Ammonia is present in agriculture and commerce in many if not most communities. This report evaluates the toxic potency of ammonia, based on three types of data: anecdotal data, in some cases predating World War I, reconstructions of contemporary industrial accidents, and animal bioassays. Standards and guidelines for human exposure have been driven largely by the anecdotal data, suggesting that ammonia at 5,000–10,000 parts per million, volume/volume (ppmv), might be lethal within 5–10 min. However, contemporary accident reconstructions suggest that ammonia lethality requires higher concentrations. For example, 33,737 ppm-v was a 5-min zero-mortality value in a major ammonia release in 1973 in South Africa. Comparisons of secondary reports of ammonia lethality with original sources revealed discrepancies in contemporary sources, apparently resulting from failure to examine old documents or accurately translate foreign documents. The present investigation revealed that contemporary accident reconstructions yield ammonia lethality levels comparable to those in dozens of reports of animal bioassays, after adjustment of concentrations to human equivalent concentrations via U.S. Environmental Protection Agency (EPA) procedures. Ammonia levels potentially causing irreversible injury or impairing the ability of exposed people to escape from further exposure or from coincident perils similarly have been biased downward in contemporary sources. The EPA has identified ammonia as one of 366 extremely hazardous substances subject to community right-to-know provisions of the Superfund Act and emergency planning provisions of the Clean Air Act. The Clean Air Act defines emergency planning zones (EPZs) around industrial facilities exceeding a threshold quantity of ammonia on-site. This study suggests that EPZ areas around ammonia facilities can be reduced, thereby also reducing emergency planning costs, which will vary roughly with the EPZ radius squared. Key words: air pollutant, ammonia, emergency planning, health risk assessment, human health, inhalation, respiratory irritant. Environ Health Perspect 107:617–627 (1999). [Online 23 June 1999]. http://ehpnet1.niehs.nih.gov/docs/1999/107p617-627michaels/abstract.html

In 1984 methyl isocyanate was released from a chemical plant in Bhopal, India. The release reportedly killed thousands of residents and irreversibly injured the eyes and lungs of approximately 20,000 (1). Internationally, governments recognized the need to identify extremely hazardous substances (EHSs) and assist communities in preparing for chemical emergencies. The U.S. Environmental Protection Agency (EPA) identified 366 EHSs, as required by the Community Right-To-Know Act (2). Community emergency planning requirements followed under the Risk Management Program (RMP) in Section 112(r) of the 1990 Clean Air Act Amendments (3).

Industrial facilities exceeding threshold quantities of EHSs on site are subject to the RMP. The RMP defines emergency planning zones (EPZs) around facilities, and requires facilities to submit to the EPA a risk management plan aimed at preventing catastrophic chemical releases and averting Bhopal-type consequences of releases. The cost of community emergency planning for a facility is likely to roughly depend on the area of its EPZ, which in turn depends on the square of the radius around the facility deemed necessary to attenuate a worst-case chemical release to specified airborne concentrations, termed acute exposure guideline levels (AEGLs).

The AEGLs for each EHS have nothing to do with routinely acceptable exposures. Acceptable community and occupational levels are set by a host of more conservative parameters. Rather, the AEGLs must be established to protect members of the general population in the context of “exposure at high levels but of short duration, usually less than one hour, and only once in a lifetime” (1). The AEGLs are under development by the National Advisory Committee (NAC) on AEGLs. NAC AEGL composition is legislatively defined to assure balance, although NAC AEGL deliberations about ammonia began before the committee reached its full complement. Ammonia was one of the first EHSs to be addressed by NAC AEGL, and is of great concern both to companies and communities (4):

During the 20th century, humanity has almost quadrupled its numbers. Although many factors have fostered this unprecedented expansion, its continuation during the past generation would not have been at all possible without a widespread—yet generally unappreciated—activity: the synthesis of ammonia.

