



# HPA Compendium of Chemical Hazards

## Ammonia

### Key Points

#### Fire

- Non-flammable, but mixtures of ammonia and air may explode when ignited
- Chemically stable under normal conditions
- Emits poisonous fumes when heated to decomposition
- Use fine water spray and liquid-tight protective clothing with breathing apparatus

#### Health

- Exposure by any route may be dangerous
- Secondary contamination may occur
- Toxic and corrosive
- Acute inhalation may result in irritation of eyes and nose with sore throat, cough, chest tightness, headache and confusion
- Acute ingestion of ammonia solutions may result in burns to the mouth and throat
- Acute skin exposure may result in deep burns
- Acute eye exposure may cause inflammation, lacrimation and photophobia
- Chronic inhalation has been associated with increased cough, phlegm production, wheeze and asthma
- Ammonia is not considered to be carcinogenic to humans
- Ammonia is not considered to be a human reproductive or developmental toxicant

#### Environment

- Dangerous for the environment
- Inform Environment Agency of substantial release incidents

## Contents

### GENERAL INFORMATION

Background .....	5
Production and Uses .....	6
Frequently Asked Questions .....	7

### INCIDENT MANAGEMENT

Hazard Identification.....	10
Standard (UK) Dangerous Goods Emergency Action Codes	10
Chemical Hazard Information and Packaging for Supply Classification	12
Specific concentration limits	13
Physicochemical Properties .....	14
Threshold Toxicity Values .....	15
Published Emergency Response Guidelines .....	16
Emergency Response Planning Guideline (ERPG) Values	16
Acute Exposure Guideline Levels (AEGLs)	16
Exposure Standards, Guidelines or Regulations.....	17
Occupational standards	17
Public health guidelines	17
Health Effects .....	18
Major routes of exposure	18
Immediate signs or symptoms of acute exposure	18
Decontamination and First Aid .....	19
Important Notes	19
Dermal exposure	19
Ocular exposure	19
Inhalation	19
Ingestion	20

### TOXICOLOGICAL OVERVIEW

Summary of Health Effects.....	22
Kinetics and Metabolism .....	23
Sources and Route of Human Exposure.....	23
Health Effects of Acute / Single Exposure.....	25
Human Data	25
Inhalation.....	25
Ingestion.....	26
Ocular / dermal exposure .....	26

Delayed effects following an acute exposure ..... 27

Health Effects of Chronic / Repeated Exposure..... 28

    Human Data ..... 28

        Inhalation..... 28

        Ingestion..... 28

        Genotoxicity..... 28

        Carcinogenicity ..... 29

        Reproductive and developmental toxicity ..... 29

    Animal and In-Vitro Data ..... 29

        Inhalation..... 29

        Ingestion..... 29

        Genotoxicity..... 30

        Carcinogenicity ..... 30

        Reproductive and developmental toxicity ..... 30

References ..... 32

# Ammonia

## General information

### Key Points

#### Fire

- Non-flammable, but mixtures of ammonia and air may explode when ignited
- Chemically stable under normal conditions
- Emits poisonous fumes when heated to decomposition
- Use fine water spray and liquid-tight protective clothing with breathing apparatus

#### Health

- Exposure by any route may be dangerous
- Secondary contamination may occur
- Toxic and corrosive
- Short-term inhalation may result in irritation of eyes and nose with sore throat, cough, chest tightness, headache and confusion
- Short term ingestion of ammonia solutions may result in burns to the mouth and throat
- Short-term skin exposure may result in deep burns
- Short-term eye exposure may cause swelling, watering and sensitivity to light
- Long-term inhalation has been associated with increased cough, phlegm production, wheeze and asthma
- Ammonia is not considered to be carcinogenic to humans
- Ammonia is not considered to be cause damage to the unborn child

#### Environment

- Dangerous for the environment
- Inform Environment Agency of substantial release incidents

## Background

Ammonia is a colourless, reactive gas that is lighter than air (approximately half as heavy) which dissolves readily in water. Ammonia has a strong smell, similar to urine, which can be detected by most people even in small amounts. Ammonia gas is non-flammable, but because some mixtures with air could explode if ignited, it is treated as flammable. Solutions of ammonia are alkali and concentrated solutions are corrosive. Names for these solutions include ammonium hydroxide, aqueous ammonia and ammonia solution.

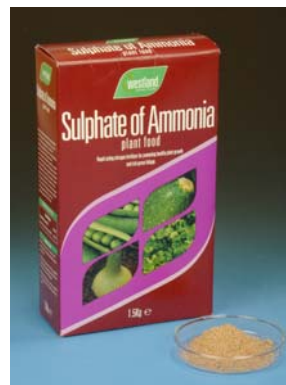


Ammonia is a very important industrial chemical, with over one million tons produced in the UK annually. Ammonia gas is produced industrially by reacting hydrogen and nitrogen at high temperature and pressure. This reaction is known as the Haber-Bosch process.

There are many uses for ammonia including the production of fertilisers, plastics, synthetic fibres, dyes, explosives and pharmaceuticals. Because it is widely used, exposure may occur in a number of situations.

Exposure may occur in the workplace although safe levels allowed are enforced to protect the employees. Such levels are below those that are thought to cause harmful effects.

In the home, ammonia is used in certain cleaning products or garden fertilisers.



Ammonia occurs naturally at low levels throughout the environment, as it is released from the natural breakdown of organic waste matter. Intensive agricultural practices may increase local levels, e.g. from lots of animal waste (slurry).



As with all chemicals, the health effects are generally related to the amount you are exposed to.

At low concentrations, ammonia may cause eye irritation, coughing or a sore throat. Inhaling high concentrations of ammonia may cause burns, swelling of the airway and lung damage and can be fatal. Ammonia solutions may cause serious burns if splashed on skin or if swallowed. Splashes in the eye may cause damage which may be irreversible in some cases and lead to loss of sight.

Children may be more sensitive to the effects of ammonia due to their smaller size.

Ammonia is unlikely to cause harm to the unborn child.

Ammonia is not considered to be a cancer-causing chemical.

## Production and Uses

### Key Points

- Ammonia is an important industrial chemical and over 1 million tonnes are produced in the UK each year
- The main use of ammonia is in the production of fertilisers
- Ammonia is also used in the manufacture of plastics, synthetic fibres, dyes, explosives and pharmaceuticals
- Ammonia is used as an industrial refrigerant and in some industrial and domestic cleaning products

Ammonia is produced from a variety of biological and industrial processes. Around 99% of atmospheric ammonia is considered to be as consequence of the natural breakdown of organic waste matter.

