, Hörold J, Juretzek U. 1988. Action of chronic peracetic acid (Wofasteril) administration on the rabbit oral mucosa, vaginal mucosa and skin. *Exp Pathol* 34:223-228.

Nims RW. 1996a. Corrositex continuous time monitor assay, test article VigorOx. Unpublished report I95-2035, Microbiological Associates, Rockville, ML, USA. FMC, Princeton, PA, USA.

Nims RW. 1996b. Bovine corneal opacity and permeability assay with histological evaluation, test article VigorOx. Unpublished report I95-2036, Microbiological Associates, Rockville, ML, USA. FMC, Princeton, PA, USA.

Nystrand R. 1985. Disinfectants in beet sugar extraction. *Zuckerind* 110:693-698 [Efficacy tests of PAA]

Palcic MN, Dunford HB. 1980. The reaction of human erythrocyte catalase with hydroperoxides to form compound I. *J Biol Chem* 255:6128-6132.

Paldy A, Berencsi G, Kramer A, Weuffen W, Spiegelberger E. 1984. Mutagene Potenz von Wofasteril, Wofasept, Formaldehyd, Chlorhexidin und Bronopol im Knochenmarkstest an der Maus. In Kramer A, Wigert H, Kemter B, eds, *Aspekte der Prophylaxe und Bekämpfung des infektiösen Hospitalismus*. In Horn H, Weuffen W, Wigert H, series eds, *Mikrobielle Umwelt und antimikrobielle Maßnahmen*. Barth, Leipzig, Germany, pp 349-352.

Pazdiora A, Kubiček V. 1967. Rapid pre-operative preparation of the hand with Persteril. *Vojenské Zdravotnické Listy* 36:116-117 [Polish; English translation].

Pehrsson R, Malone JWG, Simms RA. 1995. Verwendung von Peressigsäure für die Desinfektion in Rübenextraktionsanlagen. The use of peracetic acid formulations in the disinfection of beet sugar extraction plants. *Zuckerind* 120:S593-597 [German; English].

Petit-Poulsen V, Lamy MH, Chauvire L, Gondelle F, Bazzon M, Giacalone J, Bailleul S, Rose M. 1997. Essai d'inhibition de la croissance de l'algue d'eau douce *Pseudokirchneriella subcapitata*. Substance d'essai: solution aqueuse d'acide peracétique. Unpublished report BA567c, INERIS (Institut National de l'Environnement Industriel et des Risques), Verneuil-en-Halatte, France. Air Liquide, Chemoxal, Jouy en Josas, France.

Phillips JC. 1994a. Pharmacokinetic studies on peroxyacetic acid as a component of Proxitane 0510 in the rat. Unpublished report 1304/4/2/94, BIBRA Toxicology International, Carshalton, Surrey, UK. Johnson and Johnson Medical, Skipton, N. Yorkshire, UK.

Phillips JC. 1994b. The effects of Proxitane-0510 on the chromosomes of cultured human lymphocytes. Unpublisehd report 1295/1/3/94, BIBRA Toxicology International, Carshalton, Surrey, UK. Johnson and Johnson Medical, Skipton, N. Yorkshire, UK.

Pierre MP, Desmures MJ, Gamet JC. 2000. Procès verbal de la dégradation abiotique de l'acide peracétique, hydrolyse en fonction du pH, protocole paru au Journal Officiel des Communautés européennes L 383 A/228 du 29/12/92. Unpublished report 04/00. Bioxal-Air Liquide, Châlon sur Saône, France.

Pinkernell U, Karst U, Cammann K. 1994. Determination of peroxyacetic acid using high-performance liquid chromatography with external calibration. *Anal. Chem.* 66:2599-2602.

Pinkernell U, Effkemann S, Karst U. 1997a. Simultaneous HPLC determination of peroxyacetic acid and hydrogen peroxide. *Anal. Chem.* 69:3623-3627.

Pinkernell U, Luke JJ, Karst U. 1997b. Selective photometric determination of peroxycarboxylic acids in the presence of hydrogen peroxide. *Analyst* 122:567-571.

Pinkowski A. 1995. Verfahren zur Bestimmung von Persäuren. Patentschrift DE 42 23 228 C2. Prominent Dosiertechnik, Heidelberg, Germany.

Poffé R, De Burggrave A, Houtmeyers J, Verachtert H. 1978. Disinfection of effluents from municipal sewage treatment plant with peroxy acids. *Zbl Bakt Hyg I. Abt Orig B* 167:337-346 [Evaluation bactericidal efficacy].

Potokar M, Banduhn N, Bechstedt W, Gode, Stenzel W. 1996. Beitrag zur toxikologischen Bewertung der Peressigsäure als Desinfektionsmittel für die chemothermische Wäschedesinfektion. *Dermatosen* 44:23-28.

Price D, Worsfold PJ, Mantoura RFC. 1992. Hydrogen peroxide in the marine environment, cycling and methods of analysis. *Trends in Analytical Chemistry* 11:379-384.

Profaizer M, Massone A, Nurrizzo C, Banderta F. 1997. The Behaviour of Peracetic Acid as a Water Disinfectant. *Med Fac Landbouww Univ Gent* 62,1785-1792.

