Ambient Air Guidelines

for

Hydrogen Sulfide

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Hydrogen Sulfide – Ambient Air Guidelines

Overview

This document describes the basis for Ambient Air Guidelines (AAGs) for hydrogen sulfide. The Maine Center for Disease Control and Prevention (ME-CDC, formerly Bureau of Health) developed a protocol for deriving long term (chronic) AAGs in 2004 (ME-CDC, 2004). These AAGs are intended to serve as the most recent recommendations regarding ambient concentrations of chemicals below which there is a minimal health risk over an extended period of exposure. This document describes the public health basis for ambient air guidelines for both short-term (acute) and long-term (chronic) exposure. Section 1 presents information about sources of hydrogen sulfide gas and levels encountered in ambient air. Section 2 provides a brief review of the key toxicity data for hydrogen sulfide. Section 3 provides a summary of ambient air guidelines that have been developed by various federal and state agencies for short-term and long-term exposures. The basis for Maine's acute and chronic guidelines is then presented as section 4, and the document concludes with a discussion of appropriate averaging times for relating monitoring data to these guidelines.

Maine Ambient Air Guidelines for Hydrogen Sulfide

Duration	Value	Basis	Averaging Time	Primary Sources
Acute	30 ppb (42 ug/m^3)	Headaches and nausea in normal subjects	½-hour	CalEPA 1999
Chronic	1 ppb (2 ug/m^3)	Nasal inflammation/lesions in subchronic mouse and rat studies	1-year	US EPA 2003

1. Introduction

Hydrogen sulfide (H_2S) is a flammable, colorless gas with a characteristic odor of rotten eggs. Hydrogen sulfide occurs both naturally and from human processes. It is released from volcanoes, sulfur springs, undersea vents, swamps, salt marshes, and stagnant bodies of water, and is found in association with crude petroleum and natural gas. Hydrogen sulfide is also associated with municipal sewers and sewage treatment plants, landfill gases, manure handling operations, and pulp and paper operations.

The levels of hydrogen sulfide in air are typically low. The amount of hydrogen sulfide naturally found in the air has been estimated as 0.11-0.33 ppb (0.15-0.46 ug/m^3). Lower levels (0.02-0.07 ppb; 0.03-0.1 ug/m^3) have been observed in some remote areas.

Concentrations closer to sources of hydrogen sulfide are higher. For example, annual H_2S concentrations of ~6 ppb and 24-hour concentrations as high as 74 ppb have been reported near pulp mills in Imatra, Finland (Partti-Pellinen et al., 1996). Hydrogen sulfide from manure at dairies has been measured at 20-40 ppb (27.8-55.6 ug/m^3; Osbern and Crapo, 1981; Donham et al., 1982).

Hydrogen sulfide is also a constituent of landfill gas emissions, accounting for up to 1% by volume (ATSDR 2004). Ambient air monitoring data from residential locations in close proximity to the West Old Town, Maine landfill are available in continuous 15-minute readings over the fall of 2005 (Maine DEP 2006). While ambient air readings are generally below the detection limit of 1 ppb (1.4 ug/m^3), occasional periods of positive detection lasting up to a few hours can be observed with maximum 15-minute average concentrations of 30 ppb (42 ug/m^3). These episodic events were infrequent in this dataset; rolling 24-hour averages were generally below 1 ppb (1.4 ug/m^3), while 30-minute rolling averages occasionally exceeded 20 ppb (28 ug/m^3).

Additional monitoring data from locations adjacent to the Norridgewock landfill are available for a 1-week period in late June of 2002 (5-minute average measurements) and a 2-week period in September of 2002 (15-minute average measurements). These data are similar to those seen at the West Old Town site; hydrogen sulfide was below the detection limit aside from roughly 5 discreet, brief (15 minutes-6 hours) events per week. The maximum 30-minute rolling averages for each event ranged from 1-14 ppb. The maximum 24-hour rolling average was 0.6 ppb.

Hydrogen sulfide odor is readily detectable by humans at very low concentrations. In a report to the California Air Resources Board, Amoore (1985) synthesized many individual reports and described a lognormal distribution of odor detection thresholds with a geometric mean of 8 ppb (~11 ug/m^3) and a geometric standard deviation of 4 (CalEPA, 1999). There is a wide range of individual sensitivity to this odor. ATSDR has reported a range of individual odor detection thresholds of 0.5-300 ppb (0.7-417 ug/m^3; ATSDR, 1999) and CalEPA reports a range of 0.07-1400 ppb (0.1-1,946 ug/m^3). Age also affects the ability to detect smells, with younger people being more sensitive.