Ammonia is produced industrially using the Haber-Bosch process in which nitrogen and hydrogen are combined at high pressure over a catalyst. As an industrial chemical, ammonia is one of the most widely produced, with global production capacity estimated at approximately 160 million tonnes in 2004. Over 1 million tonnes of ammonia are manufactured in the UK each year.

The key use for ammonia is in the production of fertilisers including ammonium sulphate and ammonium nitrate. Other uses include the manufacture of plastics, synthetic fibres, dyes, explosives and pharmaceuticals. Ammonia is also used as an industrial refrigerant and is found in some household and industrial cleaning agents as the ammonium ion. Ammonium salts (liberating ammonia) have been used as “smelling salts”.

Synonyms include ammonia gas, anhydrous ammonia, and liquid ammonia. Aqueous solutions are referred to as aqueous ammonia, ammonia solution, and ammonium hydroxide.

## Frequently Asked Questions

### *What is ammonia?*

Ammonia is a colourless, irritant, reactive gas that is lighter than air (approximately half as heavy). It dissolves readily in water and has a characteristic pungent odour similar to urine.

### *What is ammonia used for?*

The main use of ammonia is in the manufacture of fertilisers including ammonium nitrate and ammonium sulphate, and also to produce plastics, synthetic fibres, dyes, pharmaceuticals, explosives and some household and industrial cleaning products.

### *How does ammonia get into the environment?*

Ammonia is mainly released into the environment from the natural breakdown of organic matter and elevated levels can be generated by intensive farming practices. Environmental ammonia may also be released from some industrial process or from accidents during transportation.

### *How will I be exposed to ammonia?*

Ammonia is produced from the natural breakdown of organic matter and so exposure to ammonia will occur at very low levels throughout the environment. Exposure to ammonia may also occur if it is used at your work or if you use it at home.

### *If there is ammonia in the environment will I have any adverse health effects?*

The presence of ammonia in the environment does not always lead to exposure. Clearly, in order for it to cause any adverse health effects you must come into contact with it. You may be exposed by breathing, eating, or drinking the substance or by skin contact. Following exposure to any chemical, the adverse health effects you may encounter depend on several factors, including the amount to which you are exposed (dose), the way you are exposed, the duration of exposure, the form of the chemical and if you were exposed to any other chemicals.

Ammonia and ammonia solutions are irritant and corrosive. Minor exposures may result in a burning sensation of the eyes and throat and more substantial exposure may cause coughing or breathing difficulties. A one-off exposure (sufficient to cause mild lung or eye irritation) is unlikely to result in long-term health effects. Exposure to high concentrations of ammonia may be potentially fatal.

### *Can ammonia cause cancer?*

Exposure to ammonia has not been linked to the development of cancer. In other words, ammonia is not thought to be carcinogenic.

### *Does ammonia affect children or damage the unborn child?*

There is no evidence to suggest that ammonia, at concentrations that do not affect the mother, can affect the health of the unborn child.

### *What should I do if I am exposed to ammonia?*

You should remove yourself from the source of exposure.

If you have got ammonia on your skin, remove soiled clothing, wash the affected area with lukewarm water and soap for at least 10 – 15 minutes and seek medical advice.

If you have got ammonia in your eyes, remove contact lenses, irrigate the affected eye with lukewarm water for at least 10 – 15 minutes and seek medical advice.

If you have inhaled or ingested ammonia, seek medical advice.

# Ammonia

## Incident management

### Key Points

#### Fire

- Non-flammable, but mixtures of ammonia and air may explode when ignited
- Chemically stable under normal conditions
- Emits toxic fumes of ammonia and oxides of nitrogen when heated to decomposition
- In the event of a fire involving ammonia, use fine water spray and liquid-tight protective clothing with breathing apparatus

#### Health



- Exposure by any route may be dangerous
- Secondary contamination may occur
- Toxic and corrosive
- Inhalation may result in irritation of eyes and nose with sore throat, cough, chest tightness, headache, ataxia and confusion
- Ingestion of ammonia solutions may cause immediate burning of the mouth and throat, drooling, difficulty swallowing with retrosternal and abdominal pain.
- Dermal exposure may result in deep burns
- Ocular exposure may cause pain, lacrimation, conjunctivitis, photophobia and corneal burns


#### Environment

- Dangerous for the environment
- Inform Environment Agency of substantial release incidents

## Hazard Identification

### Standard (UK) Dangerous Goods Emergency Action Codes<sup>(a)</sup>


<b>UN</b>		<b>1005</b>	Ammonia, anhydrous	
<b>EAC</b>		<b>2RE</b>	Use fine water spray. Wear liquid-tight chemical protective clothing in combination with breathing apparatus*. Spillages and decontamination run-off may be washed to drains with large quantities of water. There may be a public safety hazard outside the immediate area of the incident**.	
<b>APP</b>		<b>A(c)</b>	Liquefied gas with boiling point below -20 °C. Gas-tight chemical protective suit with breathing apparatus***.	
<b>Hazards</b>	<b>Class</b>	<b>2.3</b>	Toxic gases	
	<b>Sub risks</b>	<b>8</b>	Corrosive substance	
<b>HIN</b>		<b>268</b>	Toxic gas, corrosive	


<b>UN</b>		<b>2073</b>	Ammonia solution (35 – 50 %)	
<b>EAC</b>		<b>2RE</b>	Use fine water spray. Wear liquid-tight chemical protective clothing in combination with breathing apparatus*. Spillages and decontamination run-off may be washed to drains with large quantities of water. There may be a public safety hazard outside the immediate area of the incident**.	
<b>APP</b>		<b>-</b>		
<b>Hazards</b>	<b>Class</b>	<b>2.2</b>	Non flammable, non toxic gases	
	<b>Sub risks</b>	<b>-</b>		
<b>HIN</b>		<b>20</b>	Asphyxiant gas or gas with no subsidiary risk	

UN – United Nations number; EAC – Emergency Action Code; APP – Additional Personal Protection; HIN - Hazard Identification Number

<sup>a</sup> Dangerous Goods Emergency Action Code List, HM Fire Service Inspectorate, Publications Section, The Stationery Office, 2004.