Prominent. 1997 Dulcometer D1C Perox , measurement and control of H_2O_2 or PAA (AL DM 002 4/97 GB). Prominent Dosiertechnik, Heidelberg, Germany.

Qi X, Baldwin RP. 1993. Liquid chromatography and electrochemical detection of organic peroxides by reduction at an iron phthalocyanine chemically modified electrode. *Electroanalysis* 5:547-554.

Reagan EL, Becci PJ. 1983. Acute oral LD_{50} in albino rabbits of Divosan Forte disinfectant. Unpublished report, study 7586A, Food and Drug Research Laboratories, Waverly, NY, USA. Diversey Wyandotte, Wyandotte, MI, USA [Summary].

Reagan EL, Davidson TJ, Becci PJ. 1983. Acute dermal LD_{50} assay in rats, test article Divosan Forte disinfectant. Unpublished report, study 7586A, Food and Drug Research Laboratories, Waverly, NY, USA. Diversey Wyandotte, Wyandotte, MI, USA [Summary].

Reinold A. 2000. Re-equilibrium of peracetic acid (PAA). Unpublished report 87/00. Degussa-Hüls, Hanau, Germany.

Richterich K, Gode P. 1986. Abbauprüfung toxischer Stoffe, Vermeidung störender toxischer Selbsthemmung durch gestufte Prüfmusterzugabe (AT-test). Unpublished report 1986/2418, TFB-Ökologie. Henkel, Düsseldorf, Germany.

Robinson EC. 1984. Titration of the capacity of the [human] skin to tolerate primary irritating effects of peracetic acid. Unpublished report PI-3196. Monsanto, St. Louis, MO, USA.

Rodgers ML. 1991. Effects of peracetic acid and hydrogen peroxide on the growth of some cyanobacteria and micro-algae. MSc thesis. University of Bath, Bath, UK.

Rowbottom KT. 1996a. Atmospheric monitoring during filling of IBC's with peracetic acid at Ellis and Everard on the 27th March 1996. Personal communication of 28 March. Solvay Interox, Widnes, Cheshire, UK.

Rowbottom KT. 1996b. Atmospheric monitoring at North Devon District Hospital in Barnstaple, 2nd December 1996. Personal communication of 4 December. Solvay Interox, Widnes, Cheshire, UK.

Rudd T, Hopkinson LM. 1989. Comparison of disinfection techniques for sewage and sewage effluents. *J IWEM* 3:612-618.

Ruohoniemi K, Heiko J, Laakso I, Martikainen S, Väryrynen V, Jäkärä J. 1998. Experience in the use to peracetic acid in ECF and TCF bleaching. In KCL (The Finnish Pulp and Paper Research Institute), ed, *Proceedings from international pulp bleaching conference*, June 1-5, 1998, Helsinki, Finland, Vol 1. KCL, Helsinki, Finland, pp 145-150 [ISBN 951-97513-3-5].

Saito T, Kurasaki M, Kaji M, Saito K. 1984. Deficiency of erythrocyte superoxide dismutase and catalase activities in patients with malignant lymphoma and acute myeloid leukemia. *Cancer Lett.* 24:141-146.

Sandström DA, Cederborg SE, Malmström E. 1999. Utvecklingen av ECF fortsätter medan TCF planar ut. *Svensk Papperstidning* 4:38-40.

Schaffernicht H, Müller U. 1998. Zur Exposition gegenüber Peressigsäure von Beschäftigten eines Universitätsklinikums [Regarding the exposure to peracetic acid in university hospital employees]. *Zbl Arbeitsmed* 48:106-108 [German; English translation].

Schliesser TH, Wiest JM. 1979. About the temperature dependence of the bactericidal effect of some chemical disinfectants. *Zbl Bakt Hyg I. Abt Orig B* 169:560-566.

Schonbaum GR, Chance B. 1976. Catalase-mediated redox reactions. In Doyer PB, ed, *The enzymes, oxydation-reduction, dehydrogenases (II), oxidases (II), hydrogen peroxide cleavage*, 3rd ed, Vol XIII Part C. Academic Press, New York, NY, USA, pp 389-395.

Schröder W. 1982. Peressigsäure (PES) als Desinfektionswirkstoff für die Lebensmittelindustrie. *Confructa* 26:139-147.

Senf HJ. 1984. Eine modifizierte Methode zur titrimetrischen Peressigsäurebestimmung. *Zbl Pharma* 123:77-79.

Setlow B, Setlow CA, Setlow P. 1997. Killing of bacterial spores by organic peroxides. *J Ind Micro and Biotech* 18:384-388.

Shapilov OD, Kostyukovskii YL, Gramenitskaya VG. 1972. Preparation and properties of an oxidizing system based on acetic acid and hydrogen peroxide. *Zh Prikladnoi Khimii* 45:2062-2066 [Russian; English translation] [Evaluates sporicidal effectiveness of PAA solutions].

Sheehan JF, Brynjolfsson G. 1960. Ulcerative colitis following hydrogen peroxide enema: Case report and experimental production with transient emphysema of colonic wall and gas embolism. *Lab Invest* 9:150-168.

