Approaches for Deriving an OEL for Peracetic Acid and Occupational Risk Management

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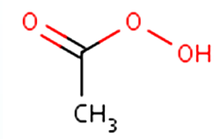

Abstract

To provide perspective on current and proposed occupational exposure limits (OELs) for peracetic acid (PAA; CAS 79-21-0) we evaluated PAA toxicity with the aim of understanding uncertainties and their implications for the resulting OEL. The database for PAA is limited and no single study is definitive. Two unpublished reports on human exposures to PAA provide some concentration-response data, indicating that a sensitive acute effect of PAA exposure is eye and respiratory tract irritation, but the studies differ quantitatively. These differences are not surprising, in light of the differences in exposures (apparently pure PAA vapor vs. an aerosol of a mixture), the subjective nature of the reporting, and the likely small sample sizes. The studies are also limited by the lack of clear concentration-duration-response data. Nonetheless, the studies provide a reasonable estimate of the threshold for the onset of irritation in humans in the range of 0.53 mg/m^3 for up to 3 hours and 1.56 mg/m^3 for up to 45 minutes. RD_{50} (concentration estimated to cause a 50% depression in respiratory rate) data in mice and rats provide additional information on the irritant potency of PAA. The RD_{50} in mice was 17 mg/m^3 for pure PAA vapor and 12 mg/m^3 for a commercial mixture. The rat RD_{50} was 21.5 to 24.1 mg/m^3. Based on the array of human data and the RD50 values in rodents, we calculated potential TWA OELs ranging from 0.26 to 1.56 mg/m^3. A similar range of 0.62 – 2 mg/m^3 is found among the published OELs, and any of these values could be justified as protective of worker health given the uncertainties in the data and the precision of the OEL methodology. More definitive sensory irritation studies would further clarify selection of a value in this range. Given the extant data, the ultimate OEL choice within a range of reasonable values is a policy-based risk management decision, not a scientific one. The optimal time averaging approach is also not clearly established by the data; however, a combination of a TWA with a STEL is the recommended risk management option.

Background

- Produced from the acid-catalyzed reaction between acetic acid and hydrogen peroxide (Sanchez and Meyers, 2000)
  - Technical grades of peracetic acid contain approximately 40% PAA in acetic acid with residual hydrogen peroxide (ACGIH, 2013)
- Used commercially as a chemical intermediate, bleaching agent, and sterilant, as well as in the formation of epoxides, epoxy resins, and the bleaching of textiles
- Potent oxidizing chemistry that is highly corrosive. Lower concentrations are irritating to eyes and mucous membranes
- Vapor pressure of 14.5 mmHg at 25°C. Saturated vapor concentration of 59,300 mg/m^3 (ACGIH, 2013)
- Pungent odor with no clearly established threshold. Odor can serve as a warning property for the presence of atmospheric PAA
- Atmospheric monitoring of PAA can be problematic, particularly in atmospheres with appreciable levels of chlorine and/or hydrogen peroxide.

Time Averaging Approach - TWA, Ceiling or STEL

- Ceiling limit often established for rapidly acting sensory irritants that lack significant secondary or chronic tissue toxicity
  - Ceiling limit should protect from not only sensory irritation, but also subclinical cytotoxic responses that could accumulate and yield other longer-term effects.
  - PAA is an irritant that can also cause cytotoxicity. Insufficient dose-response information is available to ensure that the absence of sensory response also protects from accumulating subclinical cytotoxic responses.
- **Thus, a ceiling limit approach is not recommended.**

- A short-term exposure limit (STEL) can protect protection from rapid onset and transient effects such as sensory irritation.
  - The STEL is typically accompanied by a TWA derived separately to ensure protection from longer-term effects.
  - If the upper respiratory tract (URT) irritation is the only adverse effect (i.e., tissue damage does not occur), it can be appropriate to establish a STEL in the absence of a longer-term TWA.
  - This is sound physiologically, but has practical problems.
  - In practice, the STEL is a 15-minute TWA that reflects a concentration measured over a 15-minute period. In the absence of a longer-term (e.g., 8-hour) TWA-based limit, control at the STEL is equivalent to a series of consecutive 15 minute-TWAs, and thus equivalent to a longer-term TWA.
  - Usually, where a longer-term TWA is established along with a STEL, the TWA includes an implied limit to the number and duration of excursions above the TWA and below the STEL, which means that the STEL does not become equal to the longer-term TWA value.
  - **For PAA, the data for longer-term effects are limited and the MOA suggests some cytotoxic potential. Therefore a limit based solely on the STEL is not recommended.**

Table 1. Key Peracetic Acid Worker Exposure Studies and Effect Levels

	Concentration		
Duration	**ppm**	**mg/m^3**	**Effect**
McDonagh (1997) (vapor)			
Not clear, but possibly as long as 3 hours	0.5-0.6	1.56-1.87	Not considered immediately irritating but would have been considered "unpleasant for an extended period of time"
Not clear, but possibly as long as 3 hours	0.13-0.17	0.40-0.53	Tolerable, not unpleasant
Not clear, but possibly as long as 3 hours	0.17	0.53	No lacrimation
Fraser and Thorbinson (1986) (aerosol)			
5-10 minutes	N/A - aerosol	6.23	Extreme discomfort of mucous membranes
15-20 minutes	N/A - aerosol	3.12-4.67	Discomfort of mucous membranes
25 minutes	N/A - aerosol	3.12	Discomfort tolerable
30 minutes	N/A - aerosol	1.56-3.12	Discomfort mild
35-45 minutes	N/A - aerosol	≤1.56	No discomfort