Standard (UK) Dangerous Goods Emergency Action Codes<sup>(a)</sup>

<b>UN</b>		<b>2672</b>	Ammonia solution (10 – 35 %)	
<b>EAC</b>		<b>2R</b>	Use fine water spray. Wear liquid-tight chemical protective clothing in combination with breathing apparatus*. Spillages and decontamination run-off ff may be washed to drains with large quantities of water.	
<b>APP</b>		-		
<b>Hazards</b>	<b>Class</b>	<b>8</b>	Corrosive substance	
	<b>Sub risks</b>	-		
<b>HIN</b>		<b>80</b>	Corrosive or slightly corrosive substance	

<b>UN</b>		<b>3318</b>	Ammonia solution (>50 %)	
<b>EAC</b>		<b>2RE</b>	Use fine water spray. Wear liquid-tight chemical protective clothing in combination with breathing apparatus*. Spillages and decontamination run-off may be washed to drains with large quantities of water. There may be a public safety hazard outside the immediate area of the incident**.	
<b>APP</b>		<b>B</b>	Gas-tight chemical protective suit with breathing apparatus**.	
<b>Hazards</b>	<b>Class</b>	<b>8</b>	Corrosive substance	
	<b>Sub risks</b>	-		
<b>HIN</b>		<b>268</b>	Toxic gas, corrosive	

UN – United Nations number; EAC – Emergency Action Code; APP – Additional Personal Protection; HIN - Hazard Identification Number

\* Liquid-tight chemical protective clothing (BS 8428) in combination with self-contained open circuit positive pressure compressed air breathing apparatus (BS EN 137).





\*\* People should stay indoors with windows and doors closed, ignition sources should be eliminated and ventilation stopped. Non-essential personnel should move at least 250 m away from the incident.

\*\*\* Gas-tight chemical protective clothing (BS EN 943) in combination with self-contained open circuit positive pressure compressed air breathing apparatus (BS EN 137).

<sup>a</sup> Dangerous Goods Emergency Action Code List, HM Fire Service Inspectorate, Publications Section, The Stationery Office, 2004.

*Chemical Hazard Information and Packaging for Supply Classification<sup>(a)</sup>*

*Ammonia, anhydrous*



<b>Classification</b>	<b>F</b>	Flammable	
	<b>T</b>	Toxic	
	<b>C</b>	Corrosive	
	<b>N</b>	Dangerous for the environment	
<b>Risk phrases</b>	<b>R10</b>	Flammable	
	<b>R23</b>	Toxic by inhalation	
	<b>R34</b>	Causes burns	
	<b>R50</b>	Very toxic to aquatic organisms	
<b>Safety phrases</b>	<b>S(1/2)</b>	Keep locked up out of the reach of children	
	<b>S9</b>	Keep container in a well ventilated place	
	<b>S16</b>	Keep away from sources of ignition- No smoking	
	<b>S26</b>	In case of contact with eyes, rinse immediately with plenty of water and seek medical advice	
	<b>S36/37/39</b>	Wear suitable protective clothing, gloves and eye/face protection	
	<b>S45</b>	In case of accident or if you feel unwell seek medical advice immediately (show the label where possible)	
	<b>S61</b>	Avoid release to the environment. Refer to special instructions / safety data sheet	

<sup>a</sup> European Chemicals Bureau, Classification and Labelling, Annex I of Directive 67/548/EEC; <http://ecb.jrc.it/classification-labelling/> (accessed 2/2007).

*Specific concentration limits*

Concentration	Classification
$C \geq 25 \%$	T, N; R23-34-50
$5 \% \leq C < 25 \%$	T; R23-34
$0.5 \% \leq C < 5 \%$	Xn; R20-36/37/38

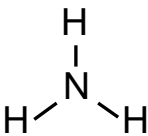
*Ammonia... %*

<b>Classification</b>	<b>C</b>	Corrosive	
	<b>N</b>	Dangerous for the environment	
<b>Risk phrases</b>	<b>R34</b>	Causes burns	
	<b>R50</b>	Very toxic to aquatic organisms	
<b>Safety phrases</b>	<b>S(1/2)</b>	Keep locked up out of the reach of children	
	<b>S26</b>	In case of contact with eyes, rinse immediately with plenty of water and seek medical advice	
	<b>S36/37/39</b>	Wear suitable protective clothing, gloves and eye/face protection	
	<b>S45</b>	In case of accident or if you feel unwell seek medical advice immediately (show the label where possible)	
	<b>S61</b>	Avoid release to the environment. Refer to special instructions / safety data sheet	

*Specific concentration limits*

Concentration	Classification
$C \geq 25 \%$	C; N; R34-50
$5 \% \leq C < 25 \%$	C; R34
$0.5 \% \leq C < 5 \%$	Xi; R36/37/38

## Physicochemical Properties

<b>CAS number</b>	7664-41-7
<b>Molecular weight</b>	17
<b>Empirical Formula</b>	NH <sub>3</sub>
<b>Common synonyms</b>	Hydrogen nitride
<b>State at room temperature</b>	Gas
<b>Volatility</b>	Vapour pressure = 7600 mm Hg at 25.7 °C
<b>Specific gravity</b>	0.8 at 21 °C (air = 1)
<b>Flammability</b>	Non flammable, but mixtures of ammonia and air may explode when ignited
<b>Lower explosive limit</b>	15 %
<b>Upper explosive limit</b>	28 %
<b>Water solubility</b>	Highly soluble, forming solutions of ammonium hydroxide and evolving heat
<b>Reactivity</b>	Stable. Incompatible with strong oxidising substances, acids, calcium hypochlorite bleaches and halogens. Liquid ammonia attacks some plastics, rubbers and coatings. Corrosive to copper and galvanised surfaces.
<b>Reaction or degradation products</b>	Emits toxic fumes of ammonia and oxides of nitrogen when heated to decomposition
<b>Odour</b>	Characteristic, pungent odour of drying urine
<b>Structure</b>	

References<sup>(a,b,c)</sup>

<sup>a</sup> Ammonia (HAZARDTEXT® Hazard Management). In: Klasco RK (Ed): TOMES® System. Thomson Micromedex, Greenwood Village, Colorado (accessed 02/2007).

<sup>b</sup> The Merck Index (14<sup>th</sup> Edition). Entry 492: ammonia, 2006.

<sup>c</sup> The Dictionary of Substances and their Effects. Ed. S Gangolli. Second Edition, Volume 1, 1999.

## Threshold Toxicity Values

EXPOSURE VIA INHALATION		
ppm	mg m <sup>-3</sup>	SIGNS AND SYMPTOMS
50	35	Slight irritation to eyes, nose and throat
100	70	Rapid irritation to eye and respiratory tract
700	488	Immediately irritating to eyes and throat
1500	1045	Pulmonary oedema and coughing
2500	1742	Life threatening

Reference<sup>(a)</sup>

---

<sup>a</sup> International Programme on Chemical Safety, Environmental Health Criteria 54: Ammonia, 1986.