Concentrations that substantially exceed the odor detection threshold can result in annoying and discomforting physiological symptoms of headache and nausea (Amoore, 1985). Several studies have been conducted to establish the ratio of discomforting annoyance threshold to detection threshold for unpleasant odors (see CalEPA, 1999). The geometric mean ratio from these studies is 5; based on an odor detection threshold of 8 ppb, the odor annoyance threshold would be 40 ppb. CalEPA estimated that ~83% of the general population should be able to detect the odor of hydrogen sulfide at 30 ppb (41.7 ug/m^3). The World Health Organization (WHO) recommends that in order to avoid substantial complaints about odor annoyance, 30-minute average hydrogen sulfide concentrations should not exceed 5 ppb (7 ug/m^3 ;WHO, 1981).

2. Hydrogen sulfide toxicity data

There are several sources of toxicity information available. Controlled studies of animals have used precise exposure methods, acute and subchronic exposure periods, and have made detailed observations of potential effects including pathology. Controlled chamber exposure studies of human volunteers have generated useful information about the potential for clinically apparent effects and markers of subclinical effects following acute exposures. Epidemiological studies of humans either living near sources of hydrogen sulfide or working at facilities that release hydrogen sulfide document a range of health symptoms or health outcomes linked with less precise exposure information, though covering a potentially more relevant range of exposure.

2.1 Mechanisms of action

The current mechanistic understanding of hydrogen sulfide toxicity is incomplete, but provides a partial basis for understanding effects on cardiac, respiratory, and nervous tissues. One of the mechanisms of hydrogen sulfide toxicity is the inhibition of cytochrome oxidase. This enzyme is involved in cellular energy production, and its inhibition leads to anaerobic metabolism, decreased cellular energy generation, and the generation of lactic acid. Cardiac tissue is particularly sensitive to the effects of cytochrome oxidase inhibition because of its high oxygen demand. The same is true of tissues in the nervous system, although indirect neurotoxicity is also thought to occur as a result of hypotension following cardiotoxicity. Other evidence indicates that hydrogen sulfide may affect the synaptic and membrane properties of brain stem neurons that control respiration (see ATSDR, 2004).

2.2 Acute toxicity

Humans: It has been estimated that symptoms of discomfort, including headaches and nausea, are experienced when the air concentration approaches five-times the odor detection threshold; assuming a detection threshold of 8 ppb this would mean that symptoms should be expected at ~ 40 ppb (55.6 ug/m^3). This relationship is based on multiple studies and is consistent with observations of odor detection and symptoms of discomfort around geyser emissions of hydrogen sulfide (CalEPA, 1999).

Hydrogen sulfide gas has been lethal to humans at acute concentrations generally exceeding 500 ppm (695,000 ug/m^3). Conditions associated with mortality included pulmonary edema, hemorrhagic bronchitis, and asphyxiation.

There have been several controlled-chamber studies of humans exposed to hydrogen sulfide, in which volunteers were exposed for a fixed period of time to a known

concentration of hydrogen sulfide under careful observation. These chamber studies have been summarized in some detail by CalEPA (1999) and ATSDR (1999 & 2004).

Bhambhani and colleagues have conducted a number of chamber studies of young healthy volunteers exposed to hydrogen sulfide via mouth-only inhalation. Bhambhani and Singh (1991) exposed sixteen male volunteers to 0 (control), 0.5, 2, and 5 ppm hydrogen sulfide on four separate occasions. In each case subjects were continuously exposed to H_2S while gradually increasing their level of exertion to exhaustion (this took variable amounts of time, no less than 12 minutes). Blood samples were taken at three stages of exertion. Heart rate and expired ventilation were unaffected as a result of the exposures during submaximal and maximal exercise; however, there was a significant increase in oxygen uptake ($V0_2$ and $V0_{2max}$) at 5 ppm and maximal exertion and significant increases in blood lactate concentrations (a marker for anaerobic metabolism) at 5 ppm hydrogen sulfide for every level of exertion.

