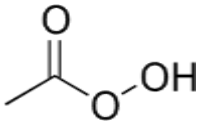
Cal/OSHA Draft Substance Summary for the December 12, 2017 HEAC Meeting

Substance name: Peracetic Acid

CAS: 79-21-0 MW: 76.05

Synonyms: Peroxyacetic Acid, ethaneperoxoic acid, acetic peroxide, acetyl hydroperoxide, proxitane, PAA

Molecular formula: $C_2H_4O_3$ 76.05 g/mol Structural formula: 

ppm to mg/M^3 conversion factors at 25 ºC and 760 mm/Hg: 0.32 ppm = 1 mg/m3

Selected GHS information:
GHS Classification (29 CFR 1910.1200): organic peroxide
GHS Label Elements:

Signal Word: Danger
Hazard Statements:
H314 Causes severe skin burns and eye damage;
H318 Causes serious eye damage
H226 Flammable liquid and vapor
H330 Fatal if inhaled
H400 Very toxic to aquatic life

Precautionary Statements: Keep away from heat/sparks/open flames/hot surfaces. No smoking
Use in a well-ventilated place

Physical characteristics at room temp: Clear liquid with sharp, pungent, vinegar-like odor

Flammability and other hazards: decomposes under fire conditions to release oxygen that intensifies the fire.

Chemical Characterization

Peracetic acid is not sold in pure form but instead is commercially available as mixtures of peracetic acid, hydrogen peroxide and acetic acid. Availability is in various ranges but as high as 30-40 % peracetic acid, approx. 45% acetic acid and approx. 10% hydrogen peroxide. Aqueous concentrated solutions of PAA are unstable, subject to explosive decomposition. For most workplace uses these concentrated solutions are heavily diluted. For example, one mixture utilized for hospital disinfection that was studied in a NIOSH HHE contained 15% peracetic acid, but was diluted for use to 200 parts per million—a reduction in concentration of 750%. In its concentrated form PAA mixtures are flammable and may be explosive if heated above the flash point [60-64ºC as a mixture]. Concentrated mixtures are hazardous to the aquatic environment. PAA breaks down rapidly in air; it has a half-life of 22 minutes. Nonetheless, diluted solutions of the mixtures stored in

containers have shelf lives of about two weeks. The PAA fraction of mixtures has a high vapor pressure. PAA and hydrogen peroxide appear to function synergistically as fast acting surface microbiocides and sporocides.

Uses/applications: Sterilant for endoscopes and kidney dialysis machines, and surface disinfectant in health care settings. Also used as a microbiocide in the dairy, wine and brewery industries for cleaning of tanks, pumps, lines and filters, as, in its diluted concentrations, PAA mixtures are non-corrosive to stainless steel. PAA mixtures are used widely in agricultural food processing settings, including poultry processing. The Department of Agriculture permits the use of up to 2000 ppm of PAA on food products. Use of PAA has been increasing in most of these applications.

Occupations with Potential Exposure to peracetic acid

Occupational exposures to PAA include hospital technicians, janitorial and housekeeping staff. Many industrial agricultural occupations may be exposed during processing of fruits, vegetables, poultry, meat and milk product lines.

Routes of exposure: The primary route of exposure is respiratory. The respiratory route of exposure to PAA occurs in particle and vapor phases. Aerosol exposures are more likely during spraying or fogging, while vapor phase exposures predominate where PAA has merely been wiped on surfaces. Skin exposure may occur during spraying or during dilution of concentrated solutions. However, significant toxic PAA exposure through the skin is unlikely due to high vapor pressure. Corrosive damage to the skin is probable from contact with concentrated solutions; corrosive damage to outer skin layers would lead to toxic skin absorption of PAA if evaporation were prevented—for example if immersion in the liquid continued, or if concentrated solution was trapped beneath impervious gloves. Ingestion would also result in PAA toxicity.