Simms RA. 1995. Peroxygen atmospheric monitoring, Glan Clwyd Hospital Bodelwyddan. Personal communication of 25 September. Solvay Interox Warrington, Cheshire, UK.

Solvay. 1997a. Proxitane AHC 5%, material safety data sheet, date prepared 22.09.1997. Solvay Interox, Houston, TX, USA.

Solvay. 1997b. Proxitane 5%, material safety data sheet, date prepared 16.01.98. Solvay Interox, Houston, TX,USA.

Solvay. 1997c. Proxitane WW-12, material safety data sheet, effective date September 9, 1997. Solvay Interox, Houston, TX, USA.

Solvay. 1997d. Proxitane 15%, material safety data sheet, date prepared 22.09.1999. Solvay Interox, Houston, TX, USA.

Solvay. 1999. Overview of existing peraceticacid (PAA) monitoring methods. Personal communication of 12 January by Smit J, Olthof H. Solvay, Expertise Centre for Industrial Hygiene Monitoring. Solvay, Weesp, Netherlands.

Solvay. 2000. Solvay acceptable exposure limits (SAEL), January 2000. Solvay, Brussels, Belgium.

Spiegelberger A, Kramer A, Weuffen W, Burmeister C. 1984. Akute epicutane bzw. Subcutane LD_{50} der Desinfektionsmittel der Liste der DDR, geprüft an der ICR-Mause. In Kramer A, Wigert H, Kemter B, eds, *Aspekte der Prophylaxe und Bekämpfung des infektiösen Hospitalismus*. In Horn H, Weuffen W, Wigert H (series eds), *Mikrobielle Umwelt und antimikrobielle Maßnahmen*. Barth, Leipzig, Germany, pp 342-343.

Steiner N. 1995. Nontoxic bleaching, evaluation of peracetic acid as an environmentally safe alternative for hypochlorite. *J. AATCC* 27:29-32.

Steiner N. 2000. Composition of Degussa-Huels peracetic acid. Personal communication of 4 July. Degussa-Hüls, Frankfurt am Main, Germany.

Swern D. 1970. *Organic peroxides* Vol 1. Wiley Interscience, New York, NY, USA, pp 340-369, 461-474.

Tanner RL, Schorran DE. 1995. Measurements of gaseous peroxides near the Grand Canyon, implication for summertime visibility impairment from aqueous-phase secondary sulfate formation, *Atmospheric Environment* 29,1113-1122.

Tecnon Consulting. 1999. Analysen, Prognosen, Nachrichten, Fakten, Zwischenprodukte, Markt für Acetaldehyde Märkte. *Europa Chemie* 99:8.

Teral G, Hamon C. 1995. Détermination de faibles teneurs en acide peracétique [seawater]. Unpublished report AT.Chem 95.05. Air Liquide, Chemoxal, Les Loges, France.

Teral G, Gouges Y. 1997. La courbe de stabilité de l'APA en fonction de la température. Personal communication of 26 May. Chemoxal, Air Liquide Chimie, Paris, France.

Terrell Y. 1986a. Acute inhalation toxicity of Divosan Forte in rats. American Standards Biosciences Corporation project 86-635. Diversey Wyandotte, Wyandotte, MI, USA [Summary].

Terrell Y. 1986b. Avian dietary quail study (limit test) of Diversey Wyandotte Divosan Forte Sanitizer 15 % peroxyacetic acid in bobwhite quail. Unpublished report, project 86-636, American Standards Biosciences Corporation, Reading, PA, USA. Diversey Wyandotte, Wyandotte, MI [Summary].

Terrell Y. 1987a. Acute toxicity bioassay of Divosan Forte on *Daphnia magna*. Unpublished report, project 86-718, American Standards Biosciences Corporation, Reading, PA, USA. Diversey Wyandotte, Wyandotte, MI USA [Summary].

Terrell Y. 1987b. Acute toxicity bioassay of Divosan Forte on rainbow trout and bluegill sunfish. Unpublished report, project 86-719/720 American Standards Biosciences Corporation, Reading, PA, USA. Diversey Wyandotte, Wyandotte, MI, USA [Summary].

Thomasfolk H, Myhrman LE, Strandell B. 1996. Mill experience with hydrogen peroxide (PO) and peracetic acid (PAA). Presented at: International Non-Chlorine Bleaching Conference, Orlando, USA, paper 13-3. Rottneros AB, Vallviks Bruk, Sweden. Miller Freeman, San Francisco, CA, USA.

Thompson AM. 1994. Oxidants in the unpolluted marine atmosphere. In Nriagu JO, Simmons MS, eds, *Environmental oxidants*. John Wiley and Sons, New York, NY, USA, pp 31-61. [ISBN 0-471-57928-9].

Thus JLG. 1994. Calculation of the octanol/water partition coefficient of peracetic acid. Personal communication of 16 May. Solvay Duphar, Weesp, Netherlands.

Thus JLF, Allan E, Feenstra AFM. 1996. The development of an analytical method for the selective determination of peracetic acid and hydrogen peroxyde in air samples. Unpublished report 56834/77/95. Solvay Duphar, Weesp, Netherlands.

Thus JLG, Groeneveld AHC, Van der Laan-Straathof JMT. 1997. Possible biodegradation of peracetic acid (preliminary experiment). Unpublished report 56834/16/97. Solvay Duphar, Weesp, Netherlands.