## Published Emergency Response Guidelines

### Emergency Response Planning Guideline (ERPG) Values<sup>(a)</sup>

	Listed value (ppm)	Calculated value (mg m <sup>-3</sup> )
<b>ERPG-1*</b>	25	18
<b>ERPG-2**</b>	150	105
<b>ERPG-3***</b>	750	525

\* Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing other than mild transient adverse health effects or perceiving a clearly defined, objectionable odour.

\*\* Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action.

\*\*\* Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing life-threatening health effects.

### Acute Exposure Guideline Levels (AEGLs)<sup>(b)</sup>

	ppm				
	10 min	30 min	60 min	4 hr	8 hr
<b>AEGL-1<sup>†</sup></b>	30	30	30	30	30
<b>AEGL-2<sup>††</sup></b>	220	220	160	110	110
<b>AEGL-3<sup>†††</sup></b>	2700	1600	1100	550	390

<sup>†</sup> The level of the chemical in air at or above which the general population could experience notable discomfort.

<sup>††</sup> The level of the chemical in air at or above which there may be irreversible or other serious long-lasting effects or impaired ability to escape.

<sup>†††</sup> The level of the chemical in air at or above which the general population could experience life-threatening health effects or death.

<sup>a</sup> American Industrial Hygiene Association (AIHA). Emergency Response Planning Guideline Values and Workplace Environmental Exposure Level Guides Handbook, Fairfax, VA, 2005.

<sup>b</sup> U.S. Environmental Protection Agency. Acute Exposure Guideline Levels, <http://www.epa.gov/oppt/aegl/pubs/chemlist.htm> (accessed 02/2007).

## Exposure Standards, Guidelines or Regulations

### *Occupational standards*

<b>WEL</b> <sup>(a)</sup>	LTEL(8 hour reference period): 25 ppm (18 mg m <sup>-3</sup> )
	STEL(15 min reference period): 35 ppm (25 mg m <sup>-3</sup> )

### *Public health guidelines*

<b>DRINKING WATER QUALITY GUIDELINE</b> <sup>(b)</sup>	0.5 mg L <sup>-1</sup> as NH <sub>4</sub>
<b>AIR QUALITY GUIDELINE</b>	No guideline value specified
<b>SOIL GUIDELINE VALUE AND HEALTH CRITERIA VALUES</b>	No guideline values specified

WEL – Workplace exposure limit; LTEL - Long-term exposure limit; STEL – Short-term exposure limit

<sup>a</sup> Health & Safety Executive. EH40/2005 Workplace Exposure Limits 2005. The Stationery Office, London, 2005

<sup>b</sup> Interim Guidance on the Water Supply (Water Quality) Regulations 2000 (England) and the Water Supply (Water Quality) Regulations 2001 (Wales). Drinking Water Inspectorate, September 2003.

## Health Effects

### *Major routes of exposure<sup>(a)</sup>*

- Exposure by any route (ingestion, inhalation, dermal or ocular exposure) may be dangerous.

### *Immediate signs or symptoms of acute exposure<sup>(b-e)</sup>*

- Inhalation may result in irritation of eyes and nose with sore throat, cough, chest tightness, headache, ataxia and confusion. Dyspnoea and stridor due to laryngeal oedema may follow.
- Ingestion may cause immediate burning of the mouth and throat, drooling, difficulty swallowing with retrosternal and abdominal pain. There is often hypersalivation and vomiting. Haematemesis and shock may complicate severe cases. The larynx may also be burned causing oedema, airway obstruction and difficulty clearing bronchial secretions. Strong alkalis such as ammonia may damage the oesophagus more than the stomach with ulceration, perforation and mediastinitis.
- Dermal exposure may result in deep, full thickness, liquefaction burns due to the solubilisation of proteins and collagen, saponification of lipids and the dehydration of tissue cells leading to extensive damage.
- Ocular exposure contact may result in pain, blepharospasm, lacrimation, conjunctivitis, palpebral oedema, photophobia and corneal burns which should be considered an ophthalmic emergency.

---

TOXBASE - <http://www.toxbase.org>

<sup>a</sup> TOXBASE: Ammonia, 2001.

<sup>b</sup> TOXBASE: Corrosives – ingestion, 2002.

<sup>c</sup> TOXBASE: Corrosives – inhalation, 2002.

<sup>d</sup> TOXBASE: Skin decontamination – corrosives, 2002.

<sup>e</sup> TOXBASE: Chemicals splashed or sprayed into the eyes, 2007.

## Decontamination and First Aid

### Important Notes

- Ambulance staff, paramedics and emergency department staff treating chemically-contaminated casualties should be equipped with Department of Health approved, gas-tight (Respirex) decontamination suits based on EN466:1995, EN12941:1998 and prEN943-1:2001, where appropriate.
- Decontamination should be performed using local protocols in designated areas such as a decontamination cubicle with adequate ventilation.
- Secondary contamination may occur.

### Dermal exposure<sup>(a)</sup>

- Remove patient for exposure.
- The patient should remove all clothing and personal effects.
- Double-bag soiled clothing and place in a sealed container clearly labelled as a biohazard.
- Wash hair and all contaminated skin with copious amounts of water (preferably warm) and soap for at least 10-15 minutes. Decontaminate open wounds first and avoid contamination of unexposed skin.
- Pay special attention to skin folds, axillae, ears, fingernails, genital areas and feet.
- Burns totalling more than 15 % of body surface in adults (>10 % in children) will require standard fluid resuscitation as for thermal burns.
- Cover affected area with a clean non-adherent dressing.

### Ocular exposure<sup>(b)</sup>

- Remove patient from exposure.
- Remove contact lenses if necessary and immediately irrigate the affected eye thoroughly with water or 0.9% saline for at least 10-15 minutes.
- Patients with corneal damage or those whose symptoms do not resolve rapidly should be referred for urgent ophthalmological assessment.

### Inhalation<sup>(c)</sup>

- Remove patient from exposure.
- Ensure a clear airway and adequate ventilation.
- Give oxygen to symptomatic patients.
- Apply other supportive measures as indicated by the patient's clinical condition.

---

TOXBASE - <http://www.toxbase.org>

<sup>a</sup> TOXBASE: Ammonia, 2001.

<sup>b</sup> TOXBASE: Chemicals splashed or sprayed into the eyes, 2007.

<sup>c</sup> TOXBASE: Corrosives - inhalation, 2002.