Three types of AEGLs are defined by the National Research Council (1): AEGL-1, to protect against nuisance exposure; AEGL-2, to protect against irreversible injury or disability (including impairment of the ability to escape); and AEGL-3, to protect against lethality. Each type of AEGL is quantified via multiple combinations of airborne concentration and exposure duration (5 min, 30 min, 1 hr, 4 hr, and 8 hr) to protect against effects of concern in exposures lasting from minutes to hours.

This assessment of the acute toxicologic potency of ammonia critically evaluates available toxicologic and accident reconstruction data, updating air dispersion modeling results to quantify concentrations to which victims probably were exposed more accurately than older models could. This investigation assumes that gaseous anhydrous ammonia is released in the vicinity of employees wearing no protective breathing apparatus, or that unprotected members of the general public encounter it. Chemical risks posed by ammonium, ammonium salts, and liquid ammonia are excluded from consideration. Also, cryogenic, high-pressure, and high temperature risks are excluded.

**Methods**

Standard procedures of technical information acquisition were used. These included online and in-house database and literature searches and the acquisition of selected documents. Specific information about the Potchefstroom, South Africa, ammonia release was provided by ERM-Four Elements (Columbus, OH), and apparently represents the same information as that published by Lonsdale (5) and Pederson and

Address correspondence to R.A. Michaels, RAM TRAC Corporation, 3100 Rosendale Road, Schenectady, NY 12309 USA. Telephone: (518) 785-0976. Fax: (518) 785-0976. E-mail: 76517.747@compuserve.com

Support for this work was provided by the Fertilizer Institute and the International Institute of Ammonia Refrigeration.

Received 5 November 1996; accepted 5 April 1999.
Selig (6). Acceptance criteria for input data for the present assessment were adopted, and articles were examined to identify toxicologic information conforming with these criteria. To be accepted for quantitative analysis, studies must have identified the test species and reported acute toxic inhalation effect(s) and exposure regimens, including concentration(s) in air and duration(s) of exposure. Concentrations to which animals were exposed in bioassays were adjusted to human equivalent concentrations (HECs) using parameters for dose conversion among species (7,8) and standard EPA methodology for irritant gases (8).

Results
Odor and Odor Threshold
The odor of ammonia is distinct, pungent, and often familiar because of its common use in cleaning. Several reports of the odor threshold for airborne ammonia have been published. These include values of 25 parts per million, volume/volume (ppm-v) (9,10), 48 ppm-v (10,11), 46.8 ppm-v (12,13), and 0.0266–39.6 mg/m³ (0.04–57 ppm-v) (13,14). The presence of airborne ammonia may become apparent to exposed individuals at concentrations in air roughly in the range of occupational exposure limits.

Vapor Density
The molecular weight of ammonia (NH₃) is 17.03 d (g/mol) (10,15–17). Its vapor density is 0.6 relative to air, which is assigned a reference vapor density of unity (=1) (13,17). The density of liquid ammonia at one atmosphere pressure (and -33.5°C) is 0.6818 (15). The density of mixtures of ammonia with water (ammonia water) depends on the ammonia fraction. The density is 0.957 for a 10% ammonia solution and 0.90 for a Spirit of Hartshorn solution, which is 28–29% ammonia.

Acute Toxic Inhalation Effects
Irreversible or clinically insignificant effects. Several reports of reversible or clinically insignificant effects exerted by ammonia on humans were located (Table 1). These effects include eye irritation (10,13,18–20), upper airway irritation (10,13,18–20), lacrimation (10,13,18–20), altered breathing patterns (10,19), minor biochemical changes (13,21), and minor blood pressure and pulse rate changes (10,19). Similar effects were also reported in animal studies. The lowest exposure concentration eliciting effects was 50 ppm-v over a duration of 10 min, causing faint to moderate irritation of the human upper airway (13,18).

Irreversible injury: animal studies. Several reports of potentially irreversible nonlethal clinical effects involving bioassay animals were located. Bioassay animals exhibiting such effects included mice (10,12,25–27), rats (10,13,28), rabbits (10,13,18,22,27,29), and cats (13,18,27,29).