Tichácek B. 1972. *Persteril*. Avenicum, Praha [Czech; title only translated].

Tinsley D, Sims I. 1987a. The acute toxicity of Oxymaster to plaice (*Pleuronectes platessa*) under semi-static conditions. Unpublished report CO1650-M/EV8687, WRc Environment, Medmenham, UK. Interox Chemicals, Widnes, Cheshire, UK.

Tinsley D, Sims I. 1987b. The acute toxicity of Oxymaster to brown shrimp (*Crangon crangon*) under semi-static conditions. Unpublished report CO1649-M/EV8687, WRc Environment, Medmenham, UK. Interox Chemicals, Widnes, Cheshire, UK.

TRGS (Technische Richtlinie Gefahrstoffe). 1997. Peroxyessigsäure, CAS-Nr. 79-21-0. In TRGS 906, Begründungen zur Bewertungen der TRGS 905, Verzeichnis krebserzeugender, erbgutverändernder oder fortpflanzungsgefährdernder Stoffe. In Kühn R, Birett K, series eds, *Merkblätter Gefährliche Arbeitsstoffe*, Vol 100, ed 7/97. Ecomed, Landsberg, Germany.

Umweltbundesamt. 2000. Peroxyessigsäure. In Umweltbundesamt, ed, Katalog wassergefährdender Stoffe, Stand 31. Oktober 2000. Einstufung aufgrund der Verwaltungsvorschrift wassergefährdender Stoffe (VwVwS). Umweltbundesamt, Berlin, Germany [http://www.umweltbundesamt.de/wgs/wgs-index.htm].

UN (United Nations). 1995. Tests and criteria for the classification of organic peroxides. In *Recommendations on the transport of dangerous goods, manual of tests and criteria*, 2nd ed, Part II, UN, New York, NY, USA, pp 185-304.

Urschel HC. 1967. Progress in cardiovascular surgery; Cardiovascular effects of hydrogen peroxide: current status. *Dis Chest* 51:180-192.

US-DOT (US Department of Transportation). 1995. Product designation, UN proper shipping name and number. Personal communication by Jones JE, October 25, 1995. FMC, Philadelphia, PA, USA.

US-EPA (Environmental Protection Agency). 1999a. TRI chemicals in waste, by chemical. 1997. In *Toxics release inventory (TRI)*. 1997 public data release, chapter 2. EPA, Washington, DC, USA, pp 79 [http://www.epa.gov/opptintr/tri/tri97/pdf/chap2.pdf].

US-EPA (Environmental Protection Agency). 1999b. Technology transfer network, Chief clearing house for inventories and emission factors. EPA, Washington, DC, USA [http://www.epa.gov/ttn/chief].

Van Beek L. 1980. Primary dermal corrosion test with Divosan Forte in albino rabbits. Personal communication, Centraal Instituut voor Voedingsonderzoek TNO, Zeist, Netherlands. Diversey, Woerden, Netherlands.

Veger J, Svihovcova P, Benesova O, Nejedly K. 1977. Toxicité subchronique du Persteril par voie buccale. *Cesk Hyg* 22:59-63 [Czech; English and French translations].

Verschueren. 1983. *Handbook of environmental data on organic chemicals*, 2nd ed. Van Nostrand Reinhold, New York, NY, USA, pp 143-144.

Veschetti E, Cutilli D, Bonadonna L, Della Libera S, Ottaviani M. 1998. Preliminary results on the possibility of using peracetic acid as disinfectant of wastewater. Presented at: AWT98 Advanced wastewater treatment, recycling and reuse, Milano 14-16 September (No further publication details] Evaluation of microbial efficacy].

Wallat S. 1984a. P3-oxonia aktiv, Prüfung auf Mutagenität im Ames-Test. Wallat S, Institut für Toxikologie. Unpublished report 840154. Henkel, Düsseldorf, Germany.

Wallat S. 1984b. P3-oxonia aktiv, Prüfung auf Mutagenität *in vivo*., Institut für Toxikologie. Unpublished report 840242. Henkel, Düsseldorf, Germany.

Wayne RP. 1991. Oxidation and transformation. In Wayne RP, ed, *Chemistry of atmospheres*, 2nd ed. Clarendon, Oxford, UK, pp214-225.

Werner. 1988. Disinfectants in dialysis: dangers, drawbacks and disinformation. *Nephron* 49:1-8.

Whitman FT. 1991. Acute inhalation toxicity study of peracetic acid 0.15 use dilution (MRD-91-004) in the rat, guideline 81-3. Unpublished report I91-1199, Exxon Biomedical Sciencies, East Millstone, NJ, USA. FMC Princeton, NJ, USA.

Wurster P. 1992. Die Peressigsäurebleiche, eine Alternative zu Bleichverfahren mit halogenhaltigen Oxidationsmitteln. *Textil Praxis* 47:960-965.

Wutzler P, Mücke H, Battke H, Goebel P, Schreiber D. 1987. Tierexperimentelle Untersuchungen über den Einfluß der Peressigsäure auf das Harnblasenurothel. *Z Urol Nephrol* 80:105-110.

