

Ammonia; CASRN 7664-41-7

Human health assessment information on a chemical substance is included in the IRIS database only after a comprehensive review of toxicity data, as outlined in the [IRIS assessment development process](#). Sections I (Health Hazard Assessments for Noncarcinogenic Effects) and II (Carcinogenicity Assessment for Lifetime Exposure) present the conclusions that were reached during the assessment development process. Supporting information and explanations of the methods used to derive the values given in IRIS are provided in the [guidance documents located on the IRIS website](#).

STATUS OF DATA FOR Ammonia

File First On-Line 05/01/1991

Category (section)	Assessment Available?	Last Revised
Oral RfD (I.A.)	not evaluated	
Inhalation RfC (I.B.)	yes	05/01/1991
Carcinogenicity Assessment (II.)	not evaluated	

I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name — Ammonia

CASRN — 7664-41-7

Not available at this time.

I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name — Ammonia

CASRN — 7664-41-7

Last Revised — 05/01/1991

The inhalation Reference Concentration (RfC) is analogous to the oral RfD and is likewise based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. The inhalation RfC considers toxic effects for both the respiratory system (portal-of-entry) and for effects peripheral to the respiratory system (extrarespiratory effects). It is expressed in units of mg/cu.m. In general, the RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily inhalation exposure of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Inhalation RfCs were derived according to the Interim Methods for Development of Inhalation Reference Doses (EPA/600/8-88/066F August 1989) and subsequently, according to Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry (EPA/600/8-90/066F October 1994). RfCs can also be derived for the noncarcinogenic health effects of substances that are carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in Section II of this file.

I.B.1. Inhalation RfC Summary

Critical Effect	Exposures*	UF	MF	RfC
Lack of evidence of decreased pulmonary function or changes in subjective syptomatology	NOAEL: 6.4 mg/cu.m (9.2 ppm) NOAEL(ADJ): 2.3 mg/cu.m NOAEL(HEC): 2.3 mg/cu.m LOAEL: None	30	1	1E-1 mg/cu.m
Occupational Study				
Holness et al., 1989				

Critical Effect	Exposures*	UF	MF	RfC
Increased severity of rhinitis and pneumonia with respiratory lesions Rat Subchronic Inhalation Study Broderon et al., 1976	NOAEL: None LOAEL: 17.4 mg/cu.m (25 ppm) LOAEL(ADJ): 17.4 mg/cu.m LOAEL(HEC): 1.9 mg/cu.m			

*Conversion Factors: MW = 17.03 Holness et al., 1989: Assuming 25C and 760 mm Hg, NOAEL (mg/cu.m) = 9.2 ppm x 17.03/24.45 = 6.4 mg/cu.m. The NOAEL is based on an 8-hour TWA occupational exposure. MVho = 10 cu.m/day, MVh = 20 cu.m/day. NOAEL(ADJ) = 6.4 mg/cu.m x (MVho/MVh) x 5 days/7 days = 2.3 mg/cu.m.

Broderon et al., 1976: Assuming 25C and 760 mm Hg, the LOAEL (mg/cu.m) = 25 ppm x 17.03/24.45 = 17.4 mg/cu.m. The LOAEL(HEC) was calculated for a gas:respiratory effect in the ExtraThoracic region. MVa = 0.14 cu.m/day, MVh = 20 cu.m/day, Sa(ET) = 11.6 sq. cm., Sh(ET) = 177 sq. cm. RGDR(ET) = (MVa/Sa) / (MVh/Sh) = 0.1068. NOAEL(HEC) = 17.4 x RGDR = 1.9 mg/cu.m.

I.B.2. Principal and Supporting Studies (Inhalation RfC)

Holness, D.L., J.T. Purdham and J.R. Nethercott. 1989. Acute and chronic respiratory effects of occupational exposure to ammonia. Am. Ind. Hyg. Assoc. J. 50: 646-650.

Broderon, J.R., J.R. Lindsey and J.E. Crawford. 1976. The role of environmental ammonia in respiratory mycoplasmosis of rats. Am. J. Pathol. 85: 115-130.