Irreversible injury: human studies. Examination of Table 1 reveals no reports of potentially irreversible nonlethal clinical effects in humans. Accident reports reveal two accidents involving permanent injuries, including impaired breathing and damage to the respiratory system, throat, and eyes (30). However, the estimated ammonia concentration range is unhelpfully broad (700–10,000 ppm-v) and exposure durations are unrated.

Fatal exposure: animal studies. Studies of ammonia-induced mortality in Animal bioassays are set forth in Table 2. A 1-hr median lethal concentration (LC₅₀) value for cats exposed to airborne ammonia was 1,071 ppm-v (31,32). Numerous bioassay reports are analyzed in Table 2, giving equivalent 5-30-, and 60-min human inhalation lowest lethal concentration (LC₅₀) and LC₉₅ values in accordance with the equation C₅₀ (t) = constant, using n = 1 (Haber's rule) and n = 2 (33).

Fatal exposure: human studies. Examination of Table 1 reveals several reports of human mortality following exposure to airborne ammonia at a concentration of 5,000 ppm-v. Concentrations are typically estimates obtained from accident reconstructions. One report indicates immediate death from spasms, inflammation, or edema of the larynx (13,34). Other reports indicate exposure durations of 5 min (27,33,36) or 30 min (10,37). A different lethality benchmark—7,000 ppm-v over 3 hr exposure—was reported in a draft Environment Canada document (13,38). Selected reports of human lethality were examined to distinguish between primary research or clinical reports versus secondary reviews. The evolution of reported lethality benchmark values is traced over time in Figure 1.

Environment Canada (38). The 1981 draft is out of print, superseded by a July 1984 final report. The 5,000-ppm-v lethality concentration remains. The Environment Canada (38) document source is the 1978 edition of the Encyclopedia of Chemical Technology (39), specifically a table referred to by Environment Canada (38) as a “Summary of Human Exposure.” In the Kirk-Othmer table (39), 5,000 ppm-v (7.179 mg/m³) is associated with “serious edema, strangulation, asphyxia; fatal almost immediately.”

Environment Canada (38) also provides Table 7.4.1 “Inhalation,” in which literature on effects and effect concentrations is cited. The Kirk-Othmer (39) citation and effect concentration are not used. However, ammonia is associated with (apparently lethal) “respiratory spasm and rapid asphyxia” in a range of 3,500–7,000 mg/m³ (approximately 2,500–5,000 ppm-v) by Braker and Mossman (40). The same range is cited in a National Research Council report (41), which also indicates a 0.5- to 1-hr exposure duration. The Environment Canada table (38) cites a Registry of Toxic Effects of Chemical Substances (RTECS) report (27) of a 5-min LC₅₀ of 21,000 mg/m³ (approximately 30,000 ppm-v). Table 7.4.1 also cites a 3-hr LC₅₀ of 7,000 μg/m³ (approximately 10,000 ppm-v) reported by the International Technical Information Institute (ITII) (42).

The Environment Canada report (38) is a secondary source; the source quality is low. See Kirk-Othmer (39), Braker and Mossman (40, ITII, 42, and RTECS 27.)

Kirk-Othmer (39). Table 13 indicates that 5,000 ppm-v ammonia is associated with the notation “serious edema, strangulation, asphyxia; fatal almost immediately” (39). The cited source of this information is Braker and Mossman (43).

This is a secondary source; the source quality is low. See Braker and Mossman (43).

Braker and Mossman (40,43). For summary purposes the sixth edition was obtained. Table 1 sets forth vapor concentrations, general effects, and exposure periods. Ammonia at 5,000–10,000 ppm-v is associated with “respiratory spasm, rapid asphyxia,” and the exposure period indicates “rapidly fatal” (40). No primary source citations are provided.

This is a secondary source; the source quality is low. The exposure period is unquantified. No primary source citation is provided. This report should be rejected in favor of more completely documented reports.

Environmental Toxicology (42). A lethal inhalation concentration of 10,000 ppm-v at exposure duration 3 hr is given. No primary source citation is provided.

This is a secondary source; the source quality is low. This report should be rejected in favor of more completely documented reports.