Subsequent studies by these researchers used a different design in which subjects were exposed continuously for 15 or 30 minutes while exercising at 50% of their maximum aerobic power. A study with thirteen men and twelve women examined the effects of 0 and 5 ppm hydrogen sulfide on respiratory physiological parameters (Bhambani et al., 1994). The results indicated that there were no significant differences between the two exposures for metabolic, cardiovascular, arterial blood, and perceptual responses in either sex. In a separate publication on apparently the same chamber study, Bhambhani et al. (1996a) reported on the effect on markers of anaerobic and aerobic metabolism, including concentrations of lactate, lactate dehydrogenase, citrate synthase, and cytochrome oxidase in muscle biopsy samples. In men (but not women), there was a significant decrease in citrate synthase concentration in muscle tissue and a tendency for lactate and lactate dehydogenase concentrations to increase and cytochrome oxidase concentration to decrease. Two additional chamber studies with exposures to 0 (control) and 10 ppm hydrogen sulfide were conducted. In a study of pulmonary function, nine men and ten women were exposed to 10 ppm hydrogen sulfide while exercising for 15 minutes; there were no significant changes in any of the measures of pulmonary function (Bhambani et al., 1996b). The second chamber study investigated cardiovascular, metabolic, and biochemical responses of fifteen men and thirteen women exposed to 10 ppm hydrogen sulfide for two 30-minute periods of exercise. A significant decrease in oxygen uptake, with a concomitant increase in blood lactate, was observed in men and women as a result of H_2S exposure. No significant changes were observed in arterial blood parameters and the cardiovascular responses under these conditions. Muscle lactate, as well as the activities of lactate dehydrogenase, citrate synthase, and cytochrome oxidase, were not significantly altered by H_2S exposure.

Collectively these mouth-only inhalation chamber studies by Bhambani and coworkers suggest an acute LOAEL for healthy adult humans of 5 ppm with evidence of inhibition of aerobic metabolism in exercising muscle being the most reproducible effect. The

authors hypothesize that this observation could explain why fatigue is commonly associated with occupational exposure to hydrogen sulfide. A factor that needs to be considered in evaluating these studies is that the inhalation exposures were by mouth only, whereas in both occupational and environmental settings inhalation exposures would be by nose and mouth. The authors note that pulmonary function might have been affected if their study subjects could have smelled hydrogen sulfide (Bhambhani et al., 1996a). CalEPA (1999) describes results from another chamber study by Bhambani and Singh (1985); the results are apparently only available as a report submitted to the Alberta Worker's Health and Safety Compensation. In this study, 42 individuals were exposed to 2.5 and 5 ppm (3,475-6,950 ug/m^3) hydrogen sulfide; coughing and throat irritation were reported after 15 minutes of exposure. As this report has yet to be obtained by ME-CDC, it is unclear whether subjects were exposed to hydrogen sulfide by mouth only (as with the other studies by this group), or by mouth and nose.

Jappinen et al. (1990) exposed 10 adult volunteers with asthma by mouth and nose to 2 ppm (2,780 ug/m^3) hydrogen sulfide for 30 minutes. All subjects reported detecting "very unpleasant" odors that they rapidly adjusted to; three subjects reported headaches after exposure. The authors reported no notable changes in the mean forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), or forced expiratory flow values ($FEV_{25-75\%}$) after exposure to hydrogen sulfide. However, airway resistance (Raw) was increased in eight of ten subjects (range –6% to +138%), with an average group increase of 25% that was of borderline statistical significance ($p = 0.06$). Specific airway conductance (sGaw) was decreased in six of ten subjects, with a range from –58% to +29% and an average group decrease of 8.4% that was not significant ($p = 0.17$). The authors noted that when assessing the changes in Raw and SGaw, two of the subjects had changes of over 30% in both Raw and SGaw indicating bronchial obstruction.

Animals: There have been multiple observations of respiratory toxicity after acute hydrogen sulfide exposure in rats (see ATSDR 1999 & 2004). The specific endpoints include increased breathing rate, inflammation and cell death in the respiratory epithelium, edema of the lungs, and congestion. All of these studies exposed rats to hydrogen sulfide concentrations in the range of 100-400 ppm (139,000-556,000 ug/m^3).

Neurotoxicity has been observed in rats, mice and rabbits at the same concentrations (100-400 ppm), with symptoms including lethargy or excitement, loss of consciousness (rabbits), and decreased behavioral response rate.

There have also been several systematic observations of mortality in animals in controlled laboratory settings. For example, 50% mortality was observed in rats exposed to 440 ppm (611,600 ug/m^3) for 4 hours. Dogs exposed to 1,000 ppm (1,390,000 ug/m^3) for 15-20 minutes experienced respiratory arrest and death (CalEPA, 1999).