### *Ingestion*<sup>(a)</sup>

- Ensure a clear airway and adequate ventilation.
- Give oxygen to symptomatic patients.
- Do not attempt gastric lavage or give neutralising chemicals as heat produced during neutralization reactions may increase injury.
- Apply other measures as indicated by the patient's clinical condition.

---

<sup>a</sup> TOXBASE: Corrosives – ingestion, 2002.

# Ammonia

## Toxicological overview

### Key Points

#### *Kinetics and metabolism*

- Ammonia dissolves in moisture in the air and on tissue or mucous membranes to form ammonium hydroxide, a strong base
- Ammonium is produced in the intestines by bacteria and is efficiently absorbed from the gastrointestinal tract
- Dermal or ocular absorptions are considered not to contribute significantly to systemic ammonium following exposure
- Ammonia is readily metabolised in the liver to urea or glutamine
- Ammonia is excreted primarily in the urine as urea

#### *Health effects of acute exposure*

- Ammonia and ammonia solutions are irritant and corrosive and may be harmful by all routes of exposure
- Acute oral exposure rapidly results in pain, excessive salivation and burns to the mouth, throat and oesophagus
- Acute inhalation may initially cause upper respiratory tract irritation. Substantial exposures can cause burns in the oral cavity, nasopharynx, larynx and trachea, together with airway obstruction, respiratory distress and bronchiolar and alveolar oedema
- Ammonia or ammonia solutions are corrosive in contact with tissue, and splashes to the eye may result in serious injury

#### *Health effects of chronic exposure*

- Effects following chronic oral exposure have not been defined in humans. Experiments in animals suggest osteoporosis, occurring secondary to chronic metabolic acidosis
- Chronic inhalation has been associated with increased cough, phlegm, wheeze and asthma
- Ammonia is considered not to be a human carcinogen
- Ammonia is considered not to be a human reproductive or developmental toxicant

## Toxicological Overview

### *Summary of Health Effects*

Ammonia and ammonium hydroxide are corrosive and can rapidly penetrate the eye and may cause permanent injury. Therefore, splashes in the eye should be considered an ophthalmic emergency.

Dermal exposure to ammonia or its solutions may result in irritation and, depending on the concentration, alkali burns. Pressurised ammonia (as a liquefied gas) may also cause cryogenic burns following skin or eye contact.

Ingestion of ammonia solutions (ammonium hydroxide) causes rapid onset of signs and symptoms including pain in the mouth, throat and chest, excessive salivation and extensive alkali burns to the aerodigestive tract. Chronic oral exposure to ammonia has not been characterised in humans. Limited animal data have shown that osteoporosis secondary to chronic metabolic acidosis may occur.

Inhalation of ammonia causes rapid onset of signs and its toxic effects are mediated through its irritant and corrosive properties. Features include irritation to the nose, throat and respiratory tract. Increased lacrimation, coughing, an increased respiratory rate as well as respiratory distress may occur. Substantial exposures can cause burns of all depths in the oral cavity, nasopharynx, larynx and trachea, together with airway obstruction and bronchiolar and alveolar oedema. Exposure to a massive concentration of ammonia gas may be fatal within minutes. There are limited data on the chronic effects of ammonia in exposed populations. In one study, an association was noted between exposure to ammonia and cough, phlegm, wheezing, dyspnoea and asthma; with a concomitant reduction in lung function.

Ammonia has no structural alerts for DNA reactivity, and is not mutagenic.

Ammonia has not been classified as a human carcinogen. Ammonia is not considered to be an animal carcinogen, ingestion by rats of ammonia as ammonium hydroxide for 2 years did not result in an increase in cancers.

It is unlikely that exposure to environmental levels of ammonia would result in reproductive or developmental toxicity. Data from animal studies show that foetal toxicity or embryotoxicity may occur but secondary to maternal toxicity after very high exposures.

### ***Kinetics and Metabolism***

Ammonia is extremely soluble in water and dissolves in the mucus fluid covering the mucous lining of the respiratory system to produce ammonium hydroxide, a strong base. Following a short term inhalation exposure, ammonia is almost entirely retained in the upper nasal mucosa [1]. Inhalation of high concentrations of ammonia may exceed the capacity of this mechanism leading to systemic absorption through the lungs.

Although ammonia rapidly enters the eye, systemic absorption is considered not to be quantitatively significant [1]. The toxicity findings after acute skin exposure to ammonia suggest that systemic absorption is not significant by this route either [2].

Ammonia is absorbed readily through mucous membranes and the intestinal tract but not through the skin [3]. It also rapidly penetrates the eye but as a route of systemic absorption, this is likely to be quantitatively insignificant.

Absorbed ammonia is well distributed throughout body compartments and reacts with hydrogen ions, depending on the pH of the compartment to produce ammonium ions [3]. The ammonium ion is less mobile due to its charged nature [1].

Ammonium ion is endogenously produced in the gut from the bacterial breakdown of nitrogenous constituents of food. Almost all of this endogenous ammonium (approximately 99% of the 4 g produced daily) is absorbed by passive diffusion from the intestinal tract before entering the hepatic portal vein [2].

In the liver, ammonium ions are extensively metabolised to urea and glutamine. Consequently, levels of ammonia that reach the circulation are low [2]. Clearly, hepatic insufficiency could affect ammonium ion metabolism.

Ammonia reaching the circulation is principally excreted by humans as urinary urea [2], excretion of absorbed ammonia in exhaled breath and faeces is not significant [3]. Small amounts of ammonia are excreted via the urine; the average daily excretion for human beings is approximately 2-3 µg, about 0.01 % of the total body burden. Small amounts of unabsorbed ammonia may also be excreted from the gastrointestinal tract in the faeces [2].

### ***Sources and Route of Human Exposure***

Apart from endogenously produced ammonia and ammonium, the major route of exposure to ammonia is by inhalation. Ammonia is released from a number of natural processes, and low levels are present in ambient air.

In Europe, agriculture is the largest source of ammonia [4], where it is liberated from manure spread on land and from livestock housing. In the UK, total ammonia emissions have been estimated at around 320,000 tonnes per year. Emissions from cattle, pig and poultry farming alone account for around 66% of this total [4] with volatilisation of some fertilisers (such as ammonium carbonate) accounting for a further 9% of total emissions. Local concentrations may therefore be elevated where organic waste matter is concentrated, such as in intensive farming environments for cattle and pig farming and chickens [4]. Non agricultural sources include sewage sludge, pets, industrial and combustion processes and petrol vehicles fitted with catalytic converters [4]. Ammonia is also produced in the human gut by bacteria.