Henderson and Haggard (37). This monograph is a secondary source (a review), and does not constitute a primary report of clinical or experimental findings. It includes a table titled “Physiological Responses to Various Concentrations of Ammonia.” The table includes an entry indicating that ammonia is “rapidly fatal for short exposure” (37) at concentrations of 5,000–10,000 ppm-v. The primary source citation is apparently the previous-line citation (Ronzani 46), and the phrase “short exposure” refers to 1/2 hr or 1/2–1 hr. The table also indicates that the maximum concentration allowable for short exposure (1/2–1 hr) is 300–500 ppm-v.
Table 1. Inhalation effects exerted by ammonia in studies involving humans.

| Concentration in air (ppm) | Exposure duration (min) | Dose times duration (ppm-v/min) | Study type | Reported effect(s) | Primary reference<sup>a</sup> | Secondary reference<sup>b</sup> |
|---------------------------|------------------------|---------------------------------|------------|--------------------|-------------------------------|-------------------------------|
| Acute exposures (within 24 hr) | 32                     | 5                               | 158        | NOAEL              | Ocular: eye irritation with lacrimation (18) |                          |
|                           | 46.8                   | -                               | -          |                    | Sensory: odor threshold (12) |                          |
|                           | 50                     | 5                               | 251        | NOAEL              | Ocular: eye irritation with lacrimation (18) |                          |
|                           | 72                     | 5                               | 359        | NOAEL              | Ocular: eye irritation with lacrimation (18) |                          |
|                           | 50                     | 10                              | 502        | TC<sub>10</sub>     | Respiratory: faint to moderate (5 of 6) irritation (18) |                          |
|                           | 135                    | 5                               | 675        | TC<sub>50</sub>     | Respiratory: nose and throat irritation (18) |                          |
|                           | 135                    | 5                               | 675        | TC<sub>50</sub>     | Respiratory: chest irritation (1 of 6) (18) |                          |
|                           | 50                     | 120                             | 6,000      | LOAEL              | Ocular: eye irritation (20) |                          |
|                           | 50                     | 120                             | 6,000      | LOAEL              | Ocular: eye irritation (20) |                          |
|                           | 500                    | 30                              | 15,000     | LOAEL              | Respiratory: nasal and throat irritation, increased minute volume, cyclic pattern of hyperpnea (19) |                          |
|                           | 500                    | 30                              | 15,000     | NOAEL              | Ocular: variable lacrimation (19) |                          |
|                           | 700                    | -                               | -          |                    | Ocular: eye irritation, permanent injury in absence of prompt remedial measures (24) |                          |
|                           | 5,000                  | 5                               | 25,000     | LC<sub>0</sub>      | Lethality: specific cause of death not reported (36) |                          |
|                           | 5,000                  | 30                              | 150,000    | Case report        | Lethality: rapidly fatal (37) |                          |
|                           | 810                    | 240                             | 194,400    | Case report        | Biochemistry: some biochemical effects (27) |                          |
|                           | 7,000                  | 180                             | 1,260,000  | LC<sub>0</sub>      | Lethality: Environment Canada benchmark (draft) (38) |                          |
|                           | 5,000                  | -                               | -          | Lethality          | Lethality: fatal almost immediately (39) |                          |
|                           | 10,000                 | 180                             | 1,800,000  | -                  | Lethality: rapidly fatal (40) |                          |
|                           | 30,000                 | 5                               | 150,000    | LC<sub>10</sub>     | Lethality: other effects not reported (42) |                          |
|                           | 30,000                 | 5                               | 150,000    | LC<sub>10</sub>     | Lethality: but value withdrawn in later editions (27) |                          |
|                           | 330,000 (?)            | -                               | -          | Lethality          | Lethality: heart failure following lung damage (47) |                          |

Abbreviations: ?, exposure duration unquantified; LC<sub>10</sub>, lowest lethal concentration; LOAEL, lowest adverse effect level; NOAEL, no adverse effect level; TC<sub>50</sub>, lowest toxic concentration. <sup>a</sup>Original research or stated conclusion. <sup>b</sup>Source of additional information about primary source(s).