2.3 Subchronic and chronic toxicity data

Humans: Several epidemiological studies have assessed the health impact of community-level exposures to chronic low levels of hydrogen sulfide. Many of these studies deal with emissions from pulp mills or other facilities that release a mixture of reduced sulfur compounds and SO_2. The unit of exposure is sometimes Total Reduced Sulfur (TRS).

Residents near a pulp mill in southern Finland, for example, reported increased eye symptoms, lower respiratory tract symptoms, and headaches on days when the TRS concentration was 10-30 ug/m^3 (medium) or >30 ug/m^3 (high). The authors report that two-thirds of TRS in this area is H_2S (Marttila et al., 1995).

A study in another pulp mill town in Finland assessed the chronic impact of low levels of hydrogen sulfide pollution (Parti-Pellinen et al., 1996). The annual average hydrogen sulfide concentration in Varkaus, Finland was reported to be 1.4-2.2 ppb (2-3 ug/m^3), with a maximum 24-hour concentration of 17.3 ppb (24 ug/m^3) and a maximum 1-hr concentration of 109.4 ppb (152 ug/m^3). Coughs, respiratory infections, and headaches were reported to be higher in Varkaus than in a neighboring, unpolluted community as assessed by questionnaire data.

Residents of Dakota City and South Sioux City, Nebraska were exposed to reduced sulfur emissions from beef slaughter, leather tanning, and waste treatment facilities. ATSDR and EPA conducted residential air monitoring of total reduced sulfur (TRS) and hydrogen sulfide in the area in 1996 and again in 1999-2000. Time-series analyses of daily hospital visits for selected health outcomes and measures of TRS and hydrogen sulfide were performed (Campagna et al., 2004). TRS and hydrogen sulfide levels were categorized as high if at least one of the daily 30-min rolling averages was ≥ 30 ppb (41.7 ug/m^3) and as low if every rolling average was < 30 ppb. The measure of association was the mean percent change (MPC) in the average number of hospital visits recorded following a day with high exposure versus as a day with low exposure. Separate time-series analyses were perform; each using ambient air monitoring data from a distinct monitoring station. The MPC in hospital visits for all respiratory diseases including asthma was significantly increased on days following high hydrogen sulfide levels for children (but not adults) for 3 of the 5 available monitoring stations. Positive associations were less common when analyzing hospital visits for asthma alone; however, asthma cases were limited in number, raising questions about adequate statistical power to detect an effect.

A Chinese study of an occupational cohort found a significant increase in the risk of spontaneous abortion in association with exposure to hydrogen sulfide (Xu et al., 1998). This study did not include exposure estimates and the degree of potential simultaneous exposure to other chemicals is unclear.

Animals: Subchronic animal studies have observed inflammation of the nasal mucosa, degeneration of olfactory neurons, and hyperplasia subsequent to neuron damage at concentrations of 30-80 ppm (41,700-111,200 ug/m^3). These studies serve as the basis for subchronic and chronic guidelines and are discussed further below.

Adverse neurological changes have been observed in newborn rat pups exposed in utero and after birth, including altered cerebellar Purkinje cell morphology and altered neurotransmitter levels. These effects were observed at 20 ppm (28 ug/m^3), the lowest dose tested.

3. Ambient air exposure guidelines

According to protocol (ME-CDC, 2004), AAGs are intended to be the most recent health-based guidelines for long-term ambient air concentrations below which minimal adverse health effects can be expected. Federal and state agencies have developed several guidelines for hydrogen sulfide exposure. These guidelines have been subjected to internal and external peer review and are based on the same body of evidence but do not necessarily agree with one another. The protocol for deriving chronic AAGs places these values in a hierarchy in which U.S. Environmental Protection Agency (EPA) values from their Integrated Risk Information System (IRIS) database are given first rank, California Environmental Protection Agency (CalEPA) values second rank, and values from the Agency for Toxic Substance and Disease Registry (ATSDR) third rank. All three of these agencies have developed chronic ambient air guidelines for hydrogen sulfide. ME-CDC does not have formal procedures for deriving acute guidelines since such guidelines are rarely derived. Acute ambient air guidelines have been developed both by CalEPA and ATSDR and are discussed below.

EPA publishes Reference Concentrations (RfCs) for chronic inhalation exposure. These values are intended to represent a concentration "without appreciable risk of deleterious effects during a lifetime". The RfC for hydrogen sulfide was recently updated (USEPA, 2003). These values are available online through the IRIS database (USEPA, 2006).