OEL recommendations

Title 8 PEL:	None	
OSHA PEL:	None	
ACGIH TLV (2014):	STEL[15 minutes]	0.4 ppm
NIOSH REL(draft 2015):		0.55 ppm (IDLH)
Acute Exposure Guidelines (Nat. Acad. Press, 2010):		AEGL 1 - 0.17ppm AEGL 2 - 0.51ppm

Other recommendations:

None.

Health Effect Summary

Peracetic acid (PAA) is produced by the catalytic action of sulfuric acid on acetic acid and hydrogen peroxide and exits in solution in equilibrium with the reactants. Technical or commercial PAA products contain different concentrations of PA acid, acetic acid, and hydrogen peroxide, but the concentration of PAA does not exceed 40%. PAA is unstable; it decomposes to its original constituents under conditions that vary with concentration, temperature, and pH. PAA is used as a disinfectant against bacteria, fungi, and viruses in the food and medical industry, as a bleaching agent, as a polymerization catalyst or co-catalyst, in the epoxidation of fatty acid esters, as an epoxy resin precursor, and in the synthesis of other chemicals.

PAA is corrosive/irritating to the eyes, mucous membranes of the respiratory tract and skin. It causes lacrimation, extreme discomfort and irritation to the upper respiratory tract in humans after exposure to concentrations as low as 15.6 mg PAA /m^3 (5 ppm) for only 3 min. Eye irritation, clinical signs, and pathologic lesions indicative of respiratory tract irritation have been observed in laboratory animals exposed by inhalation to various concentrations of PAA aerosols. Exposure to lethal concentrations of PAA causes hemorrhage, edema, and consolidation of the lungs, whereas nonlethal concentrations cause transient weight loss or reduced weight gain in addition to slight to moderate signs of respiratory tract irritation.

Sensory irritation is the primary toxicological endpoint used to set exposure limits for PAA. A limited number of animal studies are available to evaluate this endpoint. In addition, most of these studies were submitted to regulatory agencies and their full text is not readily available for review. Summaries of these studies are reported elsewhere, the most referenced being a series of studies by Janssen (1989b, 1989c, 1990; Table 1). These studies were designed to evaluate the lethality and acute effects of PAA over a range of concentration and time. All studies were conducted in the same exposure chamber in which test atmospheres were generated from the 3 chemical mixture – as such, animals were simultaneously exposed to acetic acid and hydrogen peroxide. Test concentrations were analyzed as total peroxygen concentration corrected for the amount of hydrogen peroxide. Animals were exposed nose-only. Macroscopic examinations in the lethal studies showed effects indicative of respiratory irritation (blood around the nose, red nasal and tracheal mucosa, bloody fluid in the trachea, dark red lungs, and red or dark spots on the lungs) particularly in animals that died during the study. The animals surviving to study termination showed only red or dark spots on the lungs. Mortality occurred only at concentrations of 320 mg/m and above. The LC_{50} for a 1 hour exposure was 476 mg/m^3 and for a 4 hour exposure 204 mg/m^3.

For the non-lethal experiments, respiratory rates were determined during exposures, clinical signs of toxicity were recorded for 14 days after exposure, and body weight was measured on post-exposure days 2, 7, and 14. Postmortem studies included gross examination, measurement of lung weight, and histopathological examination of the lungs. Clinical signs observed in the non-lethal studies were indicative of effects on coordination and muscle tone, extreme discomfort, and respiratory irritation. There were no treatment-related macroscopic or microscopic findings in the lungs, and lung weights were similar in the treated and control groups. Slight to moderate to severe squamous metaplasia of the nasal turbinates and/or lateral walls and epithelial atrophy of the dorsal meatus were observed in all treated groups. The study author noted that a twofold increase in exposure time produced a smaller effect on clinical signs than a twofold increase in exposure concentration indicating that effects are due more to exposure concentration than duration.