Wyrobek, AJ, Gordon LA, Burkhaart JG *et al*. 1983. An evaluation of the mouse sperm morphology test and other sperm tests in nonhuman mammals. A report of the U.S. Environmental Protection Agency Gene-Tox Program. *Mutation Research* 115:1-72.

Yamaguchi T, Yamashita Y. 1980. Mutagenicity of hydroperoxides of fatty acids and some hydrocarbons. *Agric Biol Chem* 44:1675-1678.

Yuan Z, Ni Y, Van Heiningen ARP. 1977a. Kinetics of peracetic acid decomposition, part II: pH effect and alkaline hydrolysis. *Can J Chem Eng* 75:42-47.

Yuan Z, Ni Y, Van Heiningen ARP. 1977b. Kinetics of peracetic acid decomposition, part I: Spontaneous decomposition at typical pulp bleaching conditions. *Can J Chem Eng* 75:37-41.

Zeiger E, Anderson B, Haworth S, Lawlor T, Mortelmans K. 1988. *Salmonella* mutagenicity tests IV, results from the testing of 300 chemicals. *Env Mol Mut* 11:1-158.

11.3 References Not Quoted

The following references were consulted by the Task Force, but not quoted for the specific reasons indicated. Several references are beyond the scope of this report because they are concerned with the biocidal efficacy of PAA used as an antiseptic or disinfectant.

Agnet Y, Dorange JL, Dupuy P. 1976. Mutagenicity of peracetic acid on *Salmonella typhimurium*. *Mutation Research* 38:119 [CoR 4a; abstract covered by Agnet *et al*, 1977].

Allen DW, Newman, LM, Okazaki, IJ. 1991. Inhibition of arachidonic acid incorporation into erythrocyte phospholipids by peracetic and other peroxides. Role of arachidonyl-CoA, 1 palimotyl-*sn*-glycero-3-phosphocholine acyl transferase. *Biochimica et Biophysica Acta* 1081:267-273 [Study on enzyme, not on PAA].

Anonymous. 1982. Description of a method for a European suspension test for the evaluation of the efficacy of disinfectants in food hygiene. Unpublished report, restricted CD-P-SP (82 32), appendix B. [Efficacy].

Arturo-Schaan M, Suavager F, Mamez C, Gougeon A, Cornier M. 1996. Use of peracetic acid as a disinfectant in a water-treatment plant: effect of plasmid content of *Escherichia coli* strains. *Current Microbiology* 32:43-47 [Efficacy].

Baldry MGC. 1994. Peracetic acid residuals. Technical memo M-12-94, Solvay Interox, Widnes, Cheshire, UK [Covered by Chalkley, 1991a,b,c].

Booth RA, Lester JN. 1995. The potential formation of halogenated by-products during peracetic acid treatment of final sewage effluent. *Wat. Res.* 29:1793-1801 [Disinfection].

Brázdová K, Dluhoπ M, Veleck˝ R, Sekaninová G, Táborsk˝ I, Zajícova V. 1970. Tissue tolerance and peracetic acid toxicity in relation to plastics. *Scripta medica* 43:323-327 [Effect of PAA residues on tissue cultures; CoR 3a].

Brown GE, Schubert TS. 1987. Use of *Xanthomonas campestris* pv. *vesicatoria* to evaluate surface disinfectants for canker quarantine treatment of citrus fruit. *Plant Disease* 71:319-323 [Efficacy].

Busch A. 1973. Untersuchungen zur Toxizität PES-haltiger Desinfektionsmittel beim Auftragen auf die Haut des Schweines. Diss. Vet.-Med., Humboldt University, Berlin, Germany [Thesis covered by Busch and Werner, 1974].

Cechova L. 1969. Die Peressigsäure als Desinfektionsmittel in der Stomatologie. Wirksamkeit und Entwicklungsstand. *Wissenschaftliche Zeitschrift der Humboldt-Universität zu Berlin, Math-Nat Reihe B* 18:1179-1181 [Efficacy in disinfection of mouth protheses].

Chalkley NJ. 1992a. Degradation of peracetic acid in contact with various samples of water. Personal communication of 1 April 1992. Solvay Interox, Widnes, Cheshire, UK [Repeated experiments of Chalkley 1992; no additional information].

Chalkley NJ. 1992b. Degradation of peracetic acid in contact with various samples of water, tomato plant washing project. Personal communication of 22 April 1992. Solvay Interox, Widnes, Cheshire, UK [No aditional information].

Chanratchakool P. 1994a. Minimum bactericidal concentration of Proxitane 1507 against various shrimp pathogen. Unpublished draft report, Aquatic Animal Health Research Institute, Bangkok, Thailand. Peroxythai, Bangkok, Thailand [Efficacy, draft report].

Chanratchakool P. 1994b. Toxicity of Proxitane on shrimp, microflora and plankton. Unpublished draft report, Aquatic Animal Health Research Institute, Bangkok, Thailand. Peroxythai, Bangkok, Thailand [CoR 4e, draft report].

Christiansen B, Eggers H-J, Exner M, Gundermann K-O, Heeg P, Hingst V, Höffler U, Krämer J, Mar H, Rüden H, Schliesser Th, Schubert R, Sonntag H-G, Spicher G, Steinmann J, Thofern E, Thraenhart O, Werner H-P. 1991. Richtlinie für die Prüfung und Bewertung von Hautdesinfektionsmitteln. *Zbl Hyg* 192:99-103 [Efficacy in (hand) skin disinfection].