Holness et al. (1989) investigated production workers exposed to ammonia in a soda ash facility. All of the available 64 production workers were invited to participate and 82% agreed to be evaluated. The control group consisted of 31 other plant workers from stores and office areas of the plant without previous exposure to ammonia. The mean age of the workers was 38.9 years and duration of exposure was 12.2 years. Weight was the only statistically significant difference in demographics found after comparing height, weight, years worked, % smokers and pack-years smoked. The mean TWA ammonia exposures based on personal sampling over one work shift

(average sample collection 8.4 hours) of the exposed and control groups were 9.2 ppm (6.4 mg/cu.m) and 0.3 ppm (0.21 mg/cu.m), respectively.

A questionnaire was administered to obtain information on exposure and work histories and to determine eye, skin and respiratory symptomatology (based on the American Thoracic Society [ATS] questionnaire [Ferris, 1978]). Spirometry (FVC, FEV-1, FEF50 and FEF75) was performed according to ATS criteria at the beginning and end of each work shift on the first workday of the week (day 1) and the last workday of the week (day 2). Differences in reported symptoms and lung function between groups were evaluated using the actual values and with age, height and pack-years smoked as covariates in linear regression analysis. Baseline lung function results were expressed as percent of predicted values calculated from Crapo et al. (1981) for FVC and FEV-1 and from Lapp and Hyatt (1967) for FEF50 and FEF75.

No statistical difference in the prevalence of the reporting symptoms was evident between the exposed and control groups, although workers reported that exposure at the plant had aggravated specific symptoms including coughing, wheezing, nasal complaints, eye irritation, throat discomfort and skin problems. The percentage of exposed workers reporting hay fever or familial history of hay fever was significantly less than controls, suggesting possible self-selection of atopic individuals out of this work force. The atopic status of the worker and control groups was not determined by skin prick tests to common aeroallergens. Furthermore, the workers complained that their symptomatology was exacerbated even though there was no statistical difference between groups. Since the study was cross-sectional in design with a small population, it is possible that selection bias may have occurred.

Baseline lung functions (based on the best spirometry values obtained during the four testing sessions) were similar in the exposed and control groups. No changes in lung function were demonstrated over either work shift (days 1 or 2) or over the workweek in the exposed group compared with controls. No relationship was demonstrated between chronic ammonia exposure and baseline lung function changes either in terms of the level or duration of exposure, probably due to lack of adequate exposure data for categorizing exposures and thus precluding development of a meaningful index accounting for both level and length of exposure.

Based on the lack of subjective symptomatology and changes in spirometry, this study establishes a free-standing TWA NOAEL of 9.2 ppm (6.4 mg/cu.m). Adjustment for the TWA occupational scenario results in a NOAEL(HEC) of 2.3 mg/cu.m.

Broderick et al. (1976) exposed groups of F344 rats (6/sex/dose) continuously to 25, 50, 150 or 250 ppm ammonia (HEC = 1.9, 3.7, 11.2 or 18.6 mg/cu.m, respectively) for 7 days prior to inoculation with *Mycoplasma pulmonis* and from 28-42 days following *M. pulmonis* exposure. Each treatment group had a corresponding control group exposed only to background ammonia

and inoculated with *M. pulmonis* in order to produce murine respiratory mycoplasmosis (MRM). The following parameters were used to assess toxicity: clinical observations and histopathological examination of nasal passages, middle ear, trachea, lungs, liver and kidneys. All levels of ammonia, whether produced naturally or derived from a purified source, significantly increased the severity of rhinitis, otitis media, tracheitis and pneumonia characteristic of *M. pulmonis*. Furthermore, there was a significant concentration response between observed respiratory lesions and increasing environmental ammonia concentration for gross and microscopic lesions. All lesions observed were characteristic of MRM. Gross bronchiectasis and/or pulmonary abscesses and the extent of gross atelectasis and consolidation was consistently more prevalent in exposed animals at all concentrations than in their corresponding controls. The severity of the microscopic lesions in the nasal passages, middle ears, tracheas and lungs was significantly greater in all exposed groups compared with controls. Increasing ammonia concentration was not associated with an increasing frequency of *M. pulmonis* isolations. Additionally, rats not exposed to *M. pulmonis* and exposed to ammonia at 250 ppm developed nasal lesions (epithelial thickening and epithelial hyperplasia) unlike those observed in inoculated rats. Based upon these data in *M. pulmonis* exposed rats, a LOAEL(HEC) of 1.9 mg/cu.m was identified.