CalEPA publishes Reference Exposure Levels (RELs) for both acute (1 hour) and chronic exposures; these are analogous to RfCs. An acute REL for hydrogen sulfide was published in 1999 (CalEPA,1999) and a chronic REL was published in 2000 (CalEPA, 2000).

The Agency for Toxic Substances and Disease Registry (ATSDR) publishes Minimal Risk Levels (MRLs), which are defined as exposure concentrations "without appreciable risk of adverse noncancer health effects". MRLs are derived for acute (1-14 days), intermediate (15 days-1 year), and chronic (more than one year) exposure periods. These values are published in ATSDR Toxicological Profiles; the current profile for hydrogen sulfide is from 1999. We can also consider the information described in a draft update to

this profile published in 2004; a final update will not be available until sometime in 2006 (S. Chou, ATSDR, personal communication).

3.1 Acute guidelines

California's acute REL for hydrogen sulfide is intended to protect against both odor nuisance and physiological symptoms such as headache and nausea. The 1-hour California Ambient Air Quality Standard (AAQS) for hydrogen sulfide was originally based on an odor detection study (California State Department of Health, 1969). The individual thresholds of the panel of sixteen individuals ranged from 12-69 ppb (16.7-95.9 ug/m^3) and the geometric mean was 29 ppb (41.7 ug/m^3). The California Air Resources Board (CARB) reviewed the AAQS for hydrogen sulfide in 1984, and found that the standard was not only necessary to reduce annoyance odors, but also to reduce the physiological symptoms of headache and nausea. CARB noted that odor detection thresholds as low as 8 ppb had been reported. Based on a central estimate of a value of 5 for the ratio of the discomforting annoyance threshold to the detection threshold, CARB estimated that the AAQS of 30 ppb would be detectable by 83% of the population and would be discomforting to 40% of the population. This concern was believed to be substantiated by reports of nausea and headache at 30 ppb exposures from geyser emissions.

The acute MRL in ATSDR (1999) was based on a study of humans exposed under controlled conditions. Jappinen et al. (1990) exposed ten asthmatic adult volunteers to hydrogen sulfide at 2 ppm (2,780 ug/m^3) for 30 minutes. Respiratory function in response to a histamine challenge was assessed in the volunteers. Two subjects showed signs of bronchial obstruction and three subjects also reported headaches. ATSDR (1999) considered this concentration (2 ppm) to be a traditional Lowest Observed Adverse Effect Level (LOAEL). An uncertainty factor (UF) of 10 was applied according to standard risk assessment practices to extrapolate from a LOAEL to a level that approximates a No Observed Adverse Effect Level or NOAEL (ASTDR, 1999). An additional UF of 3 was applied to account for variability among humans and the final MRL was 70 ppb (97.3 ug/m^3).

In the draft update ATSDR (2004) proposed changing the acute inhalation MRL based on a different interpretation of the same underlying data. The 2 ppm concentration was defined as a "minimal LOAEL" rather than a "LOAEL". An uncertainty factor of 3 was used to extrapolate to a NOAEL, rather than a factor of 10. This change results in a threefold increase in the acute inhalation MRL to 200 ppb (278 ug/m^3).

3.2 Chronic guidelines

Long-term (chronic) exposure guidelines are based on subchronic rodent studies that focused on changes in the nasal mucosa. Brenneman et al. (2000) exposed rats to

hydrogen sulfide for 10 weeks[1], and observed loss of olfactory neurons and subsequent hyperplasia at 30 ppm (41,700 ug/m^3; LOAEL) but not at 10 ppm (13,900 ug/m^3; NOAEL). CIIT (1983) exposed mice for 90 days[2] and observed inflammation of the nasal mucosa at 80 ppm (111,200 ug/m^3; LOAEL) but not at 30.5 ppm (42,400 ug/m^3; NOAEL). The chronic guidelines described below differ in choice of study and selection of uncertainty factors.

The EPA reference concentration (RfC) is based on the rat study (Brenneman et al. 2000). The NOAEL was converted to a human equivalent concentration of 0.46 ppm (639 ug/m^3) and adjusted with a cumulative uncertainty factor of 300, yielding an RfC of 1.4 ppb (1.9 ug/m^3).

The California chronic reference exposure level (REL) is based on the mouse study (CIIT 1983). The NOAEL from this study was converted to a human equivalent concentration of 0.85 ppm (1,182 ug/m^3) and adjusted with a cumulative uncertainty factor of 100. The final REL is 8 ppb (11.1 ug/m^3; CalEPA, 2000).