CPR (Commissie Preventie van Rampen door gevaarlijke stoffen [Dutch Committee for the Prevention of Disasters caused by dangerous substances]). 1997. Storage of organic peroxides. Report CPR 3E, 2nd ed. Sdu, Den Haag, Netherlands [National guidance on safe handling following UN and EU directives].

Davenport L. 1990. Oxymaster treated samples received 4th October 1989, conclusion of the report on the mutagenic potential detectable in sewage effluents received from Interox. Personal communication 3 April with continuation of report 5 December 1989, Severn-Trent Laboratories, Finham, Coventry, UK. Solvay Interox, Widnes, Cheshire, UK [Efficacy; non-standard test].

Davidson KA, McClanahan MA, Rodgers G, Morawetz J. 1998. Acute exposure guideline levels (AEGLs) for peracetic acid, June 5. 1998. Unpublished draft report by Lockheed Martin Energy Research/US Department of Energy to Tobin, PS, NAC/AEGL. US Environmental Protection Agency, Washington, DC, USA [Review].

Degussa. 1977. Orientierende Prüfung der akuten Toxizität von 40%iger Peressigsäure bei Sprague-Dawley Ratten. Unpublished report by Leuschner F, Laboratorium für Pharmakologie und Toxikologie, Hamburg, Germany. Degussa, Frankfurt am Main, Germany.

Degussa. 1992a. Desodorierung von Klärschlamm mit Peressigsäure 15%. Report IC-AO-AT/BC 106/92 by Del Grosso B and Schmidt K, Asta Pharma, Bielefeld, Germany. Degussa, Hanau, Germany [Efficacy to remove smell from cat litter made of sewage sludge].

Degussa. 1992b. Desodorierung von Klärschlamm mit Peressigsäure 15%. Report IC-AO-AT/BC 129/92 by Del Grosso B, Asta Pharma, Bielefeld, Germany. Degussa, Hanau, Germany [Efficacy to remove smell from cat litter made of sewage sludge].

Degussa. 1993. Stabilität von Peressigsäure-Konzentrationen im ppm-Bereich in Leitungswasser und dest. Wasser. Unpublished report BC108/93 by Del Grosso B, Asta Pharma, Bielefeld, Germany. Degussa, Hanau, Germany [Stability test in drinking/distilled water, no additional information].

DFG (Deutsche Forschungsgemeinschaft, Senatskommission zur Prüfung gesundheitsschädlicher Arbeitsstoffe). 1988. Peroxyessigsäure. In: Henschler D (ed), Gesundheitsschädliche Arbeitsstoffe, toxikologish-arbeitsmedizinische Begründing von MAK-Werten, 14th ed. VCH, Weinheim, Germany [Review].

DOE (UK Department of the Environment). 1988. Review of operational and experimental techniques for the removal of bacteria, viruses and pathogens from sewage effluents. Unpublished report PECD 7/7260. Consultants in Environmental Sciences, DOE, London, UK [Review, disinfection].

Euler J, Werner HP. 1978. Untersuchungen über den Einfluß von Peressigsäure auf Ehrlich-Lettre-Mäuse-Aszitestumorzellen. Krebsgeschehen 10:30-33 [Non-standard test and cell line, interpretation unclear].

Flemming HC. 1984. Die Peressigsäure als Desinfektionsmittel, ein Überblick. *Zbl Bakt Hyg, I. Abt Orig B* 179:97-111 [Review, disinfection].

Fordham JP. 1978. Safe handling of peracetic acid in a closed environment. *Laboratory Animals* 12:247-248 [Safe handling in laboratory, no additional information].

Geiler W, Otto J, Mücke H. 1989. Einhaltung der arbeitshygienischen Grenzwerte in der Raumluft bei Flächendesinfektion mit Peressigsäure durch Alkalisierung der Lösung. *Z Klin Med* 44:349-352 [Disinfection, OEL/odour threshold compliance].

Gode P, Winkler J. 1982. Biologische Abbaubarkeit und Toxizität von 19 P3-Desinfektionsmitterohstoffen. Unpublished report 1982/2088, ZR-FE-ALAB-Ökologie. Henkel, Düsseldorf, Germany [CoR 3a; test substance and method not specified].

Gould DJ. 1989. Microbiological and biological monitoring at Southend-on-Sea, Essex 1989. Unpublished report 50, interim draft, Marine Environmental Consultants, Baldock, Herts, UK [Efficacy in sewage disinfection].

Greenspan FP, MacKellar DG. 1951. The application of peracetic acid germicidal washes to mold control of tomatoes. *Food Technol* 5:95-97 [Efficacy].

Grussel T, Busch W. 1997. Experimental studies of the effect of peracetic acid on the endometrium of cattle. *Tierärztl. Prax.* 25:28-34 [CoR 3a; no additional information].

Heinze W, Nattermann H. 1984. Zur Wirkung von Wofasteril-Aerosolen auf tierpathogene Keime. *Monatshefte Vet Med* 39:776-779 [Efficacy].