A group of 295 pathogen free F344 rats was inoculated with *M. pulmonis* and exposed to either trace or 100 ppm ammonia (HEC=7.4 mg/cu.m) (Schoeb et al., 1982). Growth of *M. pulmonis* was greater in exposed rats than in controls. Similarly, serum immunoglobulin antibody responses to the inoculum were greater in the exposed population. It was further demonstrated that the nasal passages absorbed virtually all the ammonia at concentrations <500 ppm, indicating that the increased numbers of *M. pulmonis* in the lungs and the consequent exacerbation of lung lesions in MRM are secondary to events in the nasal passages rather than a direct effect of ammonia in the lung itself. These results are consistent with those of Broderick et al. (1976) detailed above.

The use of Holness et al. (1989) as the principal study can only be supported in the context of the data array. It is not surprising that no effects were seen on screening spirometry since the exposure levels were low. Comparing the 9.2 TWA of Holness et al. (1989) with other data on the respiratory effects of ammonia, a trend is observed that at lower concentrations the extrathoracic region of the respiratory system is affected due to the chemical's solubility and reactivity; while at higher concentrations, the lower part of the respiratory system is involved in both experimental animals (Dahlman, 1956; Gamble and Clough, 1976) and humans (Flury et al., 1983). Thus, no effects were observed in the lower respiratory system as reflected by pulmonary function. Pulmonary function may not be a particularly sensitive test because exposure to this type of agent at low concentrations is not expected to result in significant exposure of the lower respiratory region. No objective investigation of the workers' nasal epithelium was performed and the complaint of exacerbated upper respiratory symptoms

suggests sensory irritation and supports the extrathoracic region as the critical region for an effect. The possibility of selection bias against atopic predispositions in the population is suggested by the significantly lower prevalence of hay fever in the exposed versus control cohort. Thus, there is a concentration-response in the extrathoracic region in experimental animals beginning at a LOAEL at essentially the same HEC as the NOAEL in Holness et al. (1989) and the NOAEL may be based on a less sensitive endpoint. Also the apparent discrepancy of a lower LOAEL(HEC) from Broderson et al. (1976) and the identified NOAEL(HEC) of the Holness et al. (1989) study may be the result of differences in air flow patterns since rats are obligate nose- breathers and humans breathe oronasally. The use of the NOAEL from Holness et al. (1989) can be supported as marginal in this context due to the symptomatology complaints and because human data engenders less uncertainty than extrapolation from the experimental animal data.

I.B.3. Uncertainty and Modifying Factors (Inhalation RfC)

UF — An uncertainty factor of 10 is used to allow for the protection of sensitive individuals. A factor of 3 was used to account for several data base deficiencies including the lack of chronic data, the proximity of the LOAEL to the NOAEL and the lack of reproductive and developmental toxicology studies. This factor is not larger than 3, however, since studies in rats (Schaerdel et al., 1983) have shown no increases in blood ammonia levels at exposures 32 ppm and only minimal increases at 300-1000 ppm, suggesting that no significant distribution is likely to occur at the HEC level calculated.

MF — None

I.B.4. Additional Studies/Comments (Inhalation RfC)

Groups of four healthy human volunteers were exposed weekly (5 days/week) to 25 (2 hours/day), 50 (4 hours/day) or 100 (6 hours/day) ppm ammonia (1.0, 4.1 or 12.1 mg/cu.m) for 6 weeks; or to 50 ppm (6.2 mg/cu.m) 6 hours/day for 6 weeks. Subjective and objective indications of eye and respiratory tract irritation, pulse rate, respiration rate, FVC, FEV and difficulty in performing simple cognitive tasks were used to assess toxicity. No abnormalities of the chest, heart, vital organs, neurological response, apparent motor function, or significant weight changes were observed during weekly medical examinations. Transient irritation of the nose and throat was observed at 50 ppm (duration-adjusted to 4.1 mg/cu.m) or greater (Ferguson et al., 1977).

Flury et al. (1983) reported on a 5-year follow-up case study of a 50- year-old male patient who sustained a high-concentration exposure to ammonia fumes when a refrigerator coolant tank exploded. The patient had no prior history of smoking, pulmonary disease, wheezing or atopy and no family history of atopy or asthma before the industrial accident. The patient was

hospitalized with acute respiratory failure. Laryngoscopy demonstrated membranous formation involving the entire tracheal wall. Chest examination revealed bilateral rhonchi, and chest x-rays on admission revealed bilateral perihilar infiltrates. Subsequent serial pulmonary function testing (spirometry and diffusion capacity) was performed and although the initial peripheral airway abnormality resolved over the 5-year period, a persistent expiratory obstruction and recurrent bronchospasm, suggestive of hyperreactive airways, was demonstrated. It is proposed that reepithelialization and probable reinnervation of the bronchial mucosa following the initial inflammation resulted in drastically altered irritant receptors.

