

Title: Comprehensive Review on Human Health Effects of Pork
Production Emissions – **NPB# 00-173**

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Introduction

The rapid growth of intensive swine operations over the years has resulted in increased community complaints particularly about the problems associated with swine waste. State and federal agencies have been concerned with the industry's impact on the health of nearby residents, the environment, and the overall quality of life in the surrounding community. Malodors emanating from swine waste, anaerobic lagoons, and production facilities have increased the odor-related complaints from residents of surrounding communities where such facilities are more intensified. Production of odorous compounds can also pose potential health problems to both animals and farm workers. Most of the gaseous compounds found in livestock buildings are listed as "hazardous pollutants" in the Clean Air Act (CAA). The presence of odorous and toxic compounds such as ammonia, hydrogen sulfide and other gases in livestock buildings is well documented (Xue, 1998), and government agencies (OSHA and EPA), have set occupational exposure limit levels in the workplace for these compounds. Although all livestock operations generate odors, the odors are more intense from larger intensive swine operations. These operations are wet-based waste management systems with water used to flush the waste periodically from the growing-finishing houses. About 400 organic compounds have been identified from air samples collected in these facilities, and 94 are suspected as being odorous compounds. The most intense and unpleasant odors were caused by p-cresol, carboxylic acids (C₂-C₇), and some ketones (Louhelainen et.al, 2001). In a review, O'Neil and Phillips (1992) summarized the concentrations of 168 compounds identified in livestock air, and their odor detection thresholds, with 30 compounds having odor detection thresholds lower than or equal to 0.001 mgm⁻³. The most important odorous components of livestock house air seem to be the volatile fatty acids, p-cresol, indole, skatole, diacetyl and ammonia, by virtue either of their relatively high concentrations or of their low detection thresholds (O'Neil and Phillips, 1992). A partial listing of some of the odorous compounds detected in livestock waste and air as grouped by their common chemical characteristics is shown in Table 1. (Kim-Yang, 2002).

Numerous articles have been published regarding the adverse respiratory health effect of working in intensive swine housing (Haglund, et. al, 1987; Jacobs, 189; Donham, et. al, 1993; Heederik et. al, 1997; Jolie et. al, 1998). A review of recent studies indicates that the main complaints of health symptoms from odors include: eye, nose, and throat irritation, headache, sputum, cough, nausea, dizziness, fainting, plugged ears, runny nose, breath shortness, chest

tightness, wheezing and drowsiness (Schiffman, 1998). Odors can also potentially affect mood and memory (Donham, 1993; Thu et. al, 1997; Schiffman,1998; Okun, 1999).

Objectives of this study were to conduct a comprehensive literature review of published data dealing with human health effects of emissions generated during pork production with emphasis on odor metabolites emanating from microbial fermentation of swine manure. The review was approached from two angles: (1) Search and compilation of literature on identification of chemical compounds detected in swine production emissions and their physical properties and range in concentrations, (2) Search and compilation of literature on the toxicity of the compounds to humans and animals.

Table 1. The odorous compounds found in swine wastes and air (Kim-Yang, 2002).

Carboxylic acids	Alcohols	Aldehydes & ketones	Nitrogen heterocycles
formic acid	methanol	formaldehyde	indole
acetic acid	ethanol	acetaldehyde	skatole
propanoic acid	n-propanol	propionaldehyde	pyridine
n-butyric acid	n-butanol	acrolein	3-aminopyridine
Iso-butyric acid	2-butanol	butyaldehyde	2-methylpyrazine
n-valeric acid	2-methyl-1-propanol	iso-butyraldehyde	methylpyrazine
isol-valeric acid	3-methylbutanol	2-butenal	trimethylpyrazine
2-methylbutanoic acid	hex-3-ene-1-ol	pentanal	tetramethylpyrazine
			2,3-dihydro-4-methyl-1H-indole
2-methyl-2-butenoic acid	2-methyl-2-pentanol	3-methylbutanal	
n-caproic acid	1-heptanol	hexanal	Others
2-methylpentanoic acid	1-heptanol	2-heptenal	methane
heptanoic acid	2-ethylhexanol	octanal	ammonia
octanoic acid	2-methoxyethanol	nonanal	hydrogen sulfide
decanoic acid	2-ethoxy-1-propanol	2-nonenal	sulfur dioxide
undecanoic acid	2,3-butanediol	2,4-nonadienal	pentane
dodecanoic acid	2-phenylethanol	decanal	hexane
tridecanoic acid	1-decanol	2,4-decadienal	octane
tetradecanoic acid	1-dodecanol	benzaldehyde	benzene
benzenecarboxylic acid	benzyl alcohol	2-propanone	toluene
phenylethanoic acid		2,3-butanedione	xylene
phenylpropanoic acid		methylethylketone	indane
hydrocinnamic acid		3-hydroxy-2-butanone	naphthalene
	Amines	diethylketone propione	methylnaphthalene
	methylamine	cyclopentanone	chloroform
	ethylamine	2-methyl cyclopentanone	hydrazine
	n-propylamine	2-octanone	2-methylfuran
	l-propylamine	amylvinylketone	2-pentylfuran
	pentylamine	acetophenone	2-methylthiophene
	trimethylamine		2,4-dimethylthiophene
	triethylamine		diethyl ether
		Phenolics	1-bromodecane
	Sulfides	phenol	butylated hydroxytoluene
	carbon disulfide	p-cresol	1,1,3-trimethyl-dihydroindene
	carbonylsulfide	m-cresol	2-amino acetophenone
	dimethylsulfide	o-cresol	bis(2-ethylhexyl) phthalate
	diethylsulfide		benzothiazole
		o-methoxyphenol	benzthiazole
	dimethyldisulfide	2,6-dimethylphenol	2,3-dihydro-indole-carboxyaldehyde
	dimethyltrisulfide	3,4-dimethylphenol	
	diethyldisulfide		
		p-ethylphenol	
	dipropyldisulfide	p-(1,1dimethylpropyl)phenol	
Esters			
methylformate			
methylacetate			
ethylformate			
ethyl acetate			
propylacetate			
Iso-propylacetate			
butylacetate			
Iso-butylacetate			
Iso-propylpropionate			
hexadecanoic acid methyl ester			
Thiols			
methanethiol			
propanethiol			
2-propanethiol			

Targeted Airborne Compounds

For this review, emphasis was placed on the major chemical components identified in the microbial fermentation of swine manure including: ammonia, hydrogen sulfide, phenol, p-cresol, indole, skatole, and volatile fatty acids (acetic, propionic, butyric, and valeric). Data was also compiled for dust and endotoxin. The chemical formula, molecular mass and odor detection threshold of these compounds are shown in Table 2. The concentration (mg/m³) of these compounds in air emissions from swine confinements is shown in Table 3.

Table 2. Targeted odorous chemical compounds and gases identified in air from swine production facilities

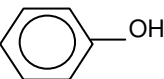
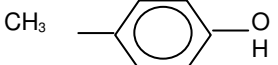
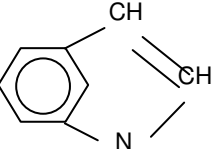
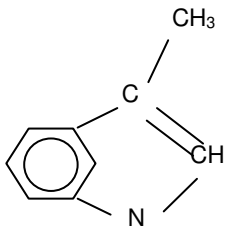
Compound (name)	Chemical formula	Molecular mass	Odor detection threshold (mg/m ³)
Ammonia	NH ₃	17	0.03-37.8
Hydrogen sulfide	H ₂ S	35	0.000051-0.0001
Phenol		94	0.022-4
p-cresol		108	0.00005-0.024
Indole		117	0.0006-0.0071
Skatole		131	0.00035-0.00078
acetic acid	CH ₃ COOH	60	0.025-10
propionic acid	C ₂ H ₅ COOH	74	0.003-0.89
n-butyric acid	C ₃ H ₇ COOH	88	0.0004-42
n-valeric acid	C ₄ H ₉ COOH	102	0.0008-0.12

Table 3. Concentration of targeted airborne compounds identified in swine confinements

Compound	Reported concentrations, (mg/m ³)								
	Ref.1	Ref.2	Ref.3	Ref.4	Ref.5	Ref.6	Ref.7	Ref.8	Ref. 9
Ammonia	18	-	-	2.8-15.3	-	0.01-1.9	-	0.1-18	1-24
Hydrogen sulfide	0.004	-	-	-	-	-	-	-	-
Phenol	0.005	2.5x10 ⁻⁶	-	0.04	0.05	-	-	0.0015-0.065	0.001-0.043
p-Cresol	0.04	4.5x10 ⁻⁶	0.0025-0.025	0.04	0.05	-	0.0073	-	0.002-0.075
Indole	0.003	-	-	-	-	-	-	-	-
Skatole	0.003	-	-	-	-	-	-	-	-
Acetic acid	6.7	1.5x10 ⁻⁶	-	-	-	0.02-0.08	0.08-1.2	0.08-1.2	0.005-0.326
Propionic acid	1.1	2x 10 ⁻⁶	-	-	-	0.002-0.03	0.08-1.2	-	0.004-0.29
n-Butyric acid	0.7	-	-	-	-	0.001-0.01	0.08-1.2	-	0.002-0.617
i-Butyric acid	0.16	1x 10 ⁻⁶	-	-	-	-	0.08-1.2	-	0.001-0.078
n-Valeric acid	0.08	-	-	-	-	-	0.08-1.2	-	0.002-0.063
i-Valeric acid	0.21	1.2x10 ⁻⁶	-	-	-	-	0.08-1.2	-	0.002-0.092

Excerpt from table2, D.H.O'Neil; V.R. Philips. 1992.

(-): means not determined in reference.

1. Schaefer,(1974); 2. Miner, (1975); 3. Schaefer, (1977); 4. Hilliger, (1981);,5.Hartung, (1980),
6. Kowalewshy (1980); 7. Hammond, (1981); 8. Klarenbeek (1982), 9. Van Geelen (1982),

Table 4. Minimal risk level (MRL) of targeted airborne compound

Name	Route	Duration	MRL	Factors	Endpoint	CAS Number
Ammonia	Inhal.	Acute	0.5 ppm	100	Resp.	7664-41-7
		Chronic	0.3 ppm	10	Resp.	
	Oral	Intermediate	0.3 mg/kg/day	100	Other	
p-Cresol	Oral	Acute	0.05 mg/kg/day	100	Neurol.	106-44-5
Hydrogen sulfide	Inhal.	Acute	0.07 ppm	30	Resp.	7783-06-4
		Intermediate	0.03 ppm	30	Resp.	

Agency for Toxic Substances and Disease Registry (ATSDR), 1992

Resp.: Respiratory, Neurol.; Neurology, Inhal.; Inhalation

CAS Number : A accession number assigned by the Chemical Abstracts Service

Endpoint: An observable or measurable biological event or chemical concentration (e.g., metabolite concentration in a target tissue) used as an index of an effect of a chemical exposure.

Table 4. shows the minimal risk level (MRL) for ammonia, p-cresol, hydrogen sulfide, and phenol. Even if a waste contains less than the regulated amounts of hazardous compound it does not mean it is appropriate for release either to the sewer or for disposal.

MRLs are estimates of levels posing a minimal risk to humans which may be of interest to health professionals and citizens alike. The MRLs were derived from human and animal data for short-term and long-term exposure and provide a basis for comparison with levels that people might encounter either in the air, in food or drinking water. If a person is exposed to ammonia at a level below the MRL, it is not expected that harmful (noncancerous) health effects will occur. Because these levels are based only on information currently available, some uncertainty is always associated with them. Also, because the method for deriving MRLs does not use any information about carcinogenicity, an MRL does not imply anything about the presence, absence, or level of risk for cancer.

Table 5. Reference exposure level (REL) of targeted airborne compounds

	Chronic		Acute	
	Inhalation REL (ug/m3)	Target organ	Inhalation REL (ug/m3)	Target organ
Ammonia	200	Respiratory System	3200	Respiratory System
Cresol mixture	600	Nervous system	-	-
Hydrogen sulfide	10	Respiratory System	42	Headache and nausea in response to odor (toxicologic endpoint: respiratory irritation)
Phenol	200	Alimentary system, Cardiovascular system, kidney, nervous system	5800	Respiratory System; eye

Office of Environmental Health Hazard Assessment (OEHHA), 1999

Table 5. shows the REL for ammonia, p-cresol, hydrogen sulfide, and phenol. OEHHA, (1999) recommended exposure limit (REL) of each concentration for each compound for occupational exposure to reduce the risk of developing adverse health effect as a result of occupational exposure. Conversion factors between ppm and mg/m³ in air are shown below in table 6.