Table 2. Human exposures to airborne ammonia predicted to be lethal, based on human and animal data.

| Statistic | Unit | Parameter | Haber’s rule [C<sub>n</sub> (t = constant; n = 1)] 5 min | Ten Barge adjustment (n = 2) 5 min | 30 min | 60 min | 5 min | 30 min | 60 min |
|-----------|------|-----------|------------------------------------------------------|----------------------------------|--------|--------|-------|--------|--------|
| Human lethality, based on human studies | | | | | | | | | |
| Number of reported lethality values (n<sup>a</sup>) | | | 4 | | | | | | |
| Minimum<sup>b</sup> | | | 5,000 | | | | | | |
| Geometric mean<sup>c</sup> | | | 59,482 | | | | | | |
| Arithmetic mean<sup>d</sup> | | | 95,000 | | | | | | |
| SD<sup>e</sup> | | | 98,234 | | | | | | |
| Coefficient of variation<sup>f</sup> | | | 103 | | | | | | |
| Human lethality, based on animal studies | | | 4 | | | | | | |
| Number of reported lethality values (n<sup>a</sup>) | | | 5 | | | | | | |
| Minimum<sup>b</sup> | | | 77,540 | | | | | | |
| Geometric mean<sup>c</sup> | | | 67,540 | | | | | | |
| Arithmetic mean<sup>d</sup> | | | 233,923 | | | | | | |
| SD<sup>e</sup> | | | 153,537 | | | | | | |
| Coefficient of variation<sup>f</sup> | | | 118 | | | | | | |

Abbreviations: LC<sub>10</sub>, median lethal concentration; LC<sub>50</sub>, lowest lethal concentration; SD, standard deviation. <sup>a</sup>Reported lethality values may appear in multiple references, and some references may report more than one of the tabulated lethality values. Thus, the number of reported lethality values differs from the number of reference citations. References are human LC<sub>10</sub> based on human studies (34,38–42,43,45,47); human LC<sub>50</sub> or LC<sub>10</sub> based on animal studies: cat (29,38); mouse (26,30,74–78); rabbit (29,38); and rat (23,24,28,31,33,36,61,71,72,75,77). <sup>b</sup>Minimum: lowest among n values. <sup>c</sup>Geometric mean = nth root of the product of n values = sum of logarithms of n values, divided by n. <sup>d</sup>Arithmetic mean = sum of n values, divided by n. <sup>e</sup>SD = square root of the variance, where the variance = sum of squared deviations from the arithmetic mean, divided by (n - 1). <sup>f</sup>Coefficient of variation = 100 x SD/arithmetic mean.
Ronzani (44) and Lehmann (45); and that 2,500–4,500 ppm-v is dangerous for even short exposure (1/2 hr) (44).

This is a secondary source; the source quality is old but acceptable; more recent and better documented sources would be preferable. The phrase "short exposure" associated with lethality can refer to 1/2 hr or 1/2–1 hr, but seems to have been erroneously interpreted as meaning 5–10 min in derivative contemporary sources (Figure 1).

Maass (35,36). The German words for ammonia are Ammoniak (gas) and Salmiakgeist (solution). Maass (39) primarily introduced principles of biology and toxicology of chemical agents used in warfare. However, ammonia appears to be unmentioned, and its citation in the RTECS report (27) is erroneous. Maass (36) presented a table titled "Approximate Effectiveness of Gases and Vapors for Humans" [translated title] lists Ammoniak. Ammonia is listed as lethal at 5,000 ppm-v following exposure of 5–10 min duration. No primary source citation is provided for this entry. General literature is provided in an appendix on pages 249–250. However, the appendix presumably pertains to previously presented information, not to subsequent tables, some of which also have appended material. Finally, the literature cited appears to be of a general nature, including no primary research reports likely to be the original source of any toxicologic data.