Eight human volunteers were exposed to 50, 80, 110 and 140 ppm ammonia (35, 56, 76 and 97 mg/cu.m, respectively) for 2 hours, with a 1-week interval between exposures. The subjects tolerated a concentration of 76 mg/cu.m, although they rated the throat irritation as a nuisance. An ammonia concentration of 97 mg/cu.m was intolerable, and all of the subjects left the exposure chamber prematurely (Verberk, 1977).

Human volunteers were exposed to 21 or 35 mg/cu.m ammonia for 10 minutes. At 35 mg/cu.m, the irritation was not found to be "discomforting or painful" and was rated "moderate" by 4/6 volunteers, "faint" by 1/6 and "none" by 1/6; at 21 mg/cu.m, irritation was rated "faint" by 2/5 and "none" by 3/5 (MacEwen et al., 1970).

Six volunteers were exposed to 500 ppm ammonia (348 mg/cu.m) for 30 minutes. Nasal and throat irritation was reported. An increase in minute volume ranging from 50-250% over control values was observed (Silverman et al., 1949).

Kane et al. (1979) determined an RD50 value (exposure concentration to evoke a 50% decrease in respiratory rate) for sensory irritation in Swiss- Webster mice for ammonia of 303 ppm (95% C.I. 159-644) by plotting the percent decrease in respiratory rate versus the logarithm of the exposure concentration. A minimal irritation level for humans was predicted at 0.01RD50 (3 ppm).

Dahlman (1956) microscopically monitored the ciliary movement in the tracheas of rats exposed to ammonia via mouth-piece continuously for 8 minutes to concentrations of 90, 45, 20 and 10 ppm (3 rats/dose); and 6.5 and 3 ppm (2 rats/dose). Ciliary activity ceased in a concentration-dependent rate upon exposure to ammonia. Time to ciliary stasis was 5, 10, 20 and 150 seconds at concentrations of 90, 45, 20 and 6.5 ppm, respectively. Time to ciliary stasis was 7-8 minutes at the 3 ppm concentration.

Gamble and Clough (1976) whole-body exposed female Porton rats to ammonia concentrations of 200 (+/- 50) ppm for 4, 8 or 12 days or 435 (+/- 135) ppm for 7 days. Duration of exposure was not otherwise specified. The total number of animals was 16, but the apportionment into

exposure groups was not provided. Hyperplasia of the tracheal epithelium was shown to be concentration- and time-dependent. At 4 days of exposure to 200 ppm, the epithelium had changed to transitional-stratified and by 8 days there was gross change: disappearance of cilia and stratification increasing to folds forming on the luminal surface. A mucilaginous exudate was also evident with a slight increase in submucosal cellularity. At 12 days at the 200 ppm concentration, the epithelialization had increased in thickness. Rats exposed for 7 days to 435 ppm showed acute inflammatory reactions with infiltration of neutrophils, large mononucleated cells, monocytes and immature fibroblasts in the trachea. Evidence of necrotic changes at the luminal surface included pyknotic nuclei and karyorrhectic cells.

Groups of 10 guinea pigs and 20 Swiss albino mice were exposed continuously to an ammonia-air concentration of 20 ppm (13.9 mg/cu.m) for up to 6 weeks. A separate group of six guinea pigs was similarly exposed to an ammonia concentration of 50 ppm (35 mg/cu.m) for 6 weeks, and a group of 21 Leghorn chickens was exposed to a 20 ppm concentration for up to 12 weeks. Controls (number not specified) were maintained under identical conditions, except for the ammonia. Smaller groups of chickens were exposed continually to either 200 ppm for up to 3 weeks or 1000 ppm for up to 2 weeks. The effects of ammonia were found to be both time- and concentration-dependent. While no effects were observed in guinea pigs, mice, or chickens sacrificed after 1, 2, 3 or 4 weeks of exposure at 20 ppm, darkening/reddening, edema, congestion, and hemorrhage were seen in the lungs of all three species at sacrifice after 6 weeks of exposure at that concentration. In guinea pigs exposed to 50 ppm ammonia for 6 weeks, grossly enlarged and congested spleens, congested livers and lungs, and pulmonary edema were seen. In chickens exposed to 200 ppm for 17-21 days, liver congestion and slight clouding of the cornea were observed in addition to those effects observed in the chickens exposed to 20 ppm ammonia for 6 weeks. At 1000 ppm, the same effects, in addition to congestion of the spleen, were seen in chickens after just 2 weeks of exposure, and corneal opacities developed within just 8 days of exposure. In a second series of experiments, it was found that a 72-hour exposure to 20 ppm ammonia significantly increased the infection rate of chickens subsequently exposed to an aerosol of Newcastle disease virus, while the same effect was observed in just 48 hours in chickens exposed to 50 ppm. Changes in gross and micropathology did not accompany the change in disease rate (Anderson et al., 1964).