Table 6. Conversion Factors

	Property	Value
Ammonia	ppm(v/v) to mg/m ³ in air (20°C)	1 ppm (v/v) = 0.708 mg/ m ³
	mg/m ³ to ppm(v/v) in air (20°C)	1 mg/ m ³ = 1.41 ppm (v/v)
Hydrogen Sulfide	ppm(v/v) to mg/m ³ in air (20°C)	1 ppm (v/v) = 1.40 mg/ m ³
	mg/m ³ to ppm(v/v) in air (20°C)	1 mg/ m ³ = 0.714 ppm (v/v)
Phenol	ppm(v/v) to mg/m ³ in air (20°C)	1 ppm (v/v) = 0.255mg/ m ³
	mg/m ³ to ppm(v/v) in air (20°C)	1 mg/ m ³ = 3.92 ppm (v/v)
Cresol	ppm(v/v) to mg/m ³ in air (20°C)	1 ppm (v/v) = 4.50 mg/ m ³
	mg/m ³ to ppm(v/v) in air (20°C)	1 mg/ m ³ = 0.22 ppm (v/v)

Agency for Toxic Substances and Disease Registry (ATSDR), 1992

Table 7. Concentration-Response Assessment of ammonia, hydrogen sulfide, phenol, and cresols.

	RfC	RfD	NOAEL		LOAEL		Carcinogenicity
			Experimental dose/ Clinical effect	Experimental dose/ Clinical effect	Experimental dose/ Clinical effect	Experimental dose/ Clinical effect	
Ammonia	1E-1 mg/m ³	-	6.4 mg/m ³ (9.2 ppm)	Lack of evidence of decreased pulmonary function or changes in subjective symptomatology	-	-	-
			-	-	17.4 mg/ m ³ (25 ppm)	Increased severity of rhinitis and pneumonia with respiratory lesions	-
Hydrogen sulfide	-	3E-3 mg/kg/day	3.1 mg/kg/day	GI disturbance	15 mg/kg/day	Pig oral toxicity study (subchronic)	-
	1E-3 mg/m ³	-	42.5 mg/m ³ (30.5 ppm)	Inflammation of the nasal mucosa	110 mg/m ³ (80 ppm)	Mouse subchronic inhalation study	
phenol	-	6E-1 mg/kg/day	60 mg/kg/day	Reduced fetal body weight in rats	120 mg/kg/day	Rat oral developmental study	D
o-cresol	-	5E-2 mg/kg/day	50 mg/kg/day	Decreased body weights and neurotoxicity	150 mg/kg/day	90-day oral subchronic neurotoxicity study in rat	C
m-cresol	-	5E-2 mg/kg/day	50 mg/kg/day	Decreased body weights and neurotoxicity	150 mg/kg/day	90-day oral subchronic neurotoxicity study in rat	C
p-cresol	-	withdrawn	-	-	-	-	C

Integrated Risk Information System (IRIS), 1998 ; ACGIH (1998); NIOSH (1992)

(-): None listed

PEL-TWA: permissible exposure limit time-weighted average

In a hazard identification, scientists evaluate all available information about the effects of a toxic compound to estimate the likelihood that a chemical will cause a certain effect in humans. Table 7 shows the concentration-response assessment of ammonia, hydrogen sulfide, phenol, and cresols. Weight of evidence for health problems of concern are classified with 4 categories (A, B, C, and D). Category A. Human carcinogens: good evidence in human studies; category B. Probable human carcinogens: Some evidence in human studies, or two or more good studies; category C. Possible human carcinogens: one good animal

study, no human studies; category D. Inadequate data. The RfC is defined as an estimate, with uncertainty spanning perhaps an order of magnitude of a daily exposure to the human population (including sensitive subgroups) which is likely to be without adverse effects during a lifetime (USEPA, 1990). The derivation of the RfC is based on a complete review of the toxicological literature and encompasses adjustments for exposure duration and dosimetry and utilized uncertainty factors accounted for by specific extrapolations between the population in which the effect was observed and the human population. The critical, usually the most sensitive, effect is the focus of the RfC derivation and for this effect the no-observed-adverse-effect level (NOAEL), or lowest-observed-adverse-effect level (LOAEL) if a NOAEL is not available, is identified (USEPA, 1993). The RfC for hydrogen sulfide is $1\text{E-}3\text{ mg/m}^3$ and was derived from the NOAEL for inflammation of the nasal mucosa in mice (Toxigenics, 1983c, USEPA, 1993). Principal and supporting studies for inhalation RfC of H_2S are based on subchronic 90-day vapor inhalation toxicity study of H_2S in B6C3F1 mice (USEPA, 1983a).

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg/day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime (IRIS, 1991). The RfD of 0.6 mg/kg/day (IRIS, 1998) for phenol is based on a NOAEL of 60 mg/kg/day for developmental effects (decreased fetal weights) observed in rats at a dose of 120 mg/kg/day (Jones Price et al. 1983a). Principal supporting studies for oral RfD of H_2S are based on adult pigs showed digestive disorders when their diet was replaced by a high percentage of dried greens containing H_2S at an approximate intake of 15 mg/kg/day. This dose may be considered a LOAEL (IRIS, 1998). The NOAEL value of 3.1 mg/kg/day is based on data from Watteran et al (1964). They tested pigs for 105 days at three lower doses and compared body weight gain with controls, an intermediate dose of 3.1 mg/kg/day shows no change in body weight gain.

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Ammonia

Ammonia is a colorless gas with a very sharp odor. Exposure to higher than normal amounts, will result in some adverse effects. Ammonia can be detected when it is in the air at levels higher than 50 ppm. Ammonia can be detected as an odor before exposure to a concentration that may be harmful. OSHA has set a short-term (15 minute) exposure limit of 35 ppm for ammonia. NIOSH recommends that the level in workroom air be limited to 50 ppm for 5 minutes of exposure. Zeida et. al, (1994) reported on the incidence of chronic respiratory symptoms between exposure to high concentrations of ammonia and prevalence of chronic cough and bronchitis.

Baur et. al, (1997) show that bronchopulmonary damage caused by high exposure to ammonia may result in chronic obstructive bronchitis, bronchial hyperresponsiveness, and in rare cases also in a combined ventilation pattern. Exposure to ammonia for several years, as might occur in swine confinements is associated with a shift-related decrease of Forced Expiratory Volume (FEV1). Several studies show that ammonia at the Total Lung Volume (TLV) (20 ppm) inconstantly causes severe cough. In this connection, patients frequently cannot perform maximum forced ventilation manoeuvres. This leads to reduced spirometric values which usually do not represent bronchial obstruction. This interpretation is supported by normal values obtained by body plethysmography. Nevertheless, corresponding disorders may be associated with significant health impairment. Altogether, the results point predominantly to long-term adverse effects. Obviously, continuous inflammation of the airways favors the development of chronic bronchitis. Susceptible subjects will respond with airway symptoms, especially cough, upon re-exposure to ammonia.

Inhalation Exposure: There are many reports in the literature of human deaths resulting from inhalation of ammonia (Couturier et al. 1971; Heifer 1971; Sobonya 1977; Close et al. 1980; Price et al. 1983; Burns et al. 1985; Yang et al.1987). Most of these reports are of acute accidental exposure to concentrated aerosols of anhydrous ammonia. A review of the early literature on ammonia toxicity cites short-term exposure to 5000-10,000 ppm as being rapidly fatal in humans (Henderson and Haggard 1927, Mulder and Van der Zalm 1967). Immediate deaths resulting from acute exposure to ammonia appear to be caused by airway obstruction while infections and other secondary complications are lethal factors among those who survive for several days or weeks. Chemical burns and edema of exposed tissues, including the respiratory tract, eyes and exposed skin, are often observed after exposure to lethal levels.

No reports of human death due to intermediate or chronic exposure to ammonia have been reported in the literature.

Respiratory Effects: Ammonia is an upper respiratory irritant in humans. Exposures to levels exceeding 50 ppm result in immediate irritation to the nose and throat. However, tolerance appears to develop with repeated exposure (Verberk, 1977). Thus, human subjects exposed to 100 ppm of ammonia for 6 weeks experienced nose and throat irritation only during the first week (Ferguson et al. 1977). Acute exposure to higher levels (500 ppm) have been shown to increase respiratory minute volume (Silverman et al. 1949). Buff and Koller (1974) suggest that this is due to an effect on "irritant receptors" in the lungs resulting in increased activity of reflex respiratory muscles. Accidental exposures to concentrated aerosols of anhydrous ammonia or high concentrations of ammonia gas have resulted in nasopharyngeal and tracheal burns, airway obstruction and respiratory distress, and bronchiolar and alveolar edema (Couturier et al. 1971; Heifer 1971; Taplin et al. 1976; Sobonya 1977; Hatton et al. 1979; Close et al. 1980; Price et al. 1983; Burns et al. 1985). An acute inhalation MRL of 0.5 ppm was derived from the Verberk (1977) study, and a chronic inhalation MEL of 0.3 ppm was derived from the Holness et al. (1989) study. Studies in animals have demonstrated similar dose-effect and duration effect patterns for the respiratory tract. Acute exposures to low concentrations of ammonia (1000 ppm) irritate the upper respiratory tract whereas exposures to high concentrations (4000 ppm) result in severe damage to the upper and lower respiratory tract and alveolar capillaries (Stombaugh et al. 1969; Coon et al. 1970; Mayan and Merilan 1972; Richard et al. 1978a,b; Kapeghian et al. 1982; Schaerdel et al. 1983). Prolonged or repeated exposures to lower levels (150 ppm) produce inflammation and lesions of the respiratory tract (Coon et al. 1970; Broderson et al. 1976).

Cardiovascular Effects: Acute exposure to highly concentrated aerosols of ammonia may cause elevated pulse and blood pressure and cardiac arrest in humans (White 1971; Hatton et al. 1979; Montague and Macneil 1980). These effects do not occur after acute exposure to 500 ppm ammonia or repeated exposure to 100 ppm ammonia (Silverman et al. 1949; Ferguson et al. 1977).

Gastrointestinal Effects: Exposure to highly concentrated aerosols of anhydrous ammonia can produce burns of the lips, oral cavity, and pharynx, along with edema of these areas (Levy et al. 1964; Hatton et al. 1979; Stroud 1981; Ward et al. 1983; Price et al. 1983; Yang et al. 1987).

Hematological Effects: Cyanosis, elevated white blood cell count, and pulmonary artery thrombosis have been observed in humans exposed to highly concentrated aerosols of

anhydrous ammonia (Voisin et al. 1970; White 1971; Taplin et al. 1976; Sobonya 1977; Ward et al. 1983).

Musculoskeletal Effects: Spasms of muscles of the extremities have resulted from acute exposure of humans to highly concentrated aerosols of anhydrous ammonia (White 1971).

Hepatic Effects: Hemorrhagic necrosis of the liver was observed in an individual exposed to a lethal concentration of ammonia vapors for a short period of time (Heifer 1971). Hepatic effects are usually not seen in animals exposed to ammonia.

Dermal/Ocular Effects: Ammonia gas and aerosols of anhydrous ammonia are dermal and ocular irritants in humans and animals.

Other Systemic Effects: A study was reported in which human subjects were exposed continuously to low levels of ammonia (3-7 ppm) for up to 37 days (Kalandarov et al. 1984). Although detailed observations were not presented, apparently this exposure was tolerated without obvious symptoms of ill health.

Immunological Effects: Secondary infections often complicate the clinical outcome of burns and respiratory lesions related to exposure to highly concentrated aerosols of anhydrous ammonia (Sobonya 1977; Taplin et al. 1976). However, there is no evidence that the decreased resistance represents a primary impairment of the immune system in humans. A significant increase in mortality was observed in mice exposed to ammonia for 168 hours followed by exposure to the LD₅₀ of *Pasteurella multocida* (Richard et al. 1978a).

Neurological Effects: Case reports of accident victims exposed to highly concentrated aerosols of anhydrous ammonia describe blurred vision, diffuse nonspecific encephalopathy, loss of consciousness, and decreased deep tendon reflexes (White 1971; Hatton et al. 1979). The lethargy has been reported following acute exposure to lower levels (100-500 ppm). Acute exposure to low levels of ammonia (100 ppm) has been shown to depress free-access wheel running behavior in rodents (Tepper et al. 1985).