Table 1: Summary of PAA studies (Janssen, 1989b, 1989c, 1990)

		Lethal effects			
Time	Conc (mg/m^3)	Mortality	Pathology		LC_{50}
Control - 90	0		URT	LRT	
15	310	1/10	1/10	3/10	
30	130	0/5	0/5	0/5	
30	310	3/10	2/10	6/10	
60	150	0/5	0/5	1/5	476
60	390	2/5	2/5	4/5	
60	1450	5/5	3/5	2/5	
240	87	0/10	-	-	
	163	0/10	-	-	204 (186 – 233)

	185	4/10	-	-	
	267	9/10	-	-	
		Non-lethal effects			
Pathology	Conc (mg/m^3)	Gross	Microscopic	Respiratory Reduction (%)	RC_{50}
Time					
Control	0	3/5	0/5		
15	499	0/5	5/5		
30	304	1/5	4/5		
30	578	1/5	5/5		
60	329	2/5	5/5		
60	589	2/5	4/5		
90	172	0/5	5/5		
90	355	1/5	5/5		
25	8.4			46.9.	
25	12.2			32.6	
25	13.9			31.9	22.7*
25	17.4			44.2	
25	36.3			67.1	
25	221			76.3/16.0*	
25	315			78.4/29.6	>299
25	461			76.3/49.2	

*Mean RD50 for all groups

*% depression during exposure / % of depression after exposure

Two studies have examined the effect of PAA alone without the mixture effects. Merka and Urban (1978) exposed groups of 10 mice in a dynamic chamber to laboratory PAA aerosols at concentrations of 70 to 140 mg/m^3 for 60 min, three times/week for 4 weeks and observed for an additional 2 weeks. The animals exposed to PA showed signs of respiratory distress and retarded weight gain compared with controls not exposed to the test chemical. Isolated small foci of inflammation were seen in the lungs of mice killed at the end of the 14-day observation period. The LOAEC for this study was reported to be 70 mg/m^3 (ECETOC).

Gagnaire (2002) directly compared the respiratory effects of pure PAA to that of the 3-chemical mixture by buffering the PAA mixture to generate only PAA vapor. Male mice were oronasally exposed to PAA in a 2.5 inhalation chamber equipped with 4 plethysmographs. The mice were restrained in the body plethysmograph while the head was enclosed in the inhalation chamber for 60 min. The respiratory rate was measured continuously during the exposure while mice were exposed to PA alone or in the mixtures. Concentrations of 1.8, 4, 6 and 24 ppm (pure PAA) and 1.6, 3.0, 5.6 and 11.6 ppm (PAA in mixture) resulted in respiratory rate declines of 22, 35, 50 and 80% and 25, 36, 55 and 65%, respectively. Concentrations of acetic and hydrogen peroxide that produced similar rate declines were roughly 20 and 10-fold greater than PAA, respectively.

In repeat exposure studies, rats showed no effects when exposed to 2.3 ppm for 60 min/day for 28 days; however exposure to 7 ppm under similar conditions caused increased lung and liver weight, depressed weight gain, and lung inflammation (Benes et al. 1966). Similar effects were observed in mice that inhaled 22.4-45 ppm, 1 h/day, 3 times per week, for 4 weeks (Merka and Urban 1978). Effects of exposure to PAA were more prevalent and more severe after exposure was terminated than during exposure. In addition, effects were more severe after doubling the exposure concentration than doubling the exposure duration.