These are secondary sources; the source quality is low. The lethal value—5,000 ppm-v over 10 min—lacks primary documentary support. The translated source table (36) title emphasizes that the tabulated values are approximate, suggesting that a definitive measurement may have been unavailable. These old reports together fail to meet current standards of technical documentation.

U.S. Coast Guard (34). The January 1991 edition contains a material safety data sheet for anhydrous ammonia that does not cite a lethal vapor concentration.

This is a secondary source; the source quality is low. This report should be rejected in favor of more completely documented source(s). If the 1984–1985 edition (34) included a lethal vapor concentration, that parameter or its value in the case of anhydrous ammonia was abandoned in the later edition. This document should be rejected.

Sax and Lewis (46). This document lists human 5-min inhalation LC10 = 30,000 ppm-v.

This is a secondary source; the source quality is low because of erroneous information. This document should be rejected in favor of more accurate source(s). See cited reference [Mulder and Van Der Zalm (47)].

Mulder and Van Der Zalm (47). A person filling a tank wagon with 25% ammonia solution failed to wear respiratory protection, and died. The report (translated from Dutch) fails to quantify the exposure duration. It is imprecise about ammonia concentrations in the breathing-zone air of the deceased, whose face had been reddened (47): Layer of lung below the superficial layer had been harmed...He had inhaled great amount of concentrated ammonia...At the moment of the mishap, the ammonia water solution spread as a thin film over the tank car. The wind direction

Figure 1. Evolution of four human lethality values for inhalation of ammonia. Abbreviations: ATSDR, Agency for Toxic Substances and Disease Registry; HSDB, Hazardous Substances Data Bank; ITII, International Technical Information Institute; RTECS, Registry of Toxic Effects of Chemical Substances. Solid lines indicate sources that are explicitly cited. Dashed lines indicate sources that are apparent but uncharted.
was toward the victim. The vapor pressure of a 25-
percent (by weight) ammonia solution is 224 mm
of mercury. As a consequence of that, the vapor
contained 33-percent ammonia (by volume), or
330,000 ppm. Of course, under these circum-
stances, there was not a saturated vapor pressure
at the level of the victim. The actual concentration
of ammonia is unknown, but is roughly estimated
to be multiple times 10,000 ppm.

The deceased had been instructed to report to
the first aid room for medical attention, but instead went to the coffee room
for milk. He then worked 3 hr. First aid was
sought only 3 hr after the exposure incident,
whereupon the patient was transferred to a
clinic to have X-rays performed. His heart
stopped, but was restarted; he was transferred
to a hospital, where his heart stopped again.
The immediate cause of death, which occurred 6 hr postexposure, was heart failure,
although the pathology report indicated that
the underlying cause was the effect of ammobi
on the deep layer of the lung, presumably
creating cardiopulmonary stress that proved
intolerable over the protracted period of
perhaps 3–6 hr between exposure and initia-
tion of medical attention.

This document is a primary source; the
source quality is imprecise but acceptable
and important. Sax and Lewis (46) incor-
rectly list a 5-min LC50 of 30,000 ppm-v
based on this source. The incorrect value
persists in the latest edition (48). This acci-
dent is further evaluated below.

**Accident reports.** Numerous articles
report lethality of anhydrous ammonia releases [e.g., (5,6,30,47,49–59)]. One of
these cited reports (47) was mentioned
above. However, reliable measurements of
concentrations and durations of exposure are
lacking. The absence of such data has moti-
vated attempts to reconstruct ambient concen-
trations during accidents retrospectively,
for example, based on air dispersion model-
ing (6,30,52,53) or evidence from ammonia-
induced damage to biota (30).

**Dutch accident.** In the Dutch accident
mentioned above (47), a tank was being refilled with 25% ammonia at an external
temperature of 10°C over an unquantified
period. Although Mulder and Van der Zalm
(47) expressed the belief that the air at the
level of the victim had not reached satu-
ration (330,000 ppm-v), presumably the
atmosphere within the tank was saturated.
The ammonia-saturated vapor must have
been displaced into the ambient air in close
proximity to the deceased while he was on
top of the tank to fill it. In addition, ammobi
vapor, lighter than air at 10°C, would have
been rising from the rich pool of ammonia from overflowed ammonia solu-
tion on the ground. Thus, the deceased, who
inhaled a great amount of concentrated
ammonia (47), appears to have been
exposed, at least sporadically, to two sources
of ammonia vapor at all or a reasonably high
fraction of the 330,000-ppm-v saturated vapor concentration during the filling and
measuring operation.