Cancer: Carcinogenic potential of ammonia by the inhalation route has not been assessed in humans or animals. One case report was found of a white male who developed epidermal carcinoma of the nasal septum 6 months after being badly burned by accidental contact with a refrigeration ammonia-oil mixture (Shimkin et al. 1954). If ammonia played a role in the development of this cancer, it was most likely due to dermal exposure, not inhalation, since the substance was oily. However, some of the ammonia was probably inhaled into the nasal vestibule and absorbed into nasal mucous.

Table 8 shows the effects on human health from breathing ammonia during short term and long term exposure. Table 9 shows the effect on pig health from breathing ammonia during short term exposure.

Table 8. Effects on Human Health from Breathing Ammonia

Short-term Exposure (less than or equal to 14 days)			
Levels in Air		Length of Exposure	Descriptions of Effects
ppm	mg/m ³		
0.5	0.354	Less than 1 day 30 minutes less than 30 minutes	- Minimal Risk Level
50	35.4		- Slight, temporary eye and throat irritation and urge to cough
500	354		- Increased air intake into lungs; sore nose and throat
5000	3540		- Kills quickly
Long-term Exposure (greater than 14 days)			
Levels in Air		Length of Exposure	Descriptions of Effects
ppm	mg/m ³		
0.3	0.2124	6 weeks	- Minimal Risk Level
100	70.8		-Eyes, nose and throat irritation

Agency for Toxic Substances and Disease Registry (ATSDR), 1992

Table 9. Effects on Pig Health from Breathing Ammonia

Short-term Exposure (less than or equal to 14 days)			
Levels in Air		Length of Exposure	Descriptions of Effects
ppm	mg/m ³		
50	35.4	3 Hours	- Coughing, eye, mouth, and nose irritation, poor weight gain and food intake in pigs

Agency for Toxic Substances and Disease Registry (ATSDR), 1992

The symptoms in human after exposure to ammonia gas at 5 to 20 ppm in air are eyes, upper respiratory irritation (Chapin et. al, 1998). The symptoms in swine after exposure to ammonia gas less than 50 ppm in air are increased susceptibility to pneumonia and other respiratory problems; less than 100 ppm are loss of appetite, sneezing; and greater than 300 ppm are mouth and snout irritation, shortness of breath (Chapin et. al, 1998).

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Hydrogen Sulfide

Hydrogen sulfide is a colorless, gas under normal conditions. It is commonly known as hydrosulfuric acid, stink damp, and sewer gas. Hydrogen sulfide smells like rotten eggs. People can smell hydrogen sulfide at concentrations as low as 0.5 ppb in air. However, olfactory fatigue can occur at concentrations of 100 ppm or greater causing a loss of odor perception, which makes it very dangerous (Leonardos et.al. 1969). Odor threshold on water is 0.000029 ppm and on air is 0.5 ppb. Hydrogen sulfide is a flammable gas and it is heavier than air. It is an extremely toxic gas and leading cause of sudden death in the workplace. Absorption of H₂S readily occurs mainly through the nasal and lung mucosa but absorption through the skin is limited.

Occurrence and Exposure: Workers on farms with manure storage pits or landfills can also be exposed to higher levels of hydrogen sulfide than the general population. Hydrogen sulfide enters your body primarily through the air that is breathed. Breathing hydrogen sulfide at concentrations greater than 500 ppm can be fatal within just a few breaths. Death is usually preceded by a loss of consciousness after one or more breaths, although a loss of consciousness does not necessarily mean that death will follow. Hydrogen sulfide is considered to be a “broad spectrum’ poison. This means that it can poison several different systems in the body. This variety of activity may be the reason that no single antidote, or treatment, has been found for hydrogen sulfide poisoning. Deaths due to breathing in large amounts of hydrogen sulfide have been reported in a variety of different work settings, including sewers, animal processing plants, waste dumps, sludge plants, oil and gas well drilling sites, and tanks and cesspools (ATSDR, 1994).

Symptoms: Exposed to lower concentrations of hydrogen sulfide, will produce symptoms, such as eye irritation, sore throat and cough, shortness of breath, and fluid in the lungs, that will usually subside within a few weeks. Other changes such as memory problems may occur. Breathing in hydrogen sulfide on a long-term basis may result in fatigue, loss of appetite, headaches, irritability, poor memory, and dizziness. Hydrogen sulfide has not been shown to cause cancer in humans, and its ability to cause cancer in animals has not been studied thoroughly. Hydrogen sulfide has not been classified for its ability to cause or not cause

cancer. There is some evidence that exposure to hydrogen sulfide may lead to an increase in spontaneous abortions in humans. The major metabolic pathway for hydrogen sulfide in the body is oxidation of sulfide to sulfate, with the sulfate being extracted in the urine (Beauchamp et al. 1984).

There is clearly less airborne ammonia and hydrogen sulfide in well-functioning compost swineries than in the poorly functioning ones. In one composting swinery, the hydrogen sulfide level was as high as 15 mg/m³ during turning work (Louhelainen et.al, 2001). Hog confinement workers are at risk of hydrogen sulfide poisoning. These and other conditions seen in confinement workers are described, and health management procedures are outlined (Von Essen and Donham,1999). Table10. shows the effects of exposure in humans at various concentrations of hydrogen sulfide in air.

Table 10. Clinical effects based on level of hydrogen sulfide

Clinical Effect	Level of Hydrogen Sulfide	
	ppm	mg/m ³
Odor Perception threshold	0.003-0.02	0.004-0.028
Offensive odor of rotten eggs	<30	<42
Offensive odor (sickening sweet)	>30	>42
Occupational Exposure Limit	10	14
Serious eye injury	50-100	70-140
Olfactory paralysis	150-200	210-350
Pulmonary edema, threat to life	300-500	420-700
Strong nervous stimulation of respiration	500-1,000	700-1,400
Respiratory paralysis, immediate collapse, death	1,000-2,000	1,400-2,800

US. Environmental Protection Agency (USEPA), 1993

At sufficiently high concentrations (>1,000 ppm; 1,390 mg/ m³), H₂S is rapidly fatal to humans, causing respiratory paralysis and apparent inhibition of cellular respiration. At levels between 500 and 1,000 ppm (694 and 1,390 mg/ m³), a period of rapid breathing (hyperpnea) is followed by cessation of breathing (apnea) and death. Damage to organs and the nervous system can result from the anoxia caused by the depression of cellular metabolism at levels above 250 ppm. At lower concentrations (50 to 100 ppm: 70 to 139 mg/ m³), the immediate and prolonged effects are irritation with inflammation of mucous membranes, particularly of the eye and respiratory tract (USEPA, 1993). Though ambient concentrations tend to be below those considered harmful to human health, no long-term, low-level epidemiological

studies have been performed to determine whether H₂S causes pulmonary changes similar to those caused by other irritant gases such as oxides of nitrogen and sulfur. At very low concentrations, offensiveness of odor, with mostly subjective reactions to stench, is the dominant effect. Also, neurological symptoms such as visual hallucination, and short-term memory loss have been recently reported at levels thought to be not harmful.

No human health data and practically no experimental data on long-term exposures at low levels exist. No epidemiological studies relating to cancer, teratogenesis, or reproductive effects have been performed (USEPA, 1993). Table 11 shows the levels of significant exposure by inhalation of hydrogen sulfide. Some regulations and recommendations for hydrogen sulfide include the following: Environmental Protection Agency (EPA) has established that hydrogen sulfide is a regulated toxic substance and is a hazardous substance as defined under the Federal Water Pollution Control Act. OSHA has established an acceptable ceiling concentration of 20 ppm for hydrogen sulfide in the workplace, with a maximum level of 50 ppm allowed for 10 minutes maximum duration if no other measurable exposure occurs. NIOSH has set a maximum Recommended Exposure Limit (REL), ceiling value (10 minutes) of 10 ppm.

Table 11. Levels of significant exposure by inhalation of hydrogen sulfide

	Exposure Time(min)	System	NOAEL (ppm)	LOAEL
				Less Serious
Human	>16	Resp.	5 M	-
		Cardio.	5 M	
		Metab.	2 M	
	30	Resp.	5	-
		Cardio.	5	
	15	Resp.	10	-
		Cardio.	10	
	2x30	Cardio.	-	10
		Metab.	-	
	30	Resp.	-	-
Intermediate exposure	17day 24hr/d	Resp Gastro Hepatic Renal Ocular Body Wt	8.5	-
Systemic				
pig				

(-): Not determined

Agency for Toxic Substances and Disease Registry (ATSDR), 1994.

Table 12. Symptoms in human and swine after exposure to hydrogen sulfide

Concentration		Symptoms
(ppm)	mg/m ³	
Human		
10	14	Red, irritated eyes
20	28	Eyes, upper respiratory irritation
50 to 100	70 to 140	Headaches, nausea, vomiting, diarrhea
200	280	Fatigue, paralysis of sense of smell, dizziness
500	700	Unconsciousness, nervousness
>600	>840	Immediate death
Swine		
20	28	Fear of light, loss of appetite, nervousness
150 to 200	210 to 280	Pulmonary edema, shortness of breath, unconsciousness, possible death

Chapin, (1998)

Table 12 shows the symptoms in human and swine after exposure to hydrogen sulfide.

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Phenol

Phenol is a colorless-to-white solid when pure; however, the commercial product, which contains some water, is a liquid. Phenol has a distinct odor that is sickeningly sweet and tarry. Most people begin to smell phenol in air at about 40 parts of phenol per billion parts of air (ppb), and begin to smell phenol in water at about 1-8 ppm of water.

Occurrence and Exposure: Phenol is not a very volatile compound. Consequently, most toxic effects occur from dermal and oral exposure (Sullivan and Krieger, 1992). Phenol is well absorbed from the gastrointestinal tract and through the skin of animals and humans. It is metabolized principally by conjugation (by sulfation and glucuronidation) with a minor oxidation pathway leading to quinone-related reactive intermediates which bind covalently to protein and are detoxified by conjugation with glutathione. Topically applied phenol is a skin irritant, and systemic toxicity is seen in liver and kidney after topical and oral dosing. Phenol is a basic feedstock for the production of phenolic resins, bis-phenol A, caprolactam, chlorophenols and several alkylphenols and xlenols. Phenol is also used in disinfectants and antiseptics. Occupational exposure to phenol has been reported during its production and use, as well as in the use of phenolic resins in the wood products industry. It has also been detected in automotive exhaust and tobacco smoke.

Symptoms: Observed effects from acute exposure may include; shock, delirium, coma, pulmonary distress, phenolic breath, scanty/dark urine, and death. Chronic exposure usually results in major damage to the liver, kidneys and eyes. A number of effects from breathing phenol in air have been reported in humans. Short-term effects reported include respiratory irritation, headaches, and burning eyes. Chronic effects of high exposures included weakness, muscle pain, anorexia, weight loss, and fatigue. Effects of chronic low-level exposures included increases in respiratory cancer, heart disease, and effects on the immune system. Irritation to skin and mucous membranes, corrosion, disturbances of the central nervous system, and hematologic disorders are described as the main symptoms of industrial poisoning by phenol and related compounds (HazDat. 1998).

Toxicity: Phenol is toxic with a probable oral lethal dose to humans of 50-500 mg/kg (HSHB, 1998). Some individual may be hypersensitive with lethality or serious effects at very low

exposures. After any route of exposure including skin can occur rapid absorption and severe systemic toxicity (HSHB, 1998). It is not known if phenol causes cancer in humans. However, cancer has been shown to occur in mice when phenol was applied to the skin several times each week during the whole lifetime of the animal. Animal carcinogenicity data is inadequate. In carcinogenicity bioassays with B6C3F1 mice and F344 rats were administered phenol in the drinking water at concentrations of 0, 2500, 5000 ppm for 103 weeks. Histopathological examination and statistical analyses revealed no phenol related toxic or carcinogenic effects in mice (IRIS,1998). When applied in combination with certain cancer-causing chemicals, a higher rate of cancer occurs than when the carcinogens are applied alone. The International Agency for Research on Cancer (IARC, 1989) considers phenol not classifiable as to its carcinogenicity in humans. The IARC classification for phenol is Group 3, not classifiable with regard to its carcinogenicity to humans (IARC 1989, ACGIH, 2000). The EPA cancer classification for phenol is D, not classifiable as to human carcinogenicity (IRIS 1998), which means that there is inadequate evidence in humans and in experimental animals for the carcinogenicity of phenol. The EPA reference dose (RfD) of 0.6 mg/kg/day (IRIS 1998) is based on a Lowest-Observed-Adverse-Effect Level (NOAEL) of 60 mg/kg/day for developmental effects (decreased fetal body weights) observed in rats at a dose of 120 mg/kg/day (Jones-Price et al. 1983a). Immediately dangerous to life or health is 250 ppm (NIOSH, 1997).