Human exposure-response data for PAA is limited to a set of ill-defined studies of short duration with small numbers of subjects. Exposure to aerosols generated from a fogger study using diluted Peratol (5% PAA) was associated with lacrimation at 5 ppm (15.6 mg/m^3), extreme discomfort and irritation to mucous membranes at 2.0 ppm (6.23 mg/m^3); slight or mild discomfort at 0.5-1.5 ppm (1.56-4.67 mg/m^3), and no discomfort at <0.5 ppm (1.56 mg/m^3) (Fraser and Thorbinson 1986). The study was conducted in a work setting and human effects were recorded as the PAA aerosol concentration was maintained for 1-hour and then dissipated after that. McDonagh (1997) and an associate measured airborne PAA concentrations in two caprolactone distillation plants. The monitoring took place over a 3-h period. PAA vapor was measured at total peroxygen content; hydrogen peroxide was not expected to comprise a large proportion of the measured substance in the vapor. In one area, PAA concentrations ranged from 0.5 to 0.6 ppm (1.56-1.87 mg/m^3); these concentrations were not considered to be immediately irritating, but would have been considered unpleasant for an extended period of time. PAA concentrations of 0.13 to 0.17 pm (0.40-0.53 mg/m^3) in another area were considered tolerable and not unpleasant. McDonagh and his associate spent most of their time in an area where the average PAA concentration measured for a 10-min sampling time was 0.17 ppm (0.53 mg/m^3). They noted no lacrimation at any time during their 3-h exposure. McDonagh (1997) recommended 0.15 ppm (0.47 mg/m^3) as an acceptable 8-h occupational exposure limit for PAA . This concentration would be perceptible, but not irritating or unpleasant.

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 irritating or slightly irritating. PA solutions are corrosive or severely irritating to the rabbit eye at concentrations of 0.2% and higher.

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

It is speculated that the cytotoxicity and genotoxicity of PAA is the result of the same mechanism at the cellular level – production of reactive oxygen species which are not detoxified at higher concentrations. No assessment of the carcinogenicity of inhaled PA have been conducted. PAA has been linked to skin tumors following dermal applications.

HEAC Health-based assessment and recommendation

There currently are no OEL standards for PAA. NIOSH has proposed an ILDH of 0.55 ppm for PA based on the human studies of Fraser and Thorbison. In this single trial study, volunteers were first exposed to 5 ppm for 7 minutes and reported lacrimation and extreme discomfort. The PA source was extinguished for 25 minutes to allow the atmosphere to return to a tolerable level (<0.5 ppm) as reported by the volunteers. The concentration was then brought to 2-3 ppm for the next 75 minutes during which volunteers reported intolerable/extreme irritation. At the end this period, the PAA source was extinguished and PA concentration dropped from 2.0 ppm to <0.5 ppm over the course of 45 minutes. From 1.5 ppm to 0.5 ppm volunteers reported various stages of discomfort until the concentration dropped below 0.5 ppm at which level no discomfort was reported. Based on the different levels of discomfort, NIOSH determined that a threshold for severe irritation resides between 2.0 and 1.5 ppm. Using 1.5 as the point of departure and adjusting to a 30-minute exposure yields a LOAEL of approximately 1.6 at 30 minutes. Applying an uncertainty factor of 3 yields an IDLH of 0.55 ppm. The NRC AEGL Committee (2010) used a similar approach to derive an AEGL-1 value of 0.17 ppm. That body used the

NOAEL from the Fraser study (<0.5 ppm) and applied an intraspecies uncertainty factor of 3 (because PAA is a corrosive and an irritant) to arrive at 0.17 ppm. This value is used for all AEGL-1 time points – 10 minutes to 8 hours – because the threshold of irritation was considered more a function of concentration than time.

A PEL of 0.15 ppm and a STEL of 0.4 ppm is proposed for discussion. The chronic toxicological effects of PAA in laboratory animals is very poorly characterized and does not provide a basis upon which to develop an exposure level in humans. Animal studies were conducted mostly at acute levels causing lethality and what limited NOAELS could be determined from these studies (2.3 ppm, Benes 1966) would justify application of a 1000x uncertainty factor (not a chronic study, interspecies and intraspecies) with very little basis in a mechanism of action. Alternatively, given the high irritancy of PA in humans, using the limited human exposure data from controlled studies and workplaces, establishing a NOAEL from these studies and applying an intraspecies UF to address potential asthma effects would provide a basis for an OEL. This is the approach adopted by NRC (2010) and results in an OEL of 0.17 ppm. A STEL of 0.4 ppm is proposed based on the interpretation from USEPA (2008) that the author (Mc Donaugh, 1997) reported that PAA vapors at levels between 0.5 and 0.6 ppm for up to 3 hours were not immediately irritating. Skin notation is recommended.