Both guidelines use a factor of 10 to account for variability within a species; this is thought to protect more sensitive individuals from harm. Both studies also use a factor of 3 to account for uncertainties in estimating effects in humans from animal data. Although a factor of 10 is often used in deriving these kinds of guidelines, some of the uncertainty has been reduced by estimating a human equivalent concentration based on dosimetry. An additional factor is often used when a subchronic study is used to estimate chronic effects. USEPA uses a default factor of 10 while CalEPA uses a factor of 3.

3.3 Occupational guidelines

Occupational limits for hydrogen sulfide have been developed by the US Occupational Health & Safety Administration (OHSA), the National Institute for Occupational Safety and Health (NIOSH), and the American Conference of Governmental Industrial Hygienists (ACGIH). These standards and guidelines are intended to prevent effects observed in workers, including eye irritation, fatigue, neurological effects, and death. The ACGIH time-weighted-average (TWA) work-day limit for hydrogen sulfide is 10 ppm (13,900 ug/m^3). ACGIH also recommends a short-term (15 minute) exposure limit (STEL) of 15 ppm (20,850 ug/m^3). The ACGIH 2005 Guide to Occupational Exposure Values "Notice of Intended Changes" announced an intention to lower the TWA to 1 ppm (1,390 ug/m^3) and the STEL to 5 ppm (6,950 ug/m^3). Both OSHA and NIOSH have developed short-term ceiling limits. OSHA's workplace standard is an 8-hour permissible exposure limit (PEL) of 20 ppm (27,800 ug/m^3). NIOSH recommends a 10-minute ceiling concentration of 10 ppm (13,900 ug/m^3). These limits are generally intended to be

[1] Sprague-Dawley rats; 0, 10, 30, 80 ppm H_2S, 6 hr/d, 7 d/wk.
[2] B6C3F1 mice; 0, 10.1, 30.5, 80 ppm H_2S; 6 hr/d, 5 d/wk.

protective of healthy workers exposed for brief periods of time and are therefore not necessarily protective of the general public.

4. Maine Ambient Air Guidelines for hydrogen sulfide

4.1 Acute Ambient Air Guideline

The acute AAG for hydrogen sulfide is 30 ppb based on California's acute REL. This value is determined to be protective against health symptoms such as headaches and nausea, resulting from brief exposure periods (30 minutes to one hour).

ME-CDC has selected CalEPA's REL of 30 ppb as the basis for an acute AAG for three reasons. First, ME-CDC considers potential headaches and nausea among a significant proportion of the population as appropriate public health endpoints for derivation of an acute AAG. There is concern that ATSDR's acute MRL would not be adequately protective of these endpoints for the general population. If 40 ppb is assumed to be a central estimate of an odor annoyance threshold, it follows that a significant fraction of the population may experience headaches and nausea at hydrogen sulfide levels above 30 ppb.

The second reason concerns supporting epidemiological data that levels above 30 ppb may be associated with increased hospital visits for respiratory symptoms. Campagna et al. (2004) reported that hospital visits for respiratory symptoms including asthma among children ≤ 18 years were increased following days on which at least one of the daily rolling 30-minute average hydrogen sulfide concentration exceeded 30 ppb as compared to days where levels did not exceed 30 ppb. It is not possible to determine from this study whether the 30 ppb cut-point for analysis represents a population threshold for response. Nonetheless, it does provide a reason to question the protectiveness of an ambient air guideline above 30 ppb.

The third reason concerns an possible alternative approach to deriving an acute ambient air guideline. ATSDR derived an acute minimal risk level (MRL) of 70 ppb based on a chamber study of ten asthmatics (Jappinen et al., 1990), and has proposed to increase this MRL to 200 ppb based on changing the magnitude of the uncertainty factor used to extrapolate from an apparent LOAEL to a NOAEL. ME-CDC has chosen not to rely on the study by Jappinen et al. (1990) as a basis for deriving an AAG because its limited sample size resulted in low statistical power, making the equivocal findings difficult to interpret.