Occupational Exposure Standards: OSHA has set a limit of 5 ppm in air to protect workers during 8-hour workshifts of a 40-hour workweek. NIOSH recommended exposure limit (REL) for 10 hr time-weighted avg. (TWA) is 5 ppm (19 mg/cu m), and REL for Ceiling Value (15 Min) is 15.6 ppm (60 mg/cu m) for skin. (NIOSH,1997). It means that the concentration in workroom air be limited to 5 ppm over 10 hour work shift, and that the workroom air concentration should not exceed 16 ppm during a 15minute period. These workplace air limits assume no skin contact with phenol. EPA has determined that the level of phenol in ambient water (lakes, streams) should be limited to 3.5 mg/L in order to protect human health from the potential toxic effects of exposure to phenol through ingestion of water and contaminated aquatic organisms. The permissible exposure limit time-weighted average (PEL-TWA) is 5 ppm (OSHA 1997). ACGIH (1998) and NIOSH (1992) also recommend a TWA exposure limit of 5 ppm for occupational exposure. The lifetime health advisory for phenol in water is 4 mg/L (EPA 1996a).

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P-Cresol

Three types of closely related cresols exist: ortho-cresol, meta-cresol, and para-cresol. Cresols do not evaporate quickly from water, but in rivers and lakes, they can be degraded quickly by bacteria. Dissolved cresols can pass through soil into under ground water sources. This may be a problem at hazardous waste sites where cresols are buried. Cresols in air quickly decomposes and break down into smaller chemicals, some of which irritate the eyes. Cresols can enter the body tissues quickly if worker breathe air containing cresol gas or mist (droplets of cresol-containing liquid in the air), or allow skin to come into contact with substances that contain cresols. Most of the cresols that the enter body are converted to other substances and excreted from the body in the urine within 1 day. The health effects data for p-cresol were reviewed by the U.S. EPA RfD/RfC Work Group and determined to be inadequate for the derivation of an inhalation RfC. The verification status for this chemical is currently not verifiable.

Occurrence and Exposure: Phenolic compounds such as phenols and p-cresol are produced from the microbial degradation of tyrosine and phenylalanine in the intestinal tract of animals (Ishaque et. al, 1985). P-cresol is the predominant metabolite of the volatile phenolic and aromatic metabolite excreted in swine feces and urine, with the urine accounting for about 90% of its total daily excretion, the remainder being made up by phenol and, to a lesser extent, 4-ethylphenol (Yokoyama et. al, 1982). Young pigs produce and excrete substantially higher amounts of p-cresol than other livestock and humans, presumably due to a more active bacterial activity in their intestinal tract. p-Cresol originates from two different sources. Urinary excretion of p-cresol produced in the intestinal tract of the pig is in the form of the glucuronide conjugate that undergoes deconjugation by bacterial glucuronidase activity once it is voided. This would account for p-cresol being present in urine contaminated bedding, dust, and under slatted floors of buildings. p-Cresol also is produced *de novo* during storage of swine manure slurry by anaerobic fermentation. This is contributory to the malodor of swine manure slurry. Because of its extremely low odor detection threshold (0.000011-0.0005 mg/m³), it is a major contributor of the characteristic malodor associated with swine manure. A review of the chemical composition of ventilation air exhausted from piggeries showed that p-cresol is the most commonly detected compound. p-Cresol production and use as a solvent, disinfectant and chemical intermediate in the production of synthetic resins may result in its release to the environment through various waste streams. p-Cresol is also released to the environment

through automobile exhaust and tobacco smoke. Cresols, including p-cresol, are widespread in nature occurring in many plants and trees. Vapor-phase p-cresol will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 8 hours. p-Cresol is expected to biodegrade in water based on reported half-lives of 4 and 6 days in Lake Tahoe, CA water. p-Cresol is not expected to undergo hydrolysis. Occupational exposure to p-cresol may occur through inhalation and dermal contact with this compound at workplaces where p-cresol is produced or used. The general population may be exposed to p-cresol via inhalation of ambient air and dermal contact with this compound.

Symptoms: Brief exposure to cresol 6 mg/m³ resulted in irritation of the throat and nose, nasal constriction, and dryness (Uzhdavini et. al, 1972). It is possible that some of the adverse effects in humans, such as kidney problems and anemia, might occur at lower concentration if exposure occurs over a longer time period. Effects on the nervous system, such as loss of coordination and twitching of muscles, are produced by low levels of cresols in animals, but it is not known whether low levels also cause such effects in humans.

Toxicity: p-Cresol is a possible human carcinogen based on an increased incidence of skin papillomas in mice in an initiation-promotion study. The three cresol isomers produced positive results in genetic toxicity studies both alone and in combination. Human carcinogenicity data is inadequate, only anecdotal data available. Garrett (1975) reported two cases of multifocal transitional cell carcinoma of the bladder following chronic occupational exposure to cresol and creosote. Wodyka (1964), as cited in U.S. EPA, (1979) described a squamous cell carcinoma of the vocal cords in a petroleum refinery worker with a long history of exposure to cresol, dichlorooctane, and chromic acid. The effects of o-cresol and p-cresol, which have similar toxicities, are generally described prior to those of m-cresol, which is somewhat less toxic. Cresols may enhance the ability of carcinogenic chemicals to produce tumors in animals. Cresols have some ability to interact with mammalian genetic material in the test tube, but they have not been shown to cause cancer in humans or animals. The EPA has determined that cresols are possible human carcinogens. Animal studies suggest that cresols probably would not produce birth defects or affect reproduction in humans. EPA determined cresols (ortho-, meta-, and para-) as possible human carcinogens, and p-cresol is most toxic of all three (ACGIH, 1986).

Animal carcinogenicity data is also limited. Four skin application studies which had positive results are reported; however, the final two studies are of limited value due to the application of a mixture of chemicals. In a study by Boutwell and Bosch (1959), female Sutter

mice (27-29/group; 2-3 months of age) received a single dermal application of 25 μ L of 0.3% dimethylbenzanthracene (DMBA) in acetone as the initiator, followed 1 week later by 25 μ L of 20% (v/v) o-, m- or p- cresol in benzene twice weekly for 12 weeks. Skin papillomas were evaluated at 12 weeks. Many of the cresol-treated mice died, presumably of cresol toxicity. There was no mortality or evidence of skin papillomas in the benzene control group (benzene weekly after DMBA initiation). The numbers of surviving mice that developed skin papillomas at 12 weeks were as follows: 10/17, o-cresol; 7/14, m-cresol; and 7/20, p-cresol. None of the 12 mice in the benzene control group died or developed skin papillomas. In an acute dermal toxicity study, technical grade o-, m-, and p-cresol caused severe skin damage on at least 2/6 shaved, female, albino New Zealand rabbits within 4 hours of application of 2000 mg/kg of technical grade cresol, 890 mg/kg of o-cresol, 2830 mg/kg of m-cresol, or 300 mg/kg p-cresol (Vernot et al. 1977). Studies on the induction of unscheduled DNA synthesis showed p-cresol to be positive in human lung fibroblast cells in the presence of hepatic homogenates (Crowley and Margard, 1978), the mixture of the three isomers to be weakly positive in primary rat hepatocytes (Litton Bionetics, 1980d), and o-cresol to be negative in rat hepatocytes (Litton Bionetics, 1981e). In cell transformation assays using BALB/3T3 cells, a mixture of 3 cresol isomers was positive (Litton Bionetics, 1980d), and o-cresol was negative. Positive mutagenic responses were found at noncytotoxic doses (Litton Bionetics, 1980e). A mixture of the three isomers was mutagenic in a mouse lymphoma forward mutation assay with mammalian liver homogenates, while o-cresol was not mutagenic both with and without liver homogenates (Litton Bionetics, 1980b, 1981b). No isomer, when tested individually, induced sister chromatid exchanges (SCEs) in vivo, but the mixture of the three isomers induced SCEs in Chinese hamster ovary (CHO) cells in vitro (Litton Bionetics, 1980c). Only o-cresol induced SCEs in human lung fibroblasts (Cheng and Kligerman, 1984) and CHO cells (Litton Bionetics, 1981c). In a screening test for putative carcinogens, infectious virus particles were produced from SV40-transformed weanling Syrian hamster kidney cells exposed to m-cresol (Moore and Coohill, 1983).

Occupational Exposure Standards: The occupational exposure limit for 8-hour workdays over a 40-hour per week is 22 milligrams of cresols per cubic meter of air (22 mg/ m³), which is equivalent to about 5ppm. The Occupational Safety and Health Administration (OSHA) has set the legal p-cresol permissible exposure limit (PEL) for 8 hr Time Weighted Avg. (TWA) at 5 ppm (22 mg/ m³). PEL is an allowable exposure level in workplace air averaged over an 8-hour shift. Threshold Limit Values (TLVs) for p-cresol is 5ppm (with skin as end point) represent the average concentration in mg/m³ for an 8-hour workday and a 40-hour work week to which nearly

all workers may be repeatedly exposed, day after day, without adverse effect (ACGIH, 1998). Recommended Exposure Limit (REL) for p-cresol is a TWA of 2.3 ppm (10 mg/m³) based on an 10-hour workshift (NIOSH, 1997). Inhalation exposure data were severely limited, but an inhalation AIC of 7.14 mg/day was estimated based on the TLV (EPA working group, 1984. EPA PG: 29, IP: VI: EPA/540/1-86/050).

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Indole and Skatole (3-methylindole)

Indole

Indole has an intense fecal odor, and its LD₅₀ orally in rats is 1 g/kg (Merck Index, 1983). The formation of indole and skatole by bacteria occurs in the rumen and may involve similar reactions in manure. The deamination and decarboxylation reactions associated with the degradation of tryptophan and tryptosine result in the formation of indole and 3-methylindole which are toxic. Formation of 3-methylindole results from fermentation of tryptophan to indoleacetic acid, with subsequent decarboxylation of indoleacetic acid to 3-methylindole by a *Lactobacillus* sp. in the intestinal tract. The 3-methylindole causes acute pulmonary edema and emphysema in ruminants as a result of mixed function oxidase metabolism in tissues. The 3-methylindole is also the cause of naturally-occurring acute bovine pulmonary edema and emphysema after abrupt pasture change (Carlson and Breeze, 1984).

Occupational exposure may be through inhalation and dermal contact with this compound at workplaces where indole is produced or used (NIOSH, 1989). The general population will be exposed to indole via inhalation of ambient air, inhalation of tobacco smoke, ingestion of food, and dermal contact with vapors, food and other products such as perfumes containing indole (NIOSH, 1983). Indole production and use as a chemical intermediate, a perfume fixative, a synthetic flavor and possibly as a kairomone (a volatile chemical released by a plant to attract phytophagous insects) may result in its release to the environment through various waste streams. Indole is released directly to the environment as a component of tobacco smoke and occurs naturally in coal tar, jasmine oil and orange-blossom oil. If released to the atmosphere, indole will mainly exist in the vapor phase based on an experimental vapor pressure of 0.0122 mm Hg at 25 deg C. Vapor-phase indole is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals, nitrate radicals, and ozone with estimated half-lives of about 2 to 3 hours, < 1 minute, and 6 hours, respectively. Indole should not volatilize from water surfaces based on its Henry's Law constant. Occupational exposure may occur through inhalation or dermal contact at workplaces where indole is produced or used.

Skatole (3-methylindole)

Skatole is a constituent of feces, beetroot, nectandra wood, and coal tar, and has a fecal odor with brownish color (Merck Index, 1983). No occupational exposure data for 3-methylindole are currently available. Limited monitoring data indicate that there may be instances of contaminated groundwater resulting in the general population possibly being exposed to 3-methylindole primarily through ingestion of contaminated groundwater and

contaminated food (HazDat. 1998). Skatole is also produced in cigarette smoke by pyrolysis of tryptophan, and industrially used as a fixative in the perfume industry and as a food additive and may be released to the environment from a variety of waste streams. It has an extrapolated vapor pressure of 0.005 mm Hg at 25 °C and exists solely in the vapor phase in the ambient atmosphere. Skatole has low mobility in soil. In water, skatole may adsorb to sediment or particulate matter based upon its Koc value. Volatilization from water surfaces is expected based upon its estimated Henry's Law constant. When exposed to natural sunlight 3-methylindole may undergo aqueous photo-oxidation.