Heneghan JB, Gates DF. 1966. Effects of peracetic acid used in gnotobiotics on experimental animals. *Laboratory Animal Care* 16:96-104 [Disinfection].

Henkel. 1998. Peressigsäure-Desinfektion/COP [Collection of exposure data during use, different applications 1994-1998]. Personal communication dated 20 January. Henkel, Düsseldorf, Germany [MAK compliance measurements for H_2O_2 and HOAc during application of undefined PAA-containing product].

Hercik J, Dachovsky V. 1975. [Use of peracetic acid for disinfection in sugar refining]. *Listy Cukrovarnicke* 91:126-132. [CoR 4d, Czech, English summary; no additional information].

James AP, Shehad NS. 1995. Peroxygen systems for consumer applications. Presented at: 86th AOCS annual meeting, American Oil Chemists' Society, Champaign, Illinois, USA. Solvay Interox, Widnes, Cheshire, UK and Deer Park, TX, USA [Review].

Kästner W. 1981. Desinfektion bei der Lebensmittelherstellung, Wirkstoffe und deren toxikologische Beurteilung. *Archiv für Lebensmittelhygiene* 32:117-125 [Review].

Kramer A, Halle W, Weuffen W, Adrian V, Herrmann M, Bremer J, Fleck H and Steiger E. 1987b. Antimikrobielle Wirkung, Zytotoxizität und Phytotoxizität als Basisinformationen zur Verträglichkeit von Desinfektionsmitteln bzw. Antiseptika [Antimicrobial effect, cytotoxicity and phytotoxicity: aspects providing basic information on the compatibility of disinfectants and antiseptics]. *Z gesamte Hyg* 33:610-615 [German; English translation] [Review, efficacy].

Kühn H. 1978. Versuche zur antimikrobiellen Behandlung von dermatologischen Zubereitungen mittels Peressigsäure, 2. *Mitteilung. Pharmazie* 33:292-293 [Efficacy].

Lai DY, Woo Y, Argus MF, Arcos JC. 1996. Carcinogenic potential of organic peroxides, prediction based on structure-activity relationships (SAR), and mechanism-based short-term tests. *Environ Carcino Ecotox Revs C* 14:63-80 [Review].

Lenon G, Hivert G, Escabasse JY. 1997. Effect, identification and control of catalase in deinking plants, literature survey, 2nd part, biological aspects. Unpublished report, CTP project FR 96-18. Centre Technique du Papier, Grenoble, France [Review of enzymatic breakdown of hydrogen peroxide; PAA briefly mentioned].

Lichtenberg F, Gutknecht J. 1987. Peressigsäure, ein universelles Desinfektionsmittel. Anwendungstechnische Vor- und Nachteile. *Brauwelt* 14:586-590 [Disinfection in brewery].

Ljarskij. 1983. Caractéristique toxicologique et hygiénique des agents désinfectants à base de peroxyde d'hydrogène et de ses dérivés. *Gig. y Sanit.* 48: 28-31 [CoR 4e; Russian; French translation; report insufficient].

Lowings PH. 1956. The fungal contamination of Kentish strawberry fruits in 1955. *Applied Microbology* 4:84-88 [Efficacy].

Mayr E. 1973. Wofasteril (= Peressigsäure). *Zbl Pharm* 112:275-280 [Review].

Merka V, Sokol D. 1972. Zum Wirkungsmechanismus von Peressigsäure, Perameisensäure und Perpropionsäure. *Z Ges Hyg* 2:638-641 [Efficacy].

Monev V. 1974. L'acide peracétique comme désinfectant. *Suvrem Med* 25:36-39 [Bulgarian; French translation] [Review, disinfection].

Morelli G. 1991. Disinfezione acque reflue e loro riutilizzo a scopo irriguo. *IA - Ingegnena Ambientale* 20:183-192 [Disinfection of wastewater for agricultural irrigation].

Morris R. 1993. Reduction of microbial levels in sewage effluents using chlorine and peracetic acid disinfectants. *Wat Sci Tech* 27:387-393 [Efficacy].

Niebling, G, Aigner R, Wabner D, Menzel R. 1996. Data reduction for curve analysis. *Sensors and Actuators* B 34:481-486 [Uses for example voltammetry analysis curves of PAA+H_2O_2 mixtures].

Rothe A, Fiss I, Wagner E. 1996. Zum Kontaktekzem durch formaldehydfreie Desinfektionsmittel. Contact dermatitis caused by formaldehyde-free disinfectants. *Hyg Med* 18:167-175 [German and English; no allergies related to PAA, covered by IVDK, 1999].

Sax I, Lewis RJ. 1989. Dangerous properties of industrial materials, 7th ed. Van Nostrand Reinhold, New York, NY, USA, pp 2693-2694 [Review, handbook].

Sosnovsky G, Zaret EH. 1970. Base-catalyzed autoxidation. In Swern D, ed, Organic peroxides Vol 1. Wiley Interscience, New York, NY, USA, pp 517-560 [Review].

Sprössig M, Mücke H. 1969. Die Virusdesinfektion durch Peressigsäure in Gegenwart von Alkoholen. *Wissenschaftliche Zeitschrift der Humboldt-Universität zu Berlin, Math-Nat Reihe B* 18:1171-1173 [Efficacy].