Given the time between exposure and
death, Mulder and Van der Zalm (47) sug-
gested that airborne ammonia concentra-
tions equal to a reasonably large fraction
of 330,000 ppm-v are not rapidly fatal. This is

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**Table 3. Synthesis of accident reports to discern ammonia effect levels.**

| Category/location | Date       | Estimated concentration From (ppm) | Geometric mean (ppm) | Release duration (min) | Exposure duration (min) | Exposed (no.) | Affected (no.) | Effect                 |
|-------------------|------------|-------------------------------------|----------------------|------------------------|------------------------|---------------|----------------|------------------------|
| Human fatality    |            |                                     |                      |                        |                        |               |               |                       |
| Potchefstroom, South Africa  | 13 Jul 73  | 2500                                | 20000                | 22,361 Instant          | --                     | --            | 2             | Fatal                  |
| Boute, LA         | 15 Dec 70  | 5000                                | 20000                | 31,623 Instant          | --                     | --            | 3             | Fatal                  |
| Creté, NE         | 18 Feb 69  | 5000                                | 20000                | 31,623 Instant          | --                     | --            | 3             | Fatal                  |
| Potchefstroom, South Africa  | 13 Jul 73  | 5000                                | 20000                | 31,623 Instant          | --                     | --            | 10            | Fatal                  |
| Houston, TX       | 11 May 76  | 5000                                | 20000                | 31,623 Instant          | --                     | --            | 2             | Fatal                  |
| Pensacola, FL     | 9 Nov 77   | 20000                               | 20000                | 63,246 240             | --                     | --            | 2             | Fatal                  |
| Permanent injury  |            |                                     |                      |                        |                        |               |               |                       |
| Barnesville, MN   | 10 Jun 81  | 700                                 | 10,000               | 2,646 30               | --                     | --            | 11            | Injury: claimed permanent, to respiratory system, eyes, throat |
| Houston, TX       | 11 May 76  | 700                                 | 10,000               | 2,646 Instant          | --                     | --            | 3             | Injury: permanent breathing impairment |
| Reversible injury |            |                                     |                      |                        |                        |               |               |                       |
| Boute, LA         | 15 Dec 70  | 300                                 | 5,000                | 1,225 3                | --                     | --            | 3             | Injury: treated, released < 24 hr |
| Conway, KS        | 6 Dec 73   | 300                                 | 5,000                | 1,225 < 480            | --                     | --            | 1             | Injury: hospitalized 1 day, injuries unspecified |
| Conway, KS        | 6 Dec 73   | 300                                 | 5,000                | 1,225 < 480            | --                     | --            | 1             | Injury: hospitalized 6 days: eye, nose, throat, lung burns |
| Boute, LA         | 15 Dec 70  | 700                                 | 10,000               | 2,646 3                | --                     | --            | 26            | Injury: hospitalized < 14 days; unspecified injuries |
| Pensacola, FL     | 9 Nov 77   | 20000                               | 20000                | 63,246 240             | --                     | --            | 2             | Injury: children hospitalized; recovery in 1 month |
| Transient or clinically insignificant effects |           |                                     |                      |                        |                        |               |               |                       |
| Houston, TX       | 11 May 76  | 300                                 | 500                  | 387 Instant            | 10                     | > 17          | > 17          | NOAEL: no apparent permanent injury |
| Barnesville, MN   | 10 Jun 81  | 300                                 | 5,000                | 1,225 30               | --                     | > 17          | > 17          | NOAEL: exposure without injury |
| Damage to flora, fauna |       |                                     |                      |                        |                        |               |               |                       |
| Verdigris, OK     | 10 Jun 79  | 12                                 | 72                   | 29 Instant             | --                     | --            | Flora: vegetative discoloration |
| Houston, TX       | 11 May 76  | 12                                 | 72                   | 29 Instant             | --                     | --            | Flora: vegetative discoloration |
| 🌸, OK            | 7 May 76   | 12                                 | 72                   | 29 Instant             | --                     | --            | Flora: wheat bleached |
| Crestview, FL     | 8 Apr 79   | 1,000                              | 3,300                | 1,817                  | --                     | --            | Flora: defoliation; other substances present, including chlorine |
| Houston, TX       | 11 May 76  | 2,000                              | 2,300                | 2,145 Instant          | --                     | --            | Fauna: birds fell from trees |
| Blair, NE         | 16 Nov 70  | 700                                | 10,000               | 2,646 150             | --                     | --            | Fauna: fatal to one of the two species (hogs or cattle) |
| Pensacola, FL     | 9 Nov 77   | 2,300                              | ?                    | 240                    | --                     | --            | Fauna: death of small birds, wildlife |
| Pensacola, FL     | 9 Nov 77   | 2,300                              | ?                    | 240                    | --                     | --            | Flora: withered trees and ground vegetation |
| Belle, WV         | 21 Jan 70  | 5,000                              | 20,000               | 10,000                 | --                     | --            | Fauna: death of nine horses |