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Volatile Fatty Acid

Volatile organic compounds (VOCs) including the volatile fatty acids, (VFA) are substances containing carbon and different proportions of other elements such as hydrogen, oxygen, fluorine, chlorine, bromine, sulfur, or nitrogen; these substances easily become vapors or gases. According to Schiffman (1998), low concentrations of multiple VOCs can result in health consequences that a single low-level VOC would not cause. In the review paper, Okun (1999) state that odors can have a lingering effect in the body. VOCs are absorbed directly by the body into the bloodstream and fatty tissues by way of gas exchange in the lungs. Once absorbed these odorants are slowly released from the bloodstream via air expired from the body. When expired, the olfactory receptors are activated. Some of the compounds found in the waste plume, when absorbed in the body, can be transmitted to the brain through the nasal route (Monath et.al, 1983).

Acetic acid

Acetic acid is colorless liquid or crystals. It has pungent odor, and is corrosive to metals (NIOSH, 1994). Acetic acid occurs ubiquitously and is a normal metabolite in animals; therefore, the general population is continually exposed to the compound. Primary routes of exposure to the general population are through consumption of foods and inhalation of air. Occupational exposure occurs through inhalation and dermal contact (NIOSH,1983). The vapor of acetic acid is irritating to the eyes and nose, causing lacrimation and hyperemia (Grant, 1986). Eye irritation has been noted at a concentration below 10 ppm (Mackison, et.al, 1981). A case study is reported where an individual ingested 200 ml of an 80% solution of acetic acid. The patient survived the intoxication by use of hemodialysis and intensive care therapy. Repeated shock due to myocardial infarction and massive intestinal bleeding led to an organic brain psychosyndrome (Hakenbeck et. al, 1984).

Workers exposed for a number of years to concentration of up to 200 ppm have been found to suffer from palpebral edema with hypertrophy of lymph nodes, conjunctival hyperemia. With repeated exposures, workers may complain of digestive disorders with pyrosis and constipation, skin on palm of hands become dry, craked and hyperkeratotic (International labour office, 1983). Bronchopneumonia and pulmonary edema may develop following acute overexposure. Chronic exposure may result in pharyngitis and catarrhal bronchitis. Ingestion, though not likely to occur in industry, may result in penetration of the esophagus, bloody vomiting, diarrhea, shock, hemolysis, and hemoglobinuria followed by anuria (Sittig, 1981). Based on a study of 5 workers exposed 7-12 years to high

concentrations of acetic acid (80-200 ppm at peak concentration), the principal findings were blackening and hyperkeratosis of the skin (Patty, 1963). When workers exposed for 7-12 years at concentration of 60 ppm, and additional one hour daily at 100-200 ppm, conjunctivitis, bronchitis, pharyngitis and erosion of exposed teeth were observed (HSDB, 1998). Employees with chronic respiratory, skin, or eye disease are at increased risk from acetic acid exposure. Employees should be screened for history of chronic respiratory, skin and, eye diseases which might place the employee at an increased risk from acetic acid exposure. (Mackison et. al, 1981). LD50 for guinea pig and mouse inhalation is 5000 ppm/1 hr (Verschueren, 1983), and LD50 for rabbit rectal is 600 mg/kg (ITII, 1982).

Occupational Exposure Standards: The Occupational Safety and Health Administration (OSHA) has set the legal acetic acid permissible exposure limit (PEL) 8-hr TWA at 10 ppm (25 mg/ m³). PEL is an allowable exposure level in workplace air averaged over an 8-hour shift. Threshold Limit Values: 8 hr Time Weighted Avg (TWA) 10 ppm; Short Term Exposure Limit (STEL) 15 ppm. (ACGIH,1998). Threshold Limit Value (TLV) is recommended guidelines for occupational exposure to airborne contaminants published by the American Conference of Governmental Industrial Hygienists (ACGIH). TLVs represent the average concentration in mg/m³ for an 8-hour workday and a 40-hour work week to which nearly all workers may be repeatedly exposed, day after day, without adverse effect. Recommended Exposure Limit (REL) for acetic acid is a TWA of 10 ppm (25 mg/m³) based on a 10-hour workshift (NIOSH, 1997). Short-Term STEL is the maximum concentration to which workers can be exposed for up to 15 min continually. The daily TLV-TWA may not be exceeded. Recommended STEL exposure limit for acetic acid is 15 ppm (37 mg/ m³) (NIOSH, 1997), and immediately dangerous to life or health: 50 ppm (NIOSH,1997).

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Propionic Acid

Propionic acid is used to control fungi and bacteria in drinking water for livestock and poultry, so it is expected to result in its direct release to the environment. It is also released to the environment with the manufacture and use of coal-derived and shale oil liquid fuels and during the disposal of coal liquefaction and gasification and wood preserving chemical waste byproducts. Textile mills, sewage treatment facilities, municipal and industrial landfills, hazardous waste sites, and gasoline and diesel fueled engines can release propionic acid to the environment. If released to air, a vapor pressure of 3.53 mm Hg at 25 °C indicates propionic acid will exist solely as a vapor in the ambient atmosphere. Vapor-phase propionic acid will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 11 days. Photolysis of propionic acid is not expected to be an important fate process. Propionic acid is miscible in water and monitoring data has shown that physical removal from air by wet deposition is an important removal mechanism. If released to soil, propionic acid is expected to have very high mobility based upon an estimated Koc of 1.2. Volatilization from moist soil surfaces is not expected to be an important fate process. Propionic acid may volatilize from dry soil surfaces based upon its vapor pressure. Biodegradation is likely to be the most important removal mechanism of propionic acid from soil. If released into water, propionic acid is not expected to adsorb to suspended solids and sediment in water based upon the estimated Koc. Biodegradation is

likely to be the most important removal mechanism of propionic acid from water. Occupational exposure to propionic acid may occur through inhalation and dermal contact with this compound at workplaces where propionic acid is produced or used. The general population may be exposed to propionic acid via inhalation of ambient air, ingestion of food and drinking water, and dermal contact with this compound and other consumer products containing propionic acid. (NIOSH, 1989).

The chief effects are those of local damage to the skin, eye, or mucosal surfaces on contact with concentrated solution of propionic acid (Clayton, 1993). Medical reports of acute exposures of workers to propionic acid show mild to moderate skin burns, mild eye redness, and one case of mild cough and asthmatic response (ACGIH, 1991). Occupational exposure to propionic acid may occur through inhalation and dermal contact with this compound at workplaces where propionic acid is produced or used. The general population may be exposed to propionic acid via inhalation of ambient air, ingestion of food and drinking water, and dermal contact with this compound and other consumer products if applicable products containing propionic acid (NIOSH, 1983).

Clean Water Act Requirements: Propionic acid is designated as a hazardous substance under section 311(b)(2)(A) of the Federal Water Pollution Control Act and further regulated by the Clean Water Act Amendments of 1977 and 1978. These regulations apply to discharges of this substance. This designation includes any isomers and hydrates, as well as any solutions and mixtures containing this substance.

Occupational Exposure Standards: Excursion Limit Recommendation: Excursions in worker exposure levels to propionic acid may exceed three times the Threshold Limit Value (TLV)-Time-Weighted Average (TWA) for no more than a total of 30 min during a work day, and under no circumstances should they exceed five times the TLV-TWA, provided that the TLV-TWA is not exceeded (ACGIH, 1998). TLV limit is recommended guidelines for occupational exposure to airborne contaminants published by the American Conference of Governmental Industrial Hygienists (ACGIH). TLVs represent the average concentration in mg/m^3 for an 8-hour workday and a 40-hour work week to which nearly all workers may be repeatedly exposed, day after day, without adverse effect. The Occupational Safety and Health Administration (OSHA) has set the legal propionic acid permissible exposure limit (PEL) TWA at 10 ppm ($30 \text{ mg}/\text{m}^3$). PEL is an allowable exposure level in workplace air averaged over an 8-hour shift. Recommended Exposure Limit (REL) for propionic acid is a TWA of 10 ppm

(30mg/m³) based on an 10-hour workshift (NIOSH, 1997). Short-Term Exposure Limit (STEL) is the maximum concentration to which workers can be exposed for up to 15 min continually. The daily TLV-TWA may not be exceeded. Recommended STEL exposure limit for propionic acid is 15 ppm (45 mg/ m³) (NIOSH, 1997).

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Butyric acid

Butyric acid has an unpleasant, rancid, penetrating odor, and is an oily and colorless liquid (Budavari, 1989, and Fenaroli's Handbook,1975). The probable routes of exposure to butyric acid are by inhalation or dermal contact during its production or use. Exposure to the general population may occur by inhalation or dermal contact if commercial products containing this compound are used in the home (NIOSH, 1989). Ingestion of butyric acid is a probable route of exposure due to its presence in foods (Coleman, et al, 1981 and Harper, et al, 1986).

Butyric acid is both a natural and a commercially produced organic compound. It may be released to the environment as a fugitive emission during its production and formulation, or in the effluent of commercial processes, sewage treatment plants, landfills, and in the exhaust of motor vehicles. If released to soil, butyric acid is expected to be relatively mobile, although adsorption may occur by attractive interactions with active sites in the soil. Butyric acid is not expected to significantly volatilize from either moist or dry soil to the atmosphere. If released to water, butyric acid will exist predominately in the dissociated form under environmental

conditions. Butyric acid is expected to biodegrade rapidly under both aerobic and anaerobic conditions. Volatilization from water to the atmosphere is not expected to occur to any significant extent. Butyric acid will not significantly adsorb to sediment and suspended organic matter, nor is it expected to significantly bioconcentrate in fish and aquatic organisms. If released to the atmosphere, butyric acid is expected to undergo a gas-phase reaction with photochemically produced hydroxyl radicals with a half-life of 8 days. Butyric acid may also undergo atmospheric removal by wet deposition. Occupational exposure to butyric acid may occur by inhalation or dermal contact during its production or use.

Butyric acid can act as a mild irritant in man. Application to intact human skin elicits a moderate burning only after 52 min and erythema is hardly noticeable. Slight epidermal scaling may follow within 24 hr (Clayton and Clayton, 1981-1982). The vapor of butyric acid is an irritant to eyes, nose, and throat. If inhaled, it will cause coughing or difficult breathing.

LD50 orally in rat is 8.79 g/kg (Merck Index, 1983). Butyrate induced a marked reduction in the growth rate, colony forming efficiency in soft agar and de novo synthesis of DNA as well as remarkable morphological changes including cell enlargement, flattening, and a decreased number of nucleoli. Secretion of alpha-fetoprotein was reduced during culture with butyrate, while that of albumin was increased (Nakagawa, et. al, 1985).

Clean Water Act Requirements: Designated as a hazardous substance under section 311(b)(2)(A) of the Federal Water Pollution Control Act and further regulated by the Clean Water Act Amendments of 1977 and 1978. These regulations apply to discharges of this substance.

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Valeric Acid (Pentanoic Acid)

n-Valeric acid is a strong skin irritant in undiluted form (Clayton, 1993-1994). It has an unpleasant odor, similar to butyric acid (Budavari,1996). Occupational exposure to valeric acid may occur through inhalation and dermal contact with this compound at workplaces where valeric acid is produced or used (NIOSH, 1983). If released to the atmosphere, valeric acid is expected to exist solely in the vapor-phase pentanoic acid will be degraded in the atmosphere by reaction with photochemically produced hydroxyl radicals (HSDS, 1998).