Usage information: EPA TSCA Chemical Data Reporting (CDR), EPA Toxics Release Inventories (TRI)), other sources:

In 2015, there were 15 TSCA CDR records (usage in excess of 25,000 lbs) for peracetic acid in U.S. Of these, 2 were in California. In 2016 there were 255 TRI records for peracetic acid of which 15 were in California. There are 1476 businesses in the State of California CERS database reporting use of peracetic acid. The average daily use of peracetic acid reported by these businesses was 55, 230 and 26,276 gallons for the 50, 75 and 99 percentiles of users.

Measurement/Implementation Feasibility

Sampling and analysis for PAA has historically been complicated by the following:

1. PAA is volatile and breaks down rapidly
2. The three constituents of the mixture interfere with each other on sample collection.
3. For many reasons t is not possible to measure the hydrogen peroxide and acetic acid concentrations in air and calculate PAA air concentrations even when the initial concentration of the three constituents in the liquid mixture are known.

A method to measure and distinguish PAA concentrations in a mixture containing hydrogen peroxide via electrical sensor was first published in 2001 (Awad, et al, American Chemical Society, 2001). Today there are at least three manufacturers of direct reading and data logging equipment that can distinguish PAA from the potential interference of the other mixture constituents via electrical sensors. According to the Federal OSHA Salt Lake City Lab, at least one of these machines is not capable of being calibrated in the field but must be certified as freshly calibrated by the manufacturer via the delivery of machines from the manufacturer several times a year. The Salt Lake City Lab was unable to obtain accurate results until it received a newly calibrated machine from the manufacturer. This is no doubt true for all of the competing machines because of PAA's volatility and lack of stability: it is not possible to make and maintain a known concentration of PAA mixture from concentrate in the field or to order a stable standard from any source. Nevertheless, NIOSH is currently evaluating the adequacy of this equipment from three manufacturers.

In 2004, Hecht, et al, published a sampling method that utilized ordinary sampling pumps. The method first used chemically treated filters to derivatize, capture and remove the hydrogen peroxide constituent of the

mixture. A different chemical was applied to silica gel media to collect the PAA constituent. Laboratory analysis of the two media was performed with common methods. Recently, federal OSHA Salt Lake City Lab has demonstrated that the method works, but was unable to recover a sufficient percentage of the PAA in its tests to validate the method. NIOSH is currently separately evaluating the Hecht method in a comprehensive study expected to take about two years.

In 2010, European researchers reported successful use of an automated "solid phase micro-extraction (SPME) fast gas chromatography-mass spectrophotometry" for quantitative evaluation of PAA concentrations in both short term and long-term exposures (Pacenti, M., et al, Ind. Health, 2010). In its current research on PAA, NIOSH plans to utilize a possibly similar lab-grade instrument (SISP Mass-Spec) to provide more accurate assessment and validation of the PAA field sampling it plans to make using the Hecht method. It is not practical to expect employers to utilize in the field an expensive lab-grade tool of this type.

Economic Impact Analysis/Assessment

The Division has made a determination that this proposal is not anticipated to result in a significant, statewide adverse economic impact directly affecting businesses, including the ability of California businesses to compete with businesses in other states. This proposal will not have any effect on the creation or elimination of California jobs nor result in the creation or elimination of existing businesses or affect the expansion of existing California businesses. The Division anticipates that any potential costs will be balanced by avoiding or minimizing the costs inherent in workers' compensation claims, lost work time, and productivity losses that would have been caused by exposure related illness of employees.

The PEL proposed is consistent with recent scientific findings, of which professional health and safety staff and consultants of these employers and others with significantly exposed employees should be aware. Many of these entities already seek to control employee exposures to substances to levels below existing PELs in the interest of business continuity and minimization of tort and workers compensation liability.