Guinea pigs were exposed to 0 or 170 ppm (118 mg/cu.m) 6 hours/day, 5 days/week for up to 18 weeks. No adverse effects were observed in animals exposed to ammonia for 6-12 weeks (HEC=21 mg/cu.m). Mild changes in the spleen, kidney suprarenal glands and livers were observed (HEC=19 mg/cu.m) in guinea pigs exposed for 18 weeks. No effects on the lungs were observed. The upper respiratory tract was not examined (Weatherby, 1952).

Swiss-Webster mice (16-24/group) were exposed to 0 or 305 ppm ammonia (212 mg/cu.m) 6 hours/day for 5 days. Nasal lesions were observed at 212 mg/cu.m which when dose duration adjusted for the RGDR, equals a LOAEL(HEC) of 4.5 mg/cu.m (Buckley et al., 1984).

Continuous exposure of rats to ammonia at 0, 40, 127, 262, 455 or 470 mg/cu.m for a minimum of 90 days (114 days for the 40 mg/cu.m group) was conducted in male and female Sprague-Dawley and Long-Evans rats. A LOAEL of 262 mg/cu.m (HEC=28 mg/cu.m) was determined based upon nasal discharge in 25% of the rats, and nonspecific circulatory and degenerative changes in the lungs and kidneys that were difficult to relate specifically to ammonia inhalation. A frank-effect-level of 455 mg/cu.m (HEC=48.7 mg/cu.m) was observed due to high mortality in the rats (90-98%). Nasal passages were not histologically examined (Coon et al., 1970).

Duroc pigs were exposed to ammonia concentrations of 10, 50, 100 and 150 ppm. Exposure to ammonia significantly decreased both food intake and body weight gain. Higher concentrations caused nasal, lacrimal and mouth secretions, which became less severe over time. No treatment-related gross or microscopic changes were observed in the bronchi, lungs or turbinates at necropsy (Stombaugh et al., 1969).

Various animal species were exposed to 0, 155 and 770 mg/cu.m for 8 hours/day, 5 days/week for 30 exposures (rats, guinea pigs, rabbits, dogs and monkeys). The LOAEL for lung inflammation is 770 mg/cu.m for rats (HEC=82.4 mg/cu.m) and guinea pigs. Ocular and nasal irritation was observed at 770 mg/cu.m in rabbits and dogs. The upper respiratory tract was not examined (Coon et al., 1970).

Atmospheric ammonia is present in relatively low concentrations in both urban and nonurban environments. Typical levels of ammonia are on the order of 5 and 20 ug/cu.m for nonurban and urban sites, respectively (WHO, 1986). The total intake of ammonia by inhalation is approximately 0.1-0.5 mg/day. Ammonia also may be excreted through expired air. Estimates of ammonia expired by humans during mouth breathing have been reported to be between 90 and 1509 ug/cu.m (Hunt and Williams, 1977) and 29-518 ug/cu.m (Larson et al., 1977). These measured values are considerably higher than the expected values from the equilibration concentrations of plasma and lung parenchyma ammonia levels (28-49 ug/cu.m). The higher-than-expected levels of ammonia in air expired by humans and other experimental animals suggests that ammonia may be synthesized by oral microflora. Furthermore, reaction products may be formed from the expired ammonia and other ambient chemicals thereby altering the toxicity and reactivity of this endogenous ammonia source. Barrow and Steinhagen (1980) measured the average expired air ammonia concentration in nose breathing rats (mean=54 ug/cu.m) and found the concentration to be in reasonable agreement with the values measured by Larson et al. (1977) in humans. However, comparison of tracheal cannulated animals to humans is not possible because in the Larson et al. (1977) study only one subject was sampled (29

ug/cu.m). Also, due to the inadequate sample size and inherent variability of breath ammonia values, some caution must be expressed in accepting the validity of the human values. Furthermore, because the oral cavity can be a "sink" or source of ammonia, comparisons to mouth breathing humans should not be made.