Ammonia is used either directly or indirectly in many industrial processes and as such exposure may occur in a range of industrial settings, some of which are described above.

Ammonia is transported in bulk as a pressurised gas and spills or leaks after accidents are another potential source of exposure.

Domestically, exposure may occur from certain cleaning agents and dyes. Reaction of cleaning products may cause liberation of ammonia gas.

Ammonia gas is not persistent and rapidly reacts in the environment to ammonium compounds. This means that the hazards associated with the pure chemical rapidly decrease after release.

## Health Effects of Acute / Single Exposure

### Human Data

#### Inhalation

The clinical manifestations of acute ammonia exposure are usually immediate in presentation and its toxic effects are mediated through its irritant and corrosive properties.

Ammonia is an upper-respiratory tract irritant and inhalation will rapidly cause irritation to the nose, throat and respiratory tract. Increased lacrimation, coughing, an increased respiratory rate as well as respiratory distress may occur [1]. The retention of ammonia in the nasal mucosa may protect against some lung effects at low concentrations.

Substantial exposures to concentrated aerosols of ammonium hydroxide, elevated levels of ammonia gas or anhydrous ammonia fumes, can cause burns of all depths in the oral cavity, nasopharynx, larynx and trachea, together with airway obstruction, respiratory distress and pulmonary oedema [2, 5, 6].

Exposure to a massive concentration of ammonia gas may be fatal within minutes and asphyxiation may occur after exposure in poorly ventilated or enclosed spaces. Findings in fatal cases include extensive oedema, full thickness burns to the entire respiratory tract, purulent bronchitis and greatly distended lungs [2, 5, 7]. Bronchial walls may also be stripped of their epithelial lining [7, 8].

Lower levels of ammonia exposure that do not result in upper-airway obstruction may cause significant alkali burns throughout the tracheo-bronchial tree [5].

Systemic effects following acute exposures to high concentrations of ammonia include an elevated pulse and blood pressure, bradycardia, cardiac arrest, cyanosis and hemorrhagic necrosis of the liver [2].

The primary features after ammonia exposure are summarised in Table 1.

**Table 1. Summary of toxic effects following acute exposure to ammonia by inhalation [2, 9].**

Dose		Signs and Symptoms
mg m <sup>-3</sup>	ppm	
35	50	Irritation to eyes, nose and throat (2 h exposure)
70	100	Rapid eye and respiratory tract irritation
174	250	Tolerable by most persons (30-60 min exposure)
488	700	Immediately irritating to eyes and throat
>1045	>1500	Pulmonary oedema, coughing, laryngospasm
1740-3134	2500-4500	Fatal (30 min)
3480-6965	5000-10000	Rapidly fatal due to airway obstruction

Values in mg m<sup>-3</sup> are approximate calculations from ppm, where mg m<sup>-3</sup> = ppm x gram molecular weight/24.45 (molar volume of air at standard temperature and pressure)

Ammonia has a pungent and characteristic odour of drying urine which is discernible at around 35 mg m<sup>-3</sup> (50 ppm) [1, 2]. However, ammonia causes olfactory fatigue (adaptation)

making its presence difficult to detect when exposure is prolonged. Odour, therefore, is not to be considered as a reliable indicator of exposure, or the extent of an exposure.

### **Ingestion**

Ingestion of ammonia solutions (ammonium hydroxide) causes rapid onset of signs and symptoms including pain in the mouth, throat and chest, excessive salivation and extensive alkali burns to the aerodigestive tract. Though there is little quantitative data, these features have been noted in one case involving ingestion (with a suicidal intent) of as little as 20-25 mL of 6% household ammonia solution [10].

Paediatric exposures to ammonia capsules (used as “smelling salts”) or small volumes of ammonia solutions may cause the child to be drooling and irritable, dysphagic and with ulcerative lesions to the buccal cavity and first degree burns to the tongue or aerodigestive tract [11-13]. Complete recovery was, however, noted in all these cases of oral paediatric poisoning.

Adult fatalities have occurred from deliberate ingestion of ammonium solutions. In one case, ingestion of an unspecified volume of 3% ammonium ion resulted in aspiration pneumonia and laryngeal and epiglottic oedema and a friable and erythematous oesophagus with severe corrosive injury. The individual died several days later from acute respiratory distress syndrome and renal failure. In another case, after the ingestion of an unspecified amount of 2.4% ammonium ion solution, findings at autopsy included haemorrhagic oesophagus, stomach and duodenum [2].

### **Ocular / dermal exposure**

Ammonia and ammonium hydroxide rapidly penetrate the eye and can be highly damaging and may cause permanent injury: therefore, splashes in the eye should be considered an ophthalmic emergency [14].

Effects may range from increased lacrimation, conjunctivitis, palpebral oedema, photophobia, blepharospasm, through to corneal ulceration, corneal opacification, iritis, anterior and posterior synechia formation, retinal atrophy, glaucoma, cataract formation and blindness [15]. Irritation arising from low atmospheric concentrations of  $>20 \text{ mg m}^{-3}$  ( $>29 \text{ ppm}$ ) is considered to be readily reversible when exposure ceases [1].

Anhydrous ammonia gas stored under pressure as a compressed liquid expands rapidly on liberation, resulting in vaporisation and a large endothermic reaction. The result may be evaporative freezing of any tissue in contact with the ammonia [16]. Ammonia readily forms ammonium hydroxide on contact with moisture in the air and skin and the resultant hydroxide saponifies lipids of the epidermal fats and cell membranes [9]. The resultant liquifactive necrosis may appear pale and without charring or blistering [3] and may cause an increased depth of injury. The combination of both cryogenic effects with an alkali burn can produce serious injuries.

Individuals with extensive burns to the eyes and skin are likely to have obstruction of the airway [5].

### **Delayed effects following an acute exposure**

Inhalation exposures to low concentrations for a short period, from which an individual recovers quickly on removal to fresh air, are unlikely to result in delayed or long term adverse health effects.

Substantial inhalation exposures to ammonia may cause long-term health effects, including persistent airway obstruction, cough, exertional dyspnoea, bronchiolitis obliterans and bronchiectasis, which for some cases may persist for many years [2, 5, 8, 9]. Dysphonia may persist for many months as a result of burns to the aerodigestive tract [5, 7].

Scarring to body tissue can be pronounced following burns from ammonia exposure [9].

## Health Effects of Chronic / Repeated Exposure

### Human Data

#### Inhalation

Minor respiratory effects have been associated with chronic inhalation exposure to low levels of ammonia in some studies.