If ME-CDC were to derive an acute AAG based on the data of Jappinen et al., we would be unlikely to derive a value any higher than 70 ppb and would possibly derive a lower value. While ME-CDC agrees with ATSDR's view that the 2 ppm exposure represents

an observable adverse effect level, we do necessarily agree with the selection of uncertainty factors used to perform intraspecies extrapolation and a LOAEL-to-NOAEL extrapolation. ATSDR applied an uncertainty factor of three for intraspecies variability rather than the conventional factor of ten; this was presumably due to their reliance on data from a chamber study of asthmatics who appropriately can be characterized as a sensitive subpopulation. It should be recognized, however, that patients with severe asthma were excluded from the study for ethical reasons, that the subjects represented a limited age range of 30 to 61 years of age (i.e., no children or elderly asthmatics), and that the number of subjects was small resulting in limited statistical power to detect an effect. We therefore do not agree that this one study of a small group of adults with moderate asthma warrants decreasing the conventional ten-fold uncertainty factor for intraspecies variability to three – especially given the positive associations for children but not adults reported by Campagna et al. (2004).

ATSDR (2004) has also proposed reducing the uncertainty factor of ten used to extrapolate from an apparent LOAEL to a NOAEL. Though not discussed by ATSDR (2004), common arguments for using less than a ten-fold uncertainty factor when relying on a LOAEL are steepness of the dose-response curve and severity of effects (Dourson et al., 1996). With only a single exposure concentration evaluated (2 ppm), the Jappinen et al. study provides no information on the steepness of the dose-response slope for asthmatics, making it difficult to evaluate the likelihood that a three-fold uncertainty factor would likely include the NOAEL. The borderline statistical significance of findings might be argued to support a less than ten-fold uncertainty factor (e.g., since results were of borderline significance, exposure may have been close to the NOAEL), but the small sample size and limited statistical power would present a stronger counter argument. The severity of effects could be argued as mild on average (e.g., see CalEPA, 1999b – Table 7), yet the authors of Jappinen et al. note that for two of the study subjects had changes in airway resistance and specific airway conductance consistent with bronchial obstruction. Consequently, ME-CDC would be hesitant to reduce the uncertainty factor for extrapolating the apparent LOAEL to a NOAEL to a factor of three.

If ME-CDC were to derive an AAG based on the data of Jappinen et al. (1990), the resulting value would likely fall between 20 and 70 ppb, depending on the magnitude of the cumulative uncertainty factor (either 30 or 100).

4.2 Chronic Ambient Air Guideline

ME-CDC selected the EPA IRIS RfC (1 ppb) as the basis for a chronic AAG for two reasons. First, in accordance with current ME-CDC procedures for developing AAGs, preference is given to EPA-IRIS toxicity values over either CalEPA or ATSDR toxicity values. Second, the EPA IRIS value was recently updated and subjected to internal and external peer review as well as opportunity for public comment.

4.3 Averaging Times

The ambient air guidelines of 30 ppb for acute exposure and 1 ppb for chronic exposure are not regulatory standards. Rather, their intended use is to provide health-based benchmarks for interpreting monitoring data. This requires that the guidelines be matched to appropriate averaging times for monitoring data. ME-CDC recommends a 30-minute (0.5 hour) averaging time for use with the acute AAG. While the California acute guideline (30 ppb) is recommended for use with a 1-hour averaging time, a 30-minute averaging time is supported by epidemiological findings (Campagna et al. 2004) and human chamber studies (Jappinen et al., 1990). ME-CDC recommends that the chronic AAG be used in evaluating annual average hydrogen sulfide concentrations (1-year averaging time). The underlying toxicity data (subchronic rodent studies) represent exposures equivalent to 10-15% of an animal's lifespan (i.e., approximately equivalent to several years of a human life).

Table 1: Inhalation exposure guidelines for hydrogen sulfide.

Duration	Value	Basis	Averaging Time	Primary Sources
Acute	30 ppb (42 ug/m^3)	Headaches and nausea in normal subjects	½-hour	CalEPA 1999
Chronic	1 ppb (2 ug/m^3)	Nasal inflammation/lesions in subchronic mouse and rat studies	1-year	US EPA 2003

References

ACGIH 1991. Documentation of the threshold limit values and biological exposure indices. 6th ed. American Conference of Governmental Industrial Hygienists, Cincinnati, OH.

Amoore JE 1985. The perception of hydrogen sulfide odor in relation to setting an ambient standard. Olfacto-Labs, Berkeley, CA: prepared for the CA Air Resources Board.

ATSDR 1999. Toxicological profile for hydrogen sulfide. US Department of Health & Human Services. Public Health Service, Agency for Toxic Substances and Disease Registry.

ATSDR 2004. Draft toxicological profile for hydrogen sulfide update. US Department of Health & Human Services. Public Health Service, Agency for Toxic Substances and Disease Registry.

Bhambhani Y and Singh M 1991. Physiological effects of hydrogen sulfide inhalation during exercise in healthy men. J Appl Physiol 71:1872-7.