Setting a Permissible Exposure Limit that is up-to-date and consistent with current scientific information and state policies on risk assessment will send appropriate market signals to employers with respect to the costs of illness and injury, which chemicals can impose on workers and their families, the government, and society at large. With appropriate market signals, employers may be better able to protect employees from exposures in the workplace and impose less of a burden on workers and society. There are no anticipated benefits to the state's environment. The economic benefits from the proposed PEL will result primarily from reduced health risk among exposed workers.

Conclusion

Toxicological information is sufficient to justify adoption of at least a 15-minute STEL of 0.4 ppm, and an 8-hour PEL of 0.15 ppm. While initially HEAC considered adoption of exposure limits at this time premature due to the sampling and analytical inadequacies discussed above, additional consideration of the practical usage by employers of the Hecht sampling and analytical method and of the available direct reading instruments indicates employee exposures to PAA can be characterized accurately enough for employers to decide on appropriate workplace controls and to thereby protect workers.

It is important to note that any uncertainties in the values of sampling results experienced using either direct reading instruments or air sampling would be underestimates of the true values. This consistent "lower than true value" effect was demonstrated by OSHA's efforts to validate the Hecht and direct reading methods to their high standard of test concentration recovery. When OSHA utilized a properly calibrated direct reading

instrument, recovery of the test concentration easily met the high OSHA standard for validation. Therefore, HEAC proposes a 15-minute STEL of 0.4 ppm, and an 8-hour PEL of 0.15 ppm, but adds the caveat to employers that their workplace exposure modeling may underestimate exposures by up to 30% with the Hecht method and may also be underestimates for direct reading instruments if the instrument manufacturer's calibration recommendations have not been followed.

HEAC also recommends a skin notation for PAA be added to Table AC-1.

References:

Benes, V., B. Tichacek, and J. Veger. 1966. Toxizizat der Peressigsaure. Pp. 114-124 in Peressigsäure und die Moglichkeit ihrer Verwertung in der Desinfektion, B.Tichacek, ed. Prag: Staatsverlag für Gesundheitswesen der CSSR (as cited in Heinze et al. 1979).

Fraser JAL and A. Thorbison. 1986. Fogging Trials with Tenneco Organics Limited June 30 1986 at Collards Farm. Solvay InterTox, Warrington, UK

Gagnaire F, Marignac B, Hecht G, Héry M. 2002. Sensory irritation of acetic acid, hydrogen peroxide, peroxyacetic acid and their mixture in mice. Ann Occup Hyg. 46(1):97-102.

Janssen PJM [1989b]. Acute inhalation toxicity studies of Proxitane 1507 in male rats (II). Report No. S. 8908, Int. Doc. No. 56645/34/89.

Janssen PJM [1989c]. Acute inhalation study to investigate the respiratory irritating properties of Proxitane 1507
in male rats. Duphar B.V., Report No. S. 8912, Int. Doc. No. 56645/40/89.

Janssen PJM [1990]. Preliminary acute inhalation study to investigate the respiratory irritating properties of Proxitane 1507 in male rats. Duphar B.V. Report No. S.9003, Int. Doc. No. 56645/33/90.

Janssen PJM, van Doorn WM [1994]. Acute inhalation toxicity study with Proxitane AHC in male and female rats. Solvay Duphar B.V., Report No. S. 9408, Int. Doc. No. 56345/48/94.

National Academies of Science 2010. Acute Exposure Guideline Levels (AEGLs) for selected airborne chemicals - Volume: 8. Peracetic acid (CAS Reg. No. 79-21-0). NAS, National Research Council, Committee onToxicology, Subcommittee on Acute Exposure Guideline Levels National Academy Press: Washington, DC.

McDonagh J [1997]. Atmospheric monitoring of peracetic acid on the existing caprolactone plant distillation houses A & B assessment of results. Solvay Interox, Warrington, Reference No. EE970192.M01, Memorandum to R.A. Haffenden et al. dated 30 April 1997.

Merka V, Urban R [1978]. Study of inhalation toxicity of performic, peracetic and perpropionic acid in mice. J Hyg Epidemiol Microbiol Immunol *20*:54–63.