I.B.5. Confidence in the Inhalation RfC

Study — Medium

Database — Medium

RfC — Medium

Confidence in the principal study is medium. Although a relatively small sample size (males only) was studied and a free standing NOAEL was determined, mild extrathoracic effects were observed in rats near the same HEC as reported in the Holness study. Additional human subchronic and acute studies support the NOAEL. Confidence in the database is medium to high. Although developmental, reproductive or chronic toxicity following ammonia exposure has not been adequately tested, pharmacokinetic data suggests systemic distribution at the HEC level is unlikely. Reflecting medium confidence in the principal studies and medium to high confidence in the database, confidence in the RfD is medium.

I.B.6. EPA Documentation and Review of the Inhalation RfC

Source Document — This assessment is not presented in any existing U.S. EPA document.

Other EPA Documentation — U.S. EPA, 1987; U.S. EPA, 1989

Agency Work Group Review — 10/13/1988, 09/19/1989, 05/16/1990, 09/19/1990, 02/20/1991

Verification Date — 02/20/1991

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfC for ammonia conducted in August 2003 identified one or more significant new studies. IRIS users may request the references for those studies from the IRIS Hotline at hotline.iris@epa.gov or 202-566-1676.

I.B.7. EPA Contacts (Inhalation RfC)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (202)566-1676 (phone), (202)566-1749 (FAX) or hotline.iris@epa.gov (internet address).

II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Ammonia
CASRN — 7664-41-7

This substance/agent has not undergone a complete evaluation and determination under US EPA's IRIS program for evidence of human carcinogenic potential.

III. [reserved]

IV. [reserved]

V. [reserved]

VI. Bibliography

Substance Name — Ammonia
CASRN — 7664-41-7

VI.A. Oral RfD References

None

VI.B. Inhalation RfC References

Anderson, D.P., C.W. Beard and R.P. Hanson. 1964. The adverse effects of ammonia on chickens including resistance to infection with Newcastle disease virus. *Avian Dis.* 8: 369-379.

Barrow, C.S. and W.H. Steinhagen. 1980. NH₃ concentrations in the expired air of the rat: Importance to inhalation toxicology. *Toxicol. Appl. Pharmacol.* 53: 116-121.

Broderson, J.R., J.R. Lindsey and J.E. Crawford. 1976. The role of environmental ammonia in respiratory mycoplasmosis of rats. *Am. J. Pathol.* 85(1): 115-130.

Buckley, L.A., X.Z. Jiang, R.A. James, K.T. Morgan and C.S. Burrow. 1984. Respiratory tract lesions induced by sensory irritants at the RD50 concentration. *Toxicol. Appl. Pharmacol.* 74: 417-429.

Coon, R.A., R.A. Jones, L.J. Jenkins Jr. and J. Siegel. 1970. Animal inhalation studies on ammonia, ethylene glycol, formaldehyde, dimethylamine and ethanol. *Toxicol. Appl. Pharmacol.* 16: 646-655.

Crapo, R.O., A.H. Morris and R.M. Gardner. 1981. Reference spirometric values using techniques and equipment that meets ATS recommendations. *Am. Rev. Respir. Dis.* 123: 659-664.

Dahlman, T. 1956. Mucus flow and ciliary activity in the trachea of healthy rats exposed to respiratory irritant gases (SO₂, NH₃ and HCHO) - a functional and morphologic (light microscopic and electron microscopic) study, with special reference to technique: VIII. The reaction of the tracheal ciliary activity to single exposure to respiratory irritant gases and studies of the pH. *Acta Physiol. Scand.* 36(Suppl 123): 93-97.

Ferguson, W.S., W.C. Koch, L.B. Webster and J.R. Gould. 1977. Human physiological response and adaptation to ammonia. *J. Occup. Med.* 19(5): 319-326.

Ferris, B.G. 1978. Epidemiology standardization project. *Am. Rev. Respir. Dis.* 118: 11-31.