A study in a fertiliser factory considered both workers and administrative staff. It was found that workers exposed to levels above  $18 \text{ mg m}^{-3}$  (26 ppm) had significantly higher relative risks for cough, phlegm, wheezing, dyspnoea and asthma than those exposed to levels below  $18 \text{ mg m}^{-3}$ . Within the exposed group, FEV<sub>1</sub>% predicted and FEV<sub>1</sub>%/FVC% were significantly lower in symptomatic than asymptomatic individuals [17]. Whilst a small study, with high levels of smoking in the controls as a possible confounder, it suggests that chronic exposures to ammonia may impact respiratory function. Similar findings have been noted in a study conducted at a series of factories producing fertiliser chemicals, with decreased performance in respiratory function tests of exposed workers when compared with controls. Data from the ammonia plants show a small statistically significant decrease in FVC<sub>1</sub> and a substantial decrease in PEF<sub>1</sub>/min. No significant decrease in FVC was noted and the specificity of these studies for an effect by ammonia alone was, however, limited as no concentrations were presented [18].

Acclimatisation to the irritant effects of ammonia at concentrations up to  $70 \text{ mg m}^{-3}$  (100 ppm) has been demonstrated after repeated exposure for 6h a day for 5 days each week over a 6 week period [19]. No further interpretation was possible due to the limited design of this study.

In another study, occupational exposures of around 12 years to low concentrations of airborne ammonia  $6 \text{ mg m}^{-3}$  (9 ppm) had no significant effect on pulmonary function in a group of workers at a factory making sodium bicarbonate [20].

#### Ingestion

There are no human data on which to assess the effects of chronic excessive ammonia intake.

Ammonium may be ingested in both food and water, however as ammonium is readily metabolised to products of low toxicity (such as urea and glutamate) within the body; it is unlikely that chronic exposures to low levels will have a significant adverse health effect.

#### Genotoxicity

There is limited data in humans on the genotoxicity of ammonia. One small study in humans examining the exposure to ammonia at a fertiliser factory noted an increase in chromosomal aberrations, sister chromatid exchanges and increased mitotic index [21]. There was a weak association reported between increased length of exposure and increased frequency of chromosomal aberrations and sister chromatid exchange. No detail was given as to how well the exposed and control group were matched for age, smoking habits etc. Furthermore, it appears that gaps were included in the cytogenetic analysis. Given these limitations and the

small size of this study, the low levels of ambient ammonia and the likely exposure to other chemicals no conclusions can be drawn regarding the mutagenicity of ammonia.

There is no other *in-vivo* human data on which to assess the genotoxicity of ammonia and there is conflicting evidence between this study and *in-vitro* studies. However, ammonia has no structural alerts for DNA damage and when the *in-vitro* data is considered, ammonia can be considered as not having significant mutagenic potential.

### **Carcinogenicity**

There is insufficient evidence to classify ammonia as a carcinogen in humans and it has not been classified by the IARC.

### **Reproductive and developmental toxicity**

No data were located on the possible developmental effects of ammonia. It is, however, unlikely that exposure to ammonia would result in reproductive or developmental toxicity in the absence of maternal toxicity.

## ***Animal and In-Vitro Data***

### **Inhalation**

Inhalation exposure of several animal species to ammonia has been conducted. In some series of studies [22], repeated exposures (8 h/5 days a week for 30 days) to ammonia (155 mg m<sup>-3</sup>/223 ppm) produced no adverse clinical signs effects in rats, guinea pigs, rabbits, dogs and monkeys. The group sizes of higher order animals were, however, small (2 or 3). After continuous exposure to 40 mg m<sup>-3</sup> (58ppm) ammonia for 114 days, there were no adverse clinical observations noted and findings at necropsy were normal. Histological examination revealed lipid filled macrophages in the lungs of 2/2 dogs, 1/3 monkeys and 1/15 rats; these findings were considered to be of uncertain toxicological significance. No lung alterations were seen in the remaining experimental or control animals [22].

A limited study in pigs compared low atmospheric exposures to ammonia of approximately 5 mg m<sup>-3</sup> (7 ppm) with moderate exposures of approximately 35 ppm/24 mg m<sup>-3</sup>. Mean daily body weight was reduced in the moderate exposure group in the first 2 weeks of exposure, which resulted in small animals at slaughter after 6 weeks of exposure [23].

### **Ingestion**

There is limited data available on the effects of chronic oral exposure to ammonia (as ammonium hydroxide).

In one study, rabbits were given ammonium hydroxide (100 mg kg<sup>-1</sup> bodyweight) as a 0.5-1% solution by oral gavage for up to 17 months. The key findings from this study included an initial fall in blood pressure, followed by an increase above the baseline and enlarged adrenal glands [1].

Long term exposure of rats, rabbits and dogs to ammonium salts such as ammonium chloride can cause metabolic acidosis. This acidosis occurs from H<sup>+</sup> ions released during conversion to urea and may produce a range of non-specific effects on cardiovascular, pulmonary (including increased ventilation), gastrointestinal and musculoskeletal functions [2]. Osteoporosis has been noted, arising from the mobilisation of bone mineral to spare bicarbonate. However, these are considered to be secondary to prolonged metabolic acidosis [1].

### **Genotoxicity**

Ammonia gas was negative in the Ames tests for *S. typhimurium* sp. TA98, TA100, TA1535, TA1537 and TA1538 in both activated and non-activated systems. Concentrations in the range 500-25000 ppm were employed. Tests conducted in *E. Coli* WRP uvrA were also negative [24].

Positive effects were noted in a separate reverse mutation study test in *E. Coli* sp but only at treatments of NH<sub>3</sub> that caused severe toxicity [1].

There is very limited *in-vivo* mammalian data on the effects of ammonia. One study with mice (single intraperitoneal dose of ammonium at dose of 12, 25 or 50 mg kg<sup>-1</sup>) reported dose dependent increases in the frequencies of micronuclei when compared to controls [21]. Few details were given (not stated if ammonia was given as a gas or a solution) and no conclusions can be drawn.

It is considered from the battery of Ames tests (all negative) that ammonia does not have any significant mutagenic properties.

Neither ammonia nor its metabolites has any structural alerts for DNA reactivity. In view of this and the negative *in vitro* data it is concluded that ammonia does not have any significant mutagenic properties.

### **Carcinogenicity**

Ammonia is considered not to be a carcinogen in animals.

The carcinogenic potential of ammonia gas has not been considered by the IARC. Mice dosed orally with 193 mg ammonia kg<sup>-1</sup> day<sup>-1</sup> as ammonium hydroxide in drinking water for 2 years did not result in a carcinogenic effects or increase the spontaneous incidence of breast cancer in the C3H female mice used in the study [2].