Bhambhani Y, Burnham R, Snydmiller G, MacLean I, Martin T. (1994). Comparative physiological responses of exercising men and women to 5 ppm hydrogen sulfide exposure. Am Ind Hyg Assoc J. 1994 Nov;55(11):1030-5.

Bhambhani Y, Burnham R, Snydmiller G, MacLean I, Lovlin R. (1996a). Effects of 10 ppm hydrogen sulfide inhalation on pulmonary function in healthy men and women. J. Occup Environ Med. 1996 Oct;38(10):1012-7.

Bhambhani Y, Burnham R, Snydmiller G, MacLean I, Martin T. (1996b). Effects of 5 ppm hydrogen sulfide inhalation on biochemical properties of skeletal muscle in exercising men and women. Am Ind Hyg Assoc J. 1996 May;57(5):464-8.

Bhambhani Y, Burnham R, Snydmiller G, MacLean I. (1997). Effects of 10 ppm hydrogen sulfide inhalation in exercising men and women. Cardiovascular, metabolic, and biochemical responses. J Occup Environ Med. 1997 Feb;39(2):122-9.

CalEPA 1999. Determination of acute reference exposure levels for airborne toxicants: hydrogen sulfide acute toxicity summary. http://www.oehha.ca.gov/air/acute_rels/pdf/7783064A.pdf

CalEPA 1999b. Air Toxics Hot Spots Program Risk Assessment Guidelines, Part I – The Determination of Acute Reference Exposure Levels for Airborne Toxicants. Mark 1999 (see Table 7). http://www.oehha.ca.gov/air/acute_rels/acuterel.html

CalEPA 2000. Hydrogen sulfide chronic toxicity summary. http://www.oehha.ca.gov/air/chronic_rels/pdf/7783064.pdf

Campagna D, Kathman SJ, Pierson R et al. 2004. Ambient hydrogen sulfide, total reduced sulfur, and hospital visits for respiratory diseases in northeast Nebraska, 1998-2000. J Exp Anal Environ Epidemiol 14:180-7.

CIIT 1983. Chemical Industry Institute of Toxicology. 90-day vapor inhalation toxicity study of hydrogen solfide in B6C3F1 mice. US EPA, Office of Toxic Substance public files. Fiche number 0000255-0. Document number FYI-OTS-0883-0255.

Donham KJ, Knapp LW, Monson R and Gustafson K 1982. Acute toxic exposure to gases from liquid manure. J Occup Med 24:142-5.

Jappinen P, Vilkka V, Marttila O, Haahtela T 1990. Exposure to hydrogen sulphide and respiratory function. Br J Ind Med 47(12):824-8.

Maine CDC (formerly Bureau of Health) 2004. Maine Bureau of Health Ambient Air Guidelines. Prepared by the Environmental and Occupational Health Program (formerly Environmental Health Unit).

Maine DEP 2006. http://www.maine.gov/dep/rwm/wotl/hydrogen.htm

Marttila O, Jaakkola JJK, Parti-Pellinen K, Vilkka V, Haahtela T 1995. South Karelia air pollution study: Daily symptom intensity in relation to exposure levels of malodorous sulfur compounds from pulp mills. Environ Res 71:122-7.

Parti-Pellinen K, Marttila O, Vilkka V, Jaakkola JJK, Jappinen P., Haahtela T 1996. South Karelia air pollution study: Effects of low-level exposure to malodorous sulfur compounds on symptoms. Arch. Environ Health 51(4):315-320.

NIOSH 2004. NIOSH Registry of Toxic Effects of Chemical Substances - http://www.cdc.gov/niosh/rtecs/mx12b128.html#TIHEEC

Osbern LN and Crapo RO 1981. Dung lung: A report of toxic exposure to liquid manure. Ann Intern Med 95:312-4.

OSHA 2004. OSHA (Safety and Health Topics – Hydrogen Sulfide http://www.osha.gov/dts/chemicalsampling/data/CH_246800.html

USEPA 2003. Integrated Risk Information System toxicity summary for hydrogen sulfide. http://www.epa.gov/iris/subst/0061.htm

USEPA 2006. Integrated Risk Information System. http://www.epa.gov/iris/

WHO, 1981. Hydrogen Sulfide. World Health Organization, Environmental Health Criteria No. 19. Geneva.

Xu X, Cho SI, Sammel M et al. 1998. Association of petrochemical exposure with spontaneous abortion. Occup Environ Med 55:31-36.