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Dust and Endotoxin

Dust in livestock building is mainly composed of organics originating from feed, skin, bedding and dried feces (Harry, 1978). It is well known that dust can adsorb and concentrate odorants and carry them considerable distance by wind, and cause intense odor sensations to human. Hammond et al. (1979) have shown that the odorous compounds in livestock building air can be adsorbed on to dust particles, as well as being molecularly dispersed. Hammond et al. (1979) listed 19 compounds identified in dust collected from pig house air including aldehydes, acids, phenolics, skatole, and sulfur compounds. They also conducted air odor evaluation on filtered air and unfiltered air. The filtered air was odorless, while the unfiltered air inside of the swine confinement building was odor intensive (Hammond, 1979). These results supported the role of dust as an odor carrier in swine facilities. Oehrl et al. conducted air analyses of odorous compounds in swine house. Dust samples were collected from the exhaust fans of a swine house. Ten volatile fatty acids (C_2 , C_3 , C_4 , iso- C_4 , C_5 , iso- C_5 , C_6 , C_7 , C_8 , and C_9) and p-cresol were found in the dust samples with acetic acid being in highest concentration (Oehrl, 2000). In a review paper, Carpenter (1986) quoted some unpublished data indicating that the 5-20 μm diameter dust particle size range is mainly responsible for transporting odors. However, the threshold of dust or particle concentration below which odor would be effectively eliminated was not indicated. In a more recent paper, Hammond et al. (1981) listed 36 compounds identified in dust collected from pig house air sampled on three different occasions. Sixteen acids, 3 phenolic compounds and 17 carbonyls were identified in their analysis. Two of the phenols, o-ethylphenol and m-ethylphenol were identified in only one of the three sets of samples, whereas phenol, p-cresol, plus all the other compounds were identified, in varying concentrations, in all three sets of samples. Jericho (1968) reported on how airborne contaminants (organic dust, bacteria and molds) and their biologically active components (endotoxin, peptidoglycan and B-1,3-glucan) influence the health of pigs, respiratory health. Dust particles, which originate predominantly from dried feces, feed, skin, and bedding can adsorb and concentrate odorants in swine facilities. Odorants can exist in much higher concentrations in the dust particles than in a equivalent volume of air. Thus, inhalation of odorous dust and deposition of the dust particles in the mucus overlying the olfactory mucosa are likely responsible for some odor-related complaints by swine farm neighbors (Harry 1978; Bottcher, 2001). Respirable dust includes fine particles of less than 10 μm in diameter (Verma, 1984). The particles greater than 10 μm are deposited in the nasal passages, while 5 – 10 μm are deposited in the upper respiratory tract and less than 5 μm are

deposited in the lungs themselves (Hayter, 1974; Wathes, 1983). Sedimentation is the chief mechanism of lung deposition for particles above 0.5 μm in diameter, with particles below this size being deposited by Brownian motion of diffusion (Davies, 1963). In the dust of pig houses, 5 compounds (phenol, p-cresol, p-ethylphenol, indole, skatole) and in hen house, 6 compounds (phenol, p-cresol, p-ethylphenol, 2,6-dimethylphenol, 3,4-dimethylphenol, indole, skatole) were identified (O'Neill and Phillips, 1992). The total concentration of the phenolic compounds amounted to 275 $\mu\text{g/g}$ dust (finishing pigs), 111 $\mu\text{g/g}$ dust (piglets) and 108 $\mu\text{g/g}$ dust (hens). Quantitatively in the finishing pig house p-cresol was highest in concentration (53 % of the total amount), while in the piglet house phenol was highest, (50%) and in the hen house 2, 6- dimethylphenol was dominant (83%). It seemed that the decrease of the odor intensity coincided with the decrease in p-cresol. The possible influence of dust borne phenol and skatole on the animals is discussed with respect to respiratory affections. (Hartung and Rokiki,1984). The literature indicates that adverse sensory reactions to strong odors and irritants may lead to the release of catecholamines and stress hormones. Physiological and biochemical measurements related to cardiovascular risk, (e.g., blood pressure, heart rate, high-density lipoprotein (HDL) cholesterol level and serum triglyceride level), maybe altered as a result of exposure to odor and irritant-induced release of catecholamines (Toxicology and Industrial Health,1999).

Endotoxins are lipopolysaccharide (LPS) complexes that are integral parts of the outer cell wall of gram-negative bacteria, and have commonly been found in organic dusts of plant and animal origin. Evidently, there are more substances present in organic dust than just endotoxin alone. For example, B(1-3)-D-glucan from fungi and peptidoglycan from Gram positive bacteria, contribute to the development of respiratory disease in exposed workers (Pedersen,2000). Toxicity is associated with the lipid component (Lipid A) and immunogenicity is associated with the polysaccharide components of bacteria such as *E. coli*, *Salmonella*, *Shigella*, *Pseudomonas*, *Neisseria*, *Haemophilus*, and other leading pathogens. The cell wall antigens (O antigens) of Gram negative bacteria are components of LPS. LPS elicits a variety of inflammatory responses in animals. Because it activates complement by the alternative pathway, it is often part of the pathology of Gram-negative bacterial infections. Among fungi identified in swine houses, the genera *Penicillium*, *Aspergillus*, *Cladosporium*, *Alternaria*, *Curvularia*, *Stemphyllium*, and *Trichoderma* have been regarded as common allergens (Burrell,1991; Chang et. al, 2001). *Aspergillus*, *Alternaria*, *Penicillium*, and *Aureobasidium* are associated with extrinsic allergic alveolitis. *Penicillium*, *Aspergillus*, *Curvularia*, *Geotrichum*, *Drechslera*, *Stemphyllium*, and *Candida* may cause allergic bronchopulmonary mycoses,

Aspergillus and *Candida* are known to be potentially pathogenic for humans (Lacey, 1975 ;Chang et al., 2001). At the workplace the respiratory exposure to airborne dust containing endotoxins is of particular interest. Numerous articles have been published regarding the adverse respiratory health effect of working in intensive swine housing (Haglund et. al, 1987, Jacobs, 1989, Donham, et. al., 1993, Carvalheiro et. al, 1995, Heederik et. al, 1997, Jolie et. al, 1998). The health effects of acute exposure to endotoxins included dry cough, shortness of breath, decreased lung function, fever, malaise, dyspnea, headache, and joint aches. The health effects of chronic exposure to endotoxins included chronic bronchitis and reduced lung function and volume (Jacobs, 1989 and Heederik et al., 1997). General clinical symptoms of endotoxin exposure, such as eye irritation, headache and tiredness, and most prevalent respiratory symptoms included cough, nasal, dry cough, cough with phlegm, wheezing, dyspnea, throat irritation, chest tightness and sinus trouble have been reported (Haglund et al., 1987, Carvalheiro et. al, 1995, and Jolie et al., 1998).

The primary biological responses to endotoxin exposures include inflammatory, hemodynamic and immunological changes in the body. The most important of these with regard to occupational exposures are the activities of endotoxin in the human lung. Secondary responses include the recruitment of white blood cells (PMNs:polymorphonuclear leukocytes) to the airways where they respond to other macrophage derived factors and to endotoxin either directly or indirectly via activated complement. Activated PMNs release a number of factors which in their proper context defend the host. Large doses or continuous insult, however, result in the damaging of host lungs by PMNs. Platelets recruited to the air blood barrier by macrophage or PMNs can effect other cell systems and structures which in turn become activated (Jacobs, 1989). Carvalheiro et. al, (1995) studied of bronchial reactivity and work related respiratory symptoms in Swedish farmers. The cohort consisted of 76 none smoking farmers in southwest Sweden who raised vegetable or grain crops, swine, or other farm animals. The prevalence of dry cough, cough with phlegm, wheezing, and dyspnea was increased in farmers who raised swine. The prevalence of eye, nose, and throat irritation was higher in the farmers than in other groups with, the highest frequency of these symptoms occurring with swine farmers. The occurrence of organic dust toxic syndrome (ODTS), mucous membrane irritation (MMI), and chronic bronchitis, as diagnosed from the questionnaire responses, was higher in farmers raising swine and other animals than in the other groups. The prevalence of bronchial reactivity to methacholine challenge was significantly increased in farmers who raised swine and other animals. The authors conclude that an increased prevalence of work related respiratory symptoms were found in farmers

raising swine and other animals. Increased bronchial reactivity, probably due to inflammation caused by chronic organic dust exposure, were found in these groups. Jolie et. al, (1999) evaluated the effects of long term exposure to airborne dust and endotoxin on the respiratory system of pigs. In their finding, exposed pigs developed a mild eosinophilia, indicating an allergic response to the airborne contaminants. Raising pigs indoors in large confinement facilities is increasingly common in U.S. agriculture, and high endotoxin, ammonia, and dust levels contribute to acute and chronic respiratory symptoms in people who work in these settings. Respiratory conditions observed include the asthma-like syndrome, bronchitis, and asthma exacerbation.

Table 13. Summary of concentrations of airborne dust, endotoxin, and ammonia identified in swine confinements

Compound	Reported concentrations													
	ref. 1	ref. 2	ref. 3	ref. 4	ref. 5	ref. 6	ref. 7	ref. 8	ref.9	ref.10	ref.11	ref.12	ref.13	ref. 14
Endotoxin	Airborne total endotoxin													
	36.8-298 EU/m ³ (3-27 ng/m ³)	404 EU/m ³ (36 ng/m ³)	-	-	-	-	176-203 EU/m ³ (16-18 ng/m ³)	-	6667 EU/m ³ (600 ng/m ³)	11443 EU/m ³ (1030 ng/m ³)	-	-	222-2111 EU/m ³ (20-1900 ng/m ³)	-
Endotoxin	Respirable endotoxin													
	14.1-129 EU/m ³ (0.15-11.61 ng/m ³)	-	-	744.4 EU/m ³ (67 ng/m ³)	1166.7 EU/m ³ (105 ng/m ³)	-	11.86 EU/m ³ (1.07 ng/m ³)	6.44-50.44 EU/m ³ (0.58-4.54 ng/m ³)	-	-	6.44-50.44 EU/m ³ (0.58-4.54 ng/m ³)	-	111-333 EU/m ³ (10-30 ng/m ³)	-
Dust	Airborne total dust													
	0.15-0.34 mg/m ³	3.54 mg/m ³	3.54 (2.15-5.60) mg/m ³	-	-	1.3-6.3 mg/m ³	3.45 mg/m ³	-	13.5 (5.6-24) mg/m ³	-	1.48-5.11 mg/m ³	1.66-21.04 mg/m ³	2.2-15.2 mg/m ³	3.2-15.3 mg/m ³
	Respirable dust													
Dust	0.14 mg/m ³	-	-	2.19 mg/m ³	2.63 mg/m ³	-	0.26 mg/m ³	5.5 (0.8-26.9) mg/m ³	-	-	0.43-1.0 mg/m ³	-	0.3-1.4 mg/m ³	-
	-	20.7 ppm	19.6 ppm	-	-	10-45 ppm	5.15 ppm	-	-	-	-	1.5-13.23 ppm	-	-
Ammonia	-	14.66 mg/m ³ (20.7 ppm)	13.88 mg/m ³ (19.6 ppm)	-	-	7.08-31.86 mg/m ³ (10-45 ppm)	3.65 mg/m ³ (5.15 ppm)	-	-	-	-	1.06-9.37 mg/m ³ (1.5-13.23 ppm)	-	-

EU: endotoxin unit

(-) : Not determined

1. C.W. Chang (2001), 2. Cormier (2000), 3. Duchaine (2000), 4. Iversen (2000), 5. Vogelzang P.
6. Gustafsson (1997), 7. Reynolds (1996), 8. Preller L, (1995), 9. Larsson, (1994), 10. Zejda, (1994), 11. Vinzents, (1992), 12. Crook, (1991), 13. Haglind, (1987), 14. Donham (1986)

According to Vogelzang et al (1998), estimated long-term average exposure to inhalable dust was 2.63 mg/m³ and to endotoxin was 105 ng/m³. They also reported annual decline in Forced Expiratory Volume (FEV₁ is volume of air that can be forcibly exhaled during the first second of expiration following a maximal inspiration). FEV₁ was significantly associated with endotoxin exposure. They concluded endotoxin exposure as a major determinant of lung function decline in pig farmers. Although dust and/or endotoxin in the pork production emission air contains less than regulated or recommended amounts, it does not imply that is safe since it may effect adverse human health synergically with other odorous and /or hazardous compounds or gases. Table 14 shows a compilation of the exposure limit recommendations (ELR) for dust, endotoxin, and ammonia in swine confinement buildings.

At present no occupational exposure limits have been established in the USA and other countries. Estimated were "no effect levels" for acute and chronic respiratory effects ranging from 90 to 1800 EU/m³ (8.1 to 162 ng/m³) based on experimental as well as epidemiological studies (Linsel and Kummer, 1998). Safe threshold limit values for dust and endotoxin in animal houses have yet to be established, because accelerated decline in lung function has been observed below values proposed as safe limits (Iversen et al., 2000).