### **Reproductive and developmental toxicity**

There is little data on the reproductive or developmental toxicity of ammonia. However, ammonia is not considered to be a developmental toxin.

Several studies have investigated the effects of ammonium ion on development using embryo culture techniques [25, 26]. There was a relationship between concentration of ammonium in the culture medium and the incidence of abnormalities or toxicity to the blastocyst [25, 26]. The relevance of this to an *in-vivo* model or indeed to humans is doubtful; as high concentrations of ammonia are unlikely to reach the foetus *in-vivo* due to its rapid and extensive metabolism.

A study in female pigs compared low exposures, (around 7 ppm ammonia/ca 5 mg m<sup>-3</sup>) and moderate exposure (around 35 ppm/ca 24 mg m<sup>-3</sup>). The female pigs were continuously exposed from 6 weeks prior to breeding until day 30 of gestation. The time of onset of puberty or number of live foetuses or size of foetus (foetal length) was not affected [23].

## References

- [1] International Programme on Chemical Safety (IPCS) (1986). Ammonia. Environmental Health Criteria 54. World Health Organisation. Geneva.
- [2] Agency for Toxic Substances and Disease Registry (ATSDR) (2004). Toxicological Profile for Ammonia.
- [3] International Programme on Chemical Safety (IPCS) (1990). Ammonia. Health and Safety Guide. World Health Organisation. Geneva.
- [4] Department for Environment Food and Rural Affairs (DEFRA) (2002). Ammonia in the UK.
- [5] Close, L. G., Catlin, F. I. and Cohn, A. M. (1980). Acute and chronic effects of ammonia burns on the respiratory tract. *Arch Otolaryngol* **106**, 151-8.
- [6] Latenser, B. A. and Lucktong, T. A. (2000). Anhydrous ammonia burns: case presentation and literature review. *J Burn Care Rehabil* **21**, 40-2.
- [7] Kass, I., Zamel, N., Dobry, C. A. and Holzer, M. (1972). Bronchiectasis following ammonia burns of the respiratory tract. A review of two cases. *Chest* **62**, 282-5.
- [8] Leduc, D., Gris, P., Lheureux, P., Gevenois, P. A., De Vuyst, P. and Yernault, J. C. (1992). Acute and long term respiratory damage following inhalation of ammonia. *Thorax* **47**, 755-7.
- [9] Amshel, C. E., Fealk, M. H., Phillips, B. J. and Caruso, D. M. (2000). Anhydrous ammonia burns case report and review of the literature. *Burns* **26**, 493-7.
- [10] Singh, S., Malhotra, P., Jain, S. and Varma, S. (1999). Gastro-esophageal burns following domestic liquid ammonia ingestion: report of two cases. *J Assoc Physicians India* **47**, 647.
- [11] Rosenbaum, A. M., Walner, D. L., Dunham, M. E. and Holinger, L. D. (1998). Ammonia capsule ingestion causing upper aerodigestive tract injury. *Otolaryngol Head Neck Surg* **119**, 678-80.
- [12] Massa, N. and Ludemann, J. P. (2004). Pediatric caustic ingestion and parental cocaine abuse. *Int J Pediatr Otorhinolaryngol* **68**, 1513-7.
- [13] Wason, S., Stephan, M. and Breide, C. (1990). Ingestion of aromatic ammonia 'smelling salts' capsules. *Am J Dis Child* **144**, 139-40.
- [14] National Poisons Information Service (NPIS) (2001). Ammonia. TOXBASE.
- [15] George, A., Bang, R. L., Lari, A. R., Gang, R. K. and Kanjoor, J. R. (2000). Liquid ammonia injury. *Burns* **26**, 409-13.
- [16] Sotiropoulos, G., Kilagblian, T., Dougherty, W. and Henderson, S. O. (1998). Cold injury from pressurized liquid ammonia: a report of two cases. *J Emerg Med* **16**, 409-12.

- [17] Ali, B. A., Ahmed, H. O., Ballal, S. G. and Albar, A. A. (2001). Pulmonary function of workers exposed to ammonia: a study in the Eastern Province of Saudi Arabia. *Int J Occup Environ Health* **7**, 19-22.
- [18] Bhat, M. R. and Ramaswamy, C. (1993). Effect of ammonia, urea and diammonium phosphate (DAP) on lung functions in fertilizer plant workers. *Indian J Physiol Pharmacol* **37**, 221-4.
- [19] Ferguson, W. S., Koch, W. C., Webster, L. B. and Gould, J. R. (1977). Human physiological response and adaptation to ammonia. *J Occup Med* **19**, 319-26.
- [20] Holness, D. L., Purdham, J. T. and Nethercott, J. R. (1989). Acute and chronic respiratory effects of occupational exposure to ammonia. *Am Ind Hyg Assoc J* **50**, 646-50.
- [21] Yadav, J. S. and Kaushik, V. K. (1997). Genotoxic effect of ammonia exposure on workers in a fertilizer factory. *Indian J Exp Biol* **35**, 487-92.
- [22] Coon, R. A., Jones, R. A., Jenkins, L. J., Jr. and Siegel, J. (1970). Animal inhalation studies on ammonia, ethylene glycol, formaldehyde, dimethylamine, and ethanol. *Toxicol Appl Pharmacol* **16**, 646-55.
- [23] Diekman, M. A., Scheidt, A. B., Sutton, A. L., Green, M. L., Clapper, J. A., Kelly, D. T. and Van Alstine, W. G. (1993). Growth and reproductive performance, during exposure to ammonia, of gilts afflicted with pneumonia and atrophic rhinitis. *Am J Vet Res* **54**, 2128-31.
- [24] Shimizu, H., Suzuki, Y., Takemura, N., Goto, S. and Matsushita, H. (1985). The results of microbial mutation test for forty-three industrial chemicals. *Sangyo Igaku* **27**, 400-19.
- [25] Sinawat, S., Hsaio, W. C., Flockhart, J. H., Kaufman, M. H., Keith, J. and West, J. D. (2003). Fetal abnormalities produced after preimplantation exposure of mouse embryos to ammonium chloride. *Hum Reprod* **18**, 2157-65.
- [26] Lane, M. and Gardner, D. K. (1994). Increase in postimplantation development of cultured mouse embryos by amino acids and induction of fetal retardation and exencephaly by ammonium ions. *J Reprod Fertil* **102**, 305-12.

This document will be reviewed not later than 3 years or sooner if substantive evidence becomes available