Flury, K.E., D.E. Dines, J.R. Rodarte and R. Rodgers. 1983. Airway obstruction due to inhalation of ammonia. *Mayo Clin. Proc.* 58: 389-393.

Gamble, M.R. and G. Clough. 1976. Ammonia build-up in animal boxes and its effect on rat tracheal epithelium. *Lab. Anim.* 10: 93-104.

Holness, D.L., J.T. Purdham and J.R. Nethercott. 1989. Acute and chronic respiratory effects of occupational exposure to ammonia. *Am. Ind. Hyg. Assoc. J.* 50(12): 646-650.

Hunt, R.D. and D.T. Williams. 1977. Spectrometric measurements of ammonia in normal human breath. *Am. Lab.* 9: 10-23.

Kane, L.E., C.S. Barrow and Y. Alarie. 1979. A short-term test to predict acceptable levels of exposure to airborne sensory irritants. *Am. Ind. Hyg. Assoc. J.* 40: 207-229.

Lapp, N.L. and R.E. Hyatt. 1967. Some factors affecting the relationship of maximal expiratory flow to lung volume in health and disease. *Dis. Chest.* 51: 475-481.

Larson, T.V., D.S. Covert, R. Frank and R.J. Charlson. 1977. Ammonia in the human airways: Neutralization of inspired acid sulfate aerosols. *Science*. 197: 161-163.

MacEwen, J.D., J. Theodore and E.H. Vernot. 1970. Human exposure to EEL concentrations of monomethylhydrazine. In: *Proc. 1st Ann. Conf. Environmental Toxicology*, Wright-Patterson Air Force Base, OH, Sept. 9-11, 1970. Aerospace Medical Research Laboratory. (AMRL-TR-70-102, Paper 23). NTIS AD727022. p. 355-363.

Schaerdel, A.D., W.J. White, C.M. Lane, B.H. Dvorchik and K. Bohner. 1983. Localized and systemic effects of environmental ammonia in rats. *Lab. Anim. Sci.* 33(1): 40-45.

Schoeb, T.R., M.K. Davidson and J.R. Lindsey. 1982. Intracage ammonia promotes growth of *Mycoplasma pulmonis* in the respiratory tract of rats. *Infect. Immun.* 38: 212-217.

Silverman, L., J.L. Whittenberger and J. Muller. 1949. Physiologic response of man to ammonia in low concentrations. *J. Ind. Hyg. Toxicol.* 31: 74-78.

Stombaugh, D.P., H.S. Teague and W.L. Roller. 1969. Effects of atmospheric ammonia on the pig. *J. Animal Sci.* 28: 844-847.

U.S. EPA. 1987. Health Effects Assessment for Ammonia. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC.

U.S. EPA. 1989. Health Issue Assessment: Summary Review of Health Effects Associated with Ammonia. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC. EPA/600/8-89-052F.

Verberk, M.M. 1977. Effects of ammonia in volunteers. *Int. Arch. Occup. Environ. Health.* 39: 73-81.

Weatherby, J.H. 1952. Chronic toxicity of ammonia fumes by inhalation. *Proc. Soc. Exp. Biol. Med.* 81: 300-301.

WHO (World Health Organization). 1986. Environmental Health Criteria 54: Ammonia. (IPCS International Programme on Chemical Safety). Geneva.

VI.C. Carcinogenicity Assessment References

None

VII. Revision History

Substance Name — Ammonia
CASRN — 7664-41-7

Date	Section	Description
05/01/1991	I.B.	Inhalation RfC summary on-line
10/28/2003	I.B.6.	Screening-Level Literature Review Findings message has been added.

VIII. Synonyms

Substance Name — Ammonia
CASRN — 7664-41-7
Last Revised — 05/01/1991

- 7664-41-7
- Ammonia
- AM-FOL
- AMMONIA GAS
- Ammonia Solution, Strong
- Ammoniac [French]
- Ammoniaca [Italian]
- Ammoniak [German]
- Amoniaco [Spanish]
- Amoniak [Polish]
- ANHYDROUS AMMONIA

- Aromatic Ammonia, Vaporole
- Caswell No. 041
- EPA Pesticide Chemical Code 005302
- HSDB 162
- Nitro-Sil
- R 717
- SPIRIT OF HARTSHORN
- UN 1005
- UN 2073
- UN 2672