Table 2. Key Peracetic Acid Data from Animal Exposures

Study	Species	Formulation	Duration	RD_{50}
Gagnaire et al. (2002, as cited by ACGIH, 2011; OECD 2008	Mouse	Pure peracetic acid vapor evaporated from a buffered (pH 7) commercial mixture containing 39% peracetic acid, 45% acetic acid and 6% hydrogen peroxide	1 hour	5.4 ppm (17 mg/m^3)
Gagnaire et al. (2002)	Mouse	Peracetic acid vapor from a commercial mixture containing 36% peracetic acid, 53% acetic acid and 11% hydrogen peroxide	1 hour	3.8 ppm (12 mg/m^3)
Janssen (1989c, as cited by OECD, 2008; NRC, 2010)	Male Wistar Rat	Aerosol generated from a mixture of 15% peracetic acid, 14% hydrogen peroxide, and 28% acetic acid	25 minutes	21.5 to 24.1 mg/m^3 (no clear exposure-response trend)

The only repeated exposure studies were conducted at 150 mg/m^3 and higher, and caused slight to severe squamous metaplasis of the nasal turbinates in all exposed groups.

Table 3. Summary of Potential and Existing Exposure Limits

Value	Basis	Point of Departure	Uncertainty Factor	Final Value
Derived here	McDonagh (1997)	0.53 – 1.56 mg/m^3 (0.17 – 0.5 ppm) (vapor)	1-3 (midpoint is 2)	0.26 – 1.56 mg/m^3 (0.09 – 0.5 ppm)
Derived here	Fraser and Thorbinson (1986)	1.56 mg/m^3 (aerosol)	1-3 (midpoint is 2)	0.56 – 1.56 mg/m^3
Derived here	RD_{50}	12-17 mg/m^3 (3.4 – 5.4 ppm) (vapor) 21.5 to 24.1 mg/m^3 (aerosol)	30 (Schaper, 1993)	0.4 – 0.57 mg/m^3 (0.13 – 0.18 ppm) based on the mouse vapor data, or 0.71-0.8 mg/m^3 based on the rat aerosol data
NRC AEGL-1 10 min – 8 hour (NRC, 2010)	McDonagh (1997); Fraser and Thorbinson (1986)	1.56 mg/m^3 (0.5 ppm) Not immediately irritating [McDonagh (1997)]; No discomfort [Fraser and Thorbinson (1986)]	3 – Human variability, Low variability based on mode of action (MOA)	0.52 mg/m^3 (0.17 ppm)
[2]NRC AEGL-2 10 min – 8 hour (NRC, 2010)	Fraser and Thorbinson (1986)	4.7 mg/m^3 (1.5 ppm) Slight to tolerable discomfort for exposure durations up to 20 minutes	3 – Human variability Low variability based on MOA	1.56 mg/m^3 (0.5 ppm)
NIC TLV-STEL (ACGIH, 2013)	McDonagh (1997); Fraser and Thorbinson (1986); RD_{50}			1.24 mg/m^3 (0.4 ppm)
15-minute STEL (Gagnaire et al., 2002)	Based on 0.1 x RD_{50} of 0.54 ppm			1.56 mg/m^3 (0.5 ppm)
TLV-TWA (Gagnaire et al., 2002)	Based on 0.3 x RD_{50} of 0.54 ppm			0.62 mg/m^3 (0.2 ppm)
ECHA Worker DNEL, local effects – acute/ short term or long-term exposure	Documentation not available			0.6 mg/m^3 (0.2 ppm)
Various MAKs Long-term value (European Commission - EC, 2000)	Documentation not available			1 to 1.4 mg/m^3 (0.32 to 0.45 ppm)
Various MAKs 30-minute value (EC, 2000)	Documentation not available			2 mg/m^3 (0.64 ppm)

Recommendations/Conclusions Regarding Time Averaging

- Based on MOA considerations, PAA may have longer-term effects for which a STEL approach alone does not provide adequate protection.
  - The selection of a STEL without a TWA should not be driven by the absence of robust longer-term effects data.
- The use of a TWA with a STEL at a higher concentration reflects the different biological responses (sensory irritation and cytotoxicity) in ways that give the risk manager flexibility.
- The use of a TWA with a STEL may also be a better reflection of the temporal patterns in biology, since some elements of the irritation response are not completely independent of exposure duration.
- The use of a TWA and STEL together provides meaningful guidance for excursion limits and is most consistent with current practice.

Overall Conclusions

- We calculated potential TWA OELs ranging from 0.26 to 1.56 mg/m^3.
- This is similar to the range of 0.62 – 2 mg/m^3 found among the published OELs
- Any value within the range could be justified as protective of worker health in light of the uncertainties in the data and the precision of the OEL methodology.
- More definitive sensory irritation studies would further clarify selection of a value in this range.
- The ultimate OEL choice is a policy-based risk management decision, not a scientific one.
- The optimal time averaging approach is not clearly established by the data; however, a combination of a TWA with a STEL is recommended as a preferred risk management option.

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