Sprössig M, Mücke H. 1982. Peroxide als Desinfektionsmittel - Wirksamkeit und Entwicklungsstand. *Wissenschaftliche Zeitschrift der Humboldt-Universität zu Berlin, Math-Nat Reihe B* 31:539-541 [Review].

Tichácek B *et al*, ed. 1966. *Kyselina peroctová a možnosti jejího vyu ití v dezinfekci, Zdravotnické aktuality* 163 [Peressigsäure und die Möglichkeiten ihrer Verwendung in der Desinfektion, Monographie 163]. Stát. Zdrav. Nakl., Praha CSSR [Staatsverlag für das Gesundheitswesen der CSSR, Prague] [CoR 4d; Czech; review, title only translated].

Tye RJ. 1989a. Investigation of the mutagenic potential detectable in sewage effluents treated with Oxymaster, interim report. Personal communication of 14 March, Severn Trent Laboratories, Finham, Coventry, UK. Solvay Interox, Widnes, Cheshire, UK [Efficacy; non-standard test].

Tye RJ. 1989b. Preliminary report on the mutagenic potential detectable in sewage effluents received from Interox. Personal communication of 5 December, Severn Trent Laboratories, Finham, Coventry, UK. Solvay Interox, Widnes, Cheshire, UK [Efficacy; non-standard test].

Wallhäußer K-H. 1995. Praxis der Sterilisation, Desinfektion, Konservierung, 5th ed. Georg-Thieme, Stuttgart, Germany, pp 397 [Efficacy; so-called 5-5-5-test for evaluation of disinfectants].

Wiedman T. 1999. P3-oxonia aktiv and P3-oxonia aktiv 150, vapour pressure and evaporation enthalpy. Unpublished report 98/154, VTA-Safety Technology. Henkel, Düsseldorf, Germany. [Covered by Caropreso, 2000].

APPENDIX A. SPECIAL ABBREVIATIONS

ABTS	2,2´-Azino-*bis*-(3-ethyl-benzo-thiazoline)-6-sulphonate
ADS	2-((-3(2-(4-amino-2-(methhylsulphanyl)phenyl)-1-diazenyl)phenyl) sulphonyl)-1-ethanol
ALAT	Alanine aminotransferase
ASAT	Asparagine aminotransferase
DMBA	7,12-Dimethylbenz[*a*]anthracene
DNA	Dexoyribonucleic acid
DOC	Dissolved organic carbon
DOT	Department of Transport
DPD	N,N'-diethyl-*p*-phenylendiamine
EC_{50}	Median concentration expected to have an effect in 50% of the test organisms
EINECS	European inventory of existing commercial chemical substances
FTIR	Fourier transform infrared (spectroscopy)
GLP	(Principles of) good laboratory practice
GSH	Glutathione
H_2O_2	Hydrogen peroxide
HOAc	Acetic acid
HPLC	High performance liquid chromatography
i.p.	Intraperitoneal
IBC	Intermediate bulk container
IUPAC	International Union of Pure and Applied Chemistry
LC_{50}	Median concentration expected to cause the death of 50% of the test organisms
LD_{50}	Median dose expected to cause the death of 50% of the test animals
LDH	Lactate dehydrogenase
MTS	Methyl *p*-tolyl sulphide
MTSO	Methyl *p*-tolyl sulphoxide
NOAEL	No-observed adverse effect level
NOEC	No-observed effect concentration
OEL	Occupational exposure limit value
PAA	Peracetic acid
ppbv	Parts per billion by volume
PPE	Personal protective equipment
RD_{50}	Concentration inducing a 50% reduction of respiratory rate
RQflex	Reflectometer quality flexible (test strips)
SADT	Self-accelerating decomposition temperature
TAED	*Tetra*-acetyl ethylenediamine
TCF	Total chlorine free
TWA	Time-weighted average
UDS	Unscheduled DNA synthesis
U	Activity unit (of enzymes)

APPENDIX B. CRITERIA FOR RELIABILITY CATEGORIES

Adapted from Klimisch et al (1997)

Code of reliability (CoR)	Category of reliability
1	**Reliable without restriction**
1a	GLP guideline study (OECD, EC, EPA, FDA, etc.)
1b	Comparable to guideline study
1c	Test procedure in accordance with national standard methods (AFNOR, DIN, etc...)
1d	Test procedure in accordance with generally accepted scientific standards and described in sufficient detail
2	**Reliable with restrictions**
2a	Guideline study without detailed documentation
2b	Guideline study with acceptable restrictions
2c	Comparable to guideline study with acceptable restrictions
2d	Test procedure in accordance with national standard methods with acceptable restrictions
2e	Study well documented, meets generally accepted scientific principles, acceptable for assessment
2f	Accepted calculation method
2g	Data from handbook or collection of data
3	**Not reliable**
3a	Documentation insufficient for assessment
3b	Significant methodological deficiencies
3c	Unsuitable test system
4	**Not assignable**
4a	Abstract
4b	Secondary literature
4c	Original reference not yet available
4d	Original reference not translated (e.g. Russian)
4e	Documentation insufficient for assessment

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