Table 14. Exposure limit recommendations in swine confinement buildings

	Ref. 1	Ref. 2	Ref. 3	Ref.4	Ref. 5
	USA	Sweden	Denmark	Netherlands	U.K.
Endotoxin	9 ng/m ³ (100 EU/m ³)	80 ng/m ³ (=889 EU/m ³)	-	4.5 ng/m ³ (=50 EU/m ³)	-
Dust	Total:2.5 mg/m ³ Respirable: 0.23 mg/m ³	Total:2.4 mg/m ³ Respirable: 0.23 mg/m ³	5.0 mg/m ³	-	10 mg/m ³
Ammonia	7 ppm	7 ppm	-	-	35 ppm

EU: endotoxin unit

(-) : Not determined

1 USA, Donham et. al., 1995: Exposure limit recommendations ; 2 Sweden, Donham, 1991: recommended maximal concentrations ; 3 Danish, Vinzents, 1992: occupational exposure limit (OEL) ;4 Netherlands, Heederick, 1997: Dutch Expert Committee on Occupational Standard

(DECOS) recommendation ; 5. U.K. Health and Safety Executive's recommended 8-hr, time-weighted exposure limit for nuisance dust of 10 mg/m³ in 21 out of 120 measurements (18 occurred in the winter months when ventilation is decrease to conserve heat. U.K. Health and Safety Executive's recommended short-term exposure limit of 35 ppm.

Preller, et.al., (1995) investigated dust and endotoxin exposure among 198 Dutch pig farmers , and estimated that the mean time-weighted average (TWA) exposure to dust was 3.0 mg/m³ and mean TWA exposure to endotoxin was 130 ng/m³. The published no effect levels for inhaling endotoxins ranged from 9 to170 ng/m³. A no observed adverse effect level of 9 ng/m³ was based on a large, well designed exposure study in which the acute respiratory effects of endotoxin exposure were determined in asymptomatic subjects. A safety factor of 2 was applied to the no observed adverse effect level to account for the sensitivities and risks of certain groups of workers. Based on this information, DECOS recommended an occupational exposure limit for airborne endotoxins of 4.5 ng/m³ (=50 EU/m³) over an 8hr exposure period.

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Discussion and Conclusion

More research is needed to better understand the potential impact to human health of air emissions from intensive pig production systems. Although the toxicity of compounds detectable in air emissions is well documented, when they are found in high concentrations, there is clearly a gap in our knowledge about their possible adverse effects at lower concentrations of either acute or chronic exposure. Furthermore, most risk assessment studies have been concerned about the risk of carcinogenicity, while fewer studies have dealt with non-carcinogenic effects. Synergistic interactions between different chemical compounds at lower concentrations of exposure may be important in human health. Further studies need to be done to assess this possibility with the air emissions from intensive pig production systems.

There are a variety of direct (sensory) and indirect (analytical) instruments methods for measuring odor intensity and for the determination of individual or key odor components. These methods have provided a better understanding of the distinct odor, which is characteristic of pig production systems, and the chemical components which contribute to the odor. However, reported concentrations of those components have been varied depending on the method of air sampling and analysis. Studies are also needed to evaluate whether the sites being sampled are the most representative indices of exposure. To be able to compare values from different systems, standardized procedures and protocols should be developed for the accurate measurements of chemical components in air emissions.

Risk assessment is essential for setting occupational safety and health priorities, and such a process is needed to estimate the probability and magnitude of human health effects that result from exposure to air emissions from intensive pig production systems.

To make an accurate assessment will require that (1) the hazardous components are identified, (2) dose/response effects are assessed, (3) exposure is assessed, and (4) the risk factors must be characterized. To strengthen the scientific foundation on which a risk assessment is base a central database of demographic, psychological, and medical variables for persons exposed to air emissions from pig production systems should be developed.

Acronyms and Abbreviations

Acceptable Daily Intake (ADI): The amount of a chemical a person can be exposed to on a daily basis over an extended period of time (usually a lifetime) without suffering deleterious effects.

ACGIH TW Booklet: American Conference of Governmental Industrial Hygienists.

Acute: Occurring over a short time, usually a few minutes or hours. An *acute* exposure can result in short-term or long-term health effects. An *acute* effect happens a short time (up to 1 year) after exposure.

Acute Exposure: One dose or multiple doses of short duration spanning less than or equal to 24 hours. Exposure to a chemical for a duration of 14 days or less, as specified in the Toxicological Profiles.

Acute Toxicity: Any poisonous effect produced within a short period of time following an exposure, usually 24 to 96 hours.

Adverse Effect: A biochemical change, functional impairment, or pathologic lesion that affects the performance of the whole organism, or reduces an organism's ability to respond to an additional environmental challenge.

Average Daily Dose (ADD) : Dose rate averaged over a pathway-specific period of exposure expressed as a daily dose on a per-unit-body-weight basis. The ADD is usually expressed in terms of mg/kg-day or other mass-time units.

Absorption The process of taking in, as when a sponge takes up water. Chemicals can be absorbed through the skin into the bloodstream and then transported to other organs. Chemicals can also be absorbed into the bloodstream after breathing or swallowing.

ATSDR: Agency for Toxic Substances and Disease Registry

Bioassay: An assay for determining the potency (or concentration) of a substance that causes a biological change in experimental animals.

Bioavailability: The degree to which a substance becomes available to the target tissue after administration or exposure.

Carcinogenesis: The origin or production of a benign or malignant tumor. The carcinogenic event modifies the genome and/or other molecular control mechanisms of the target cells, giving rise to a population of altered cells.

Case-control study: An epidemiologic study contrasting those with the disease of interest (cases) to those without the disease (controls). The groups are then compared with respect to exposure history, to ascertain whether they differ in the proportion exposed to the chemical(s) under investigation.

Chronic Effect: An effect which occurs as a result of repeated or long term (chronic: occurring over a long period of time, more than 1 year) exposures.

Chronic Exposure: Multiple exposures occurring over an extended period of time, or a significant fraction of the animal's or the individual's lifetime. Exposure to a chemical for 1 year or more, as specified in the Toxicological Profiles.

Chronic Toxicity: The capacity of a substance to cause adverse human health effects as a result of chronic exposure.

Cohort Study (or Prospective Study): An epidemiologic study comparing those with an exposure of interest to those without the exposure. These two cohorts are then followed over time to determine the differences in the rates of disease between the exposure subjects.

Critical Concentration: An ambient chemical concentration expressed in units of $\mu\text{g}/\text{m}^3$ and used in the operational derivation of the inhalation RfC. This concentration will be the NOAEL Human Equivalent Concentration (HEC) adjusted from principal study data.

Critical Effect: The first adverse effect, or its known precursor, that occurs to the most sensitive species as the dose rate of an agent increases.

CAS Number (also **CAS Registry Number**, **CAS RN**, or **CAS#**) A unique accession number assigned by the Chemical Abstracts Service, a division of the American Chemical Society. Other than being guaranteed unique to a given compound, this number has no particular meaning. CAS Registry Numbers are assigned to every uniquely-identifiable substance, so 'cis-2-hexene', 'trans-2-hexene', and '2-hexene' (a mixture with unspecified cis/trans composition) are all assigned separate CAS Numbers.

Case Study The medical or epidemiologic evaluation of a single person or a small number of individuals to determine descriptive information about their health status or potential for exposure through interview or biomedical testing.

Central Nervous System The part of the nervous system that includes the brain and the spinal cord.

CERCLA The Comprehensive Environmental Response, Compensation, and Liability Act of 1980, also known as Superfund. This is the legislation that created ATSDR.

Developmental Toxicity: Adverse effects on the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally until the time of sexual maturation. The major manifestations of developmental toxicity include death of the developing organism, structural abnormality, altered growth, and functional deficiency.

Dose-Response Assessment: A determination of the relationship between the magnitude of an administered, applied, or internal dose and a specific biological response. Response can be expressed as measured or observed incidence, percent response in groups of subjects (or populations), or as the probability of occurrence within a population.

Dose-Response Relationship: The relationship between a quantified exposure (dose), and the proportion of subjects demonstrating specific, biological changes (response).

Dermal Referring to the skin. *Dermal* absorption means absorption through the skin.

Disease- and Symptom-Prevalence Study A study designed to measure the occurrence of self-reported disease that may, in some instances, be validated through medical records or physical examination if available, and to determine those adverse health conditions that may require further investigation because they are considered to have been reported at an excess rate. This study design can only be considered hypothesis generating.

Disease Registry A system for collecting and maintaining in a structured record, information on persons having a common illness or adverse health condition.

Dose The amount of substance to which a person is exposed. *Dose* often takes body weight into account.

Effective Dose (ED₁₀): The dose corresponding to a 10% increase in an adverse effect, relative to the control response.

Endpoint: An observable or measurable biological event or chemical concentration (e.g., metabolite concentration in a target tissue) used as an index of an effect of a chemical exposure.

EHIS: Environmental Health Information Service

Estimated Exposure Dose (EED): The measured or calculated dose to which humans are likely to be exposed considering all sources and routes of exposure.

Exposure: Contact made between a chemical, physical, or biological agent and the outer boundary of an organism by swallowing, by breathing, or by direct contact (such as through the skin or eyes). Exposure is quantified as the amount of an agent available at the exchange boundaries of the organism (e.g., skin, lungs, gut). *Exposure* may be short term (acute) or long term (chronic).

Exposure Registry A system for collecting and maintaining in a structured record, information on persons with documented environmental exposure(s). The *exposure registry* evolved from the need for fundamental information concerning the potential impact on human health of long-term exposure to low and moderate levels of hazardous substances.

Extra Risk (ER): A calculation of risk of adverse effects which adjusts for background incidence rates of the same effects, by estimating risk at dose *d* only among the fraction of the population not expected to respond to the secondary (background) causes: $ER = [P(d) - P(0)] / [1 - P(0)]$. For example, if the background rate ($P(0)$) = 0.8 and the response rate at dose *d*, $P(d)$ = .9, then $ER = (0.9 - 0.8) / (1 - 0.8) = 0.1 / 0.2 = 0.5$. That is, at dose *d*, an additional 10% of the population is expected to respond adversely. But since only 20% of the population was expected to be free of adverse effects without the exposure of interest, this 10% represents 50% of the population that would otherwise have been unharmed by this exposure.

Extrapolation, low dose: An estimate of the response at a point below the range of the experimental data, generally through the use of a mathematical model.

Epidemiologic Surveillance: The ongoing, systematic collection, analysis, and interpretation of health data essential to the planning, implementation, and evaluation of public health practice, closely integrated with the timely dissemination of these data to those who need to know. The final link in the surveillance chain is the application of these data to prevention and control. A surveillance system includes a functional capacity for data collection, analysis, and dissemination linked to public health programs.

Epidemiology: The study of the occurrence and causes of health effects in human populations. An epidemiological study often compares two groups of people who are alike except for one factor, such as exposure to a chemical or the presence of a health effect. The investigators try to determine if any factor is associated with the health effect.

EPA: The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites make up the National Priorities List (NPL) and are the sites targeted for long-term federal cleanup activities.

Forced Expiratory Volume (FEV₁): The volume of air that can be forcibly exhaled during the first second of expiration following a maximal inspiration.

Forced Vital Capacity (FVC): The maximal volume of air that can be exhaled as forcibly and rapidly as possible after a maximal inspiration.

Functional Residual Capacity (FRC): The lung volume at the end of tidal expiration (TLC - IC).

Guidelines (human health risk assessment): Official, peer-reviewed documentation stating current U.S. EPA methodology in assessing risk of harm from environmental pollutants to populations.

Examples: Proposed Guidelines for Carcinogenic Risk Assessment: U.S. EPA guidelines intended to guide Agency evaluation of suspect carcinogens. EPA/600/P-92/003C, April 1996.

Hazard A potential source of harm, a source of risk that does not necessarily imply potential for occurrence. A hazard produces risk only if an exposure pathway exists, and if exposures create the possibility of adverse consequences.

Hazard Assessment: The process of determining whether exposure to an agent can cause an increase in the incidence of a particular adverse health effect (e.g., cancer, birth defect) and whether the adverse health effect is likely to occur in humans.

Hazardous Substances and Health Effects Database (HazDat) The scientific database developed by ATSDR to manage data collection, retrieval, analysis, and utilization through the sophisticated technologies provided by computerization. *HazDat* allows ATSDR to locate information on the release of hazardous substances into the environment, and to ascertain the effects of hazardous substances on health with improved uniformity, efficiency, and precision

Human Equivalent Concentration (HEC) or Dose (HED): The human concentration (for inhalation exposure) or dose (for other routes of exposure) of an agent that is believed to induce the same magnitude of toxic effect as the experimental animal species concentration or dose. This adjustment may incorporate toxicokinetic information on the particular agent, if available, or use a default procedure, such as assuming that daily oral doses experienced for a lifetime are proportional to body weight raised to the 0.75 power.

Health Surveillance The periodic medical screening of a defined population for a specific disease or for biological markers of disease for which the population is, or is thought to be, at significantly increased risk. The program should include a mechanism to refer for treatment those persons who test positive for disease (also called Medical Monitoring).

HEAST: Health Effects Assessment Summary Tables

Health Outcome Data A major source of data for public health assessments. The identification, review, and evaluation of health outcome parameters are interactive processes involving the health assessors, data source generators, and the local community. *Health outcome data* are community specific and may be derived from databases at the local, state,

and national levels, as well as from data collected by private health care organizations and professional institutions and associations. Databases to be considered include morbidity and mortality data, birth statistics, medical records, tumor and disease registries, surveillance data, and previously conducted health studies.

IARC monographs: International Agency for Research on Cancer

Interspecies Dose Conversion: The process of extrapolating from animal doses to human equivalent doses.

Inhalation Breathing. Exposure may occur from inhaling contaminants because they can be deposited in the lungs, taken into the blood, or both.

IRIS: Integrated Risk Information System

Latency Period: The time between first exposure to an agent and manifestation or detection of a health effect of interest.

Limited Evidence: A term used in evaluating study data for the classification of a carcinogen by the 1986 U.S. EPA guidelines for carcinogen risk assessment. This classification indicates that a causal interpretation is credible but that alternative explanations such as chance, bias, and confounding variables could not be completely excluded.

Linear dose response: A pattern of frequency or severity of biological response that varies proportionately with the amount of dose of an agent.

Lowest-Observed-Adverse-Effect Level (LOAEL): The lowest exposure level at which there are statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group. Also referred to as lowest-effect level (LEL).

LOAELs: classified as a "less serious" or "serious" effects.

LOAEL or NOAELs should also help in determining whether or not the effects vary with dose and /or duration, and place into perspective the possible significance of these effects to human health.

Lowest-Observed Effect Level (LOEL or LEL): In a study, the lowest dose or exposure level at which a statistically or biologically significant effect is observed in the exposed population compared with an appropriate unexposed control group.

Maximum Likelihood (ML) method, Maximum Likelihood Estimate (MLE): Statistical method for estimating model parameters. Generally provides a mean or central tendency estimate, as opposed to a confidence limit on the estimate.

Metastasis: The dissemination or secondary growth of a malignant tumor at a site distant from the primary tumor.

Minimal Risk Level (MRL) An *MRL* is defined as an estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (noncancer) over a specified duration of exposure. *MRLs* are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration via a given route of exposure. *MRLs* are based on noncancer health effects only. *MRLs* can be derived for acute, intermediate, and chronic duration exposures by the inhalation and oral routes. *MRLs* is estimates of levels posing minimal risk to humans (*MRLs*) may be of interest

to health professionals and citizens alike. The MRLs were derived from human and animal data for short-term and long-term exposure. The MRLs provide a basis for comparison with levels that people might encounter either in the air or in food or drinking water. If a person is exposed to ammonia at an amount below the MRL, it is not expected that harmful (noncancer) health effects will occur. Because these levels are based only on information currently available, some uncertainty is always associated with them. Also, because the method for deriving MRLs does not use any information about cancer, an MRL does not imply anything about the presence, absence, or level of risk for cancer.

Modifying Factor (MF): A factor used in the derivation of a reference dose or reference concentration. The magnitude of the MF reflects the scientific uncertainties of the study and database not explicitly treated with standard uncertainty factors (e.g., the completeness of the overall database). A MF is greater than zero and less than or equal to 10, and the default value for the MF is 1.

Mutagen: A substance that can induce an alteration in the structure of DNA.

NLM : National library of Medicine

No-Observed-Adverse-Effect Level (NOAEL): An highest exposure level at which there are no statistically or biologically significant increases in the frequency or severity of adverse effect between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered adverse, nor precursors to adverse effects.

No-Observed-Effect Level (NOEL): An exposure level at which there are no statistically or biologically significant increases in the frequency or severity of any effect between the exposed population and its appropriate control.

National Priorities List (NPL) The Environmental Protection Agency's (EPA) listing of sites that have undergone preliminary assessment and site inspection to determine which locations pose immediate threat to persons living or working near the release. These sites are most in need of cleanup.

National Toxicology Program (NTP) *NTP* conducts toxicological testing on those substances most frequently found at sites on the National Priorities List of the EPA, and which also have the greatest potential for human exposure.

National Exposure Registry A listing of persons exposed to hazardous substances. This listing is composed of chemical-specific subregistries. The primary purpose of the registry program is to create a large database of similarly exposed persons. This database is to be used to facilitate epidemiology research in ascertaining adverse health effects of persons exposed to low levels of chemicals over a long period.

NIOSH: National Institute for Occupational Safety and Health

OSHA: Occupational Safety and Health Administration.

Point of Departure: The dose-response point that marks the beginning of a low-dose extrapolation. This point is most often the upper bound on an observed incidence or on an estimated incidence from a dose-response model.

ppb: A unit of measure expressed as parts per billion. Equivalent to 1×10^{-9} .

ppm: A unit of measure expressed as parts per million. Equivalent to 1×10^{-6} .

Permissible Exposure Limit (PEL)- An allowable exposure level in workplace air averaged over an 8-hour shift.

Public Health Assessment The evaluation of data and information on the release of hazardous substances into the environment in order to assess any current or future impact on public health, develop health advisories or other recommendations, and identify studies or actions needed to evaluate and mitigate or prevent human health effects; also, the document resulting from that evaluation.

Reference Concentration (RfC): An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

Reference Dose (RfD): An estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors generally applied to reflect limitations of the data used. Generally used in EPA's noncancer health assessments.

Regional Gas Dose: The gas dose calculated for the region of interest as related to the observed effect for respiratory effects. The deposited dose is adjusted for ventilatory volumes and the surface area of the respiratory region effected (mg/min-sq.cm).

Relative Risk (or Risk Ratio (RR)): The relative measure of the difference in risk between the exposed and unexposed populations in a cohort study. The relative risk is defined as the rate of disease among the exposed divided by the rate of the disease among the unexposed. A relative risk of 2 means that the exposed group has twice the disease risk as the unexposed group.

Reserve Volume: The volume of air remaining in the lungs after a maximal expiration.

Residual Volume (RV): The lung volume after maximal expiration (TLC - VC).

RTECS : Registry of Toxic Effects of Chemical Substances

Risk (in the context of human health): The probability of injury, disease, or death from exposure to a chemical agent or a mixture of chemicals. In quantitative terms, risk is expressed in values ranging from zero (representing the certainty that harm will not occur) to one (representing the certainty that harm will occur). The following are examples of how risk is expressed within IRIS: $E-4$ or 10^{-4} = a risk of 1/10,000; $E-5$ or 10^{-5} = 1/100,000; $E-6$ or 10^{-6} = 1/1,000,000. Similarly, $1.3 E-3$ or 1.3×10^{-3} = a risk of 1.3/1,000=1/770; $8 E-3$ or 8×10^{-3} = a risk of 1/125 and $1.2 E-5$ or 1.2×10^{-5} = a risk of 1/83,000.

Risk Assessment (in the context of human health): The determination of potential adverse health effects from exposure to chemicals, including both quantitative and qualitative expressions of risk. The process of risk assessment involves four major steps: hazard identification, dose-response assessment, exposure assessment, and risk characterization.

Short-Term Exposure: Multiple or continuous exposure to an agent for a short period of time, usually one week.

Slope Factor: An upper bound, approximating a 95% confidence limit, on the increased cancer risk from a lifetime exposure to an agent. This estimate, usually expressed in units of proportion (of a population) affected per mg/kg/day, is generally reserved for use in the low-dose region of the dose-response relationship, that is, for exposures corresponding to risks less than 1 in 100.

Short-Term Exposure Limit (STEL): The maximum concentration to which workers can be exposed for up to 15 min continually. The daily TLV-TWA may not be exceeded.

Statistical Significance: The probability that a result likely to be due to chance alone. By convention, a difference between two groups is usually considered statistically significant if chance could explain it only 5% of the time or less. Study design considerations may influence the a priori choice of a different statistical significance level.

Subchronic Exposure: Exposure to a substance spanning approximately 10% of the lifetime of an organism.

Superfund: Federal authority, established by the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA), which created ATSDR, to respond directly to releases or threatened releases of hazardous substances that may endanger health or welfare.

Systemic Effects or Systemic Toxicity: Toxic effects as a result of absorption and distribution of a toxicant to a site distant from its entry point, at which point effects are produced. Not all chemicals that produce systemic effects cause the same degree of toxicity in all organs.

Surveillance Activities Those activities that evaluate exposure or trends in adverse health effects over a specified period of time. *Surveillance activities* address the ongoing systematic collection, analysis, and interpretation of health data in the process of describing and monitoring a health event. Data obtained through surveillance are very important for appropriate decisions regarding the planning, evaluation, or implementation of public health interventions.

Target Organ: The biological organ(s) most adversely effected by exposure to a chemical substance.

Threshold: The dose or exposure below which no deleterious effect is expected to occur.

Total Volume (V_T): The volume of air inhaled/exhaled during normal breathing.

Total Lung Volume (TLV): The lung volume at maximal inspiration.

Toxicity: The degree to which a chemical substance elicits a deleterious or adverse effect upon the biological system of an organism exposed to the substance over a designated time period.

Toxicological Profile A document about a specific substance in which ATSDR scientists interpret all known information on the substance and specify the levels at which people may

be harmed if exposed. The *toxicological profile* also identifies significant gaps in knowledge on the substance, and serves to initiate further research, where needed.

Threshold Limit Value (TLV): Recommended guidelines for occupational exposure to airborne contaminants published by the American Conference of Governmental Industrial Hygienists (ACGIH). TLVs represent the average concentration in mg/m³ for an 8-hour workday and a 40-hour work week to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.

Threshold Limit Value (TLV): A concentration of a substance to which most workers can be exposed without adverse effect. The TLV may be expressed as a TWA, as a STEL, or as a CL.

Time-Weighted Average (TWA): An allowable exposure concentration averaged over a normal 8-hour workday or 40-hour workweek.

Uncertainty Factor (UF): One of several, generally 10-fold factors, used in operationally deriving the RfD and RfC from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, i.e., interhuman or intraspecies variability; (2) the uncertainty in extrapolating animal data to humans, i.e., interspecies variability; (3) the uncertainty in extrapolating from data obtained in a study with less-than-lifetime exposure to lifetime exposure, i.e., extrapolating from subchronic to chronic exposure; (4) the uncertainty in extrapolating from a LOAEL rather than from a NOAEL; and (5) the uncertainty associated with extrapolation from animal data when the data base is incomplete.

Unit Risk: The upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 µg/L in water, or 1 µg/m³ in air. The interpretation of unit risk would be as follows: if unit risk = 1.5×10^{-6} µg/L, 1.5 excess tumors are expected to develop per 1,000,000 people if exposed daily for a lifetime to 1 µg of the chemical in 1 liter of drinking water.

Upper bound: An plausible upper limit to the true value of a quantity. This is usually not a true statistical confidence limit.

Vital Capacity (VC): The maximum volume that can be exhaled in a single breath (TLC-RC).

Weight-of-Evidence (WOE) for Carcinogenicity: A system used by the U.S. EPA for characterizing the extent to which the available data support the hypothesis that an agent causes cancer in humans. Under EPA's 1986 risk assessment guidelines, the WOE was described by categories "A through E", Group A for known human carcinogens through Group E for agents with evidence of noncarcinogenicity. The approach outlined in EPA's proposed guidelines for carcinogen risk assessment (1996) considers all scientific information in determining whether and under what conditions an agent may cause cancer in humans, and provides a narrative approach to characterize carcinogenicity rather than categories.

Ref.) ATSDR and IRIS

Databases accessed

Databases and journal literature from the following resources was accessed for human health criteria: ATSDR, IRIS, which is a general literature search site. In addition accessed HEAST, ACGIH TLV Booklet, NIOSH Pocket Guide to Chemical Hazards, RTECS, NTP management, Status Report, EPB Library, IARC Monographs, CAS on-line and NLM, Toxicology, Merck Index, and Condensed Chemical Dictionary.

Fedrip Database, National Technical Information Service (NTIS)

Annals-of-Agricultural and Environmental Medicine.

Annals-of-Occupational-Hygiene.

Crisp Data Base National Institutes Of Health.

British Journal of Industrial Medicine

Transactions of the ASAE

Journal of Occupational Medicine

J. Appl. Physiol.

American Journal of Respiratory and Critical Care Medicine

Can J. Vet. Res.

Cancer Res.

USEPA

Appl. Environ. Microbiol.

American Journal of Industrial Medicine

Chemical Senses

AIHAJ

American Journal of Res. and Critical Care Med.

J. Anim. Sci.

Semin. Respir. Med.

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