*Abbreviations: ?, unknown; NOAEL, no adverse effect level. *Adapted from Markham 138. Note that some accidents are accorded multiple listings. This is done to accommodate multiple exposure scenarios, such as might prevail at different locations in the vicinity of the accident.

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in contrast to multiple sources cited and described above, and in each case found to be questionable. Given the failure of the deceased to seek immediate medical attention, and his ability to continue working, this report suggests that both the duration and the degree of the cardiopulmonary stress to which his death was attributed may have been significantly and unnecessarily exacerbated. As early as 1927, Henderson and Haggar (37) reported that ammonia-induced pulmonary edema, if severe, usually terminates fatally, but can be and should be treated:

inhalation of oxygen tends to relieve the anoxemia and cyanosis and should always be begun as early as possible in the stage of gray cyanosis...By far the most important feature of treatment in such cases is absolute quiet and rest. Neglect of this requirement is common and frequently precipitates death by sudden heart failure.

Thus, the level of exposure to ammonia experienced by the deceased might be survivable for individuals comparably exposed, if they receive appropriate medical attention promptly.

Together, the facts educed from this incident suggest that a concentration of airborne ammonia to which brief exposure may be nonlethal is significantly in excess of 10,000 ppm-v and may be as high as 330,000 ppm-v, at least for sporadic exposure. The victim must have been exposed to 330,000 ppm-v, at least sporadically, because he was located next to the fill-hole of a tank while manually pumping ammonia into it, thereby displacing a large volume of saturated ammonia vapor at 330,000 ppm-v, and he lacked respiratory protection. His face also was reddened by ammonia.

Available data do not support 330,000 ppm-v as an accurate estimate of nonlethal continuous exposure. However, inaccuracy is intrinsic when deriving knowledge from an accident reconstruction, whose success often relies on the meta-analyses of multiple accidents. In such meta-analysis, each accident reconstruction is inaccurate, but if multiple reconstructions are reasonably consistent, they may converge on a particular potency value or range of values. The consistency of multiple accidents must be evaluated based on a minimum-error exposure estimator for each accident. The arithmetic or geometric mean of the reported range of ammonia concentrations may be the mathematically best available estimator of discontinuous (on/off) exposure. A reasonable use of the mean as an exposure estimator in this case is to conservatively assume that tank filling and measuring required only 5 min, and that the equivalent continuous exposure level was equal to the mid point (arithmetic mean) of the reported range (170,000 ppm-v). A more cautious approach would be to assume that the ammonia concentration was at the geometric mean (57,446 ppm-v) rather than at the arithmetic mean of the reported concentration range.

The Bartow accident. An accident occurred on 5 December 1996 at an ammonia plant in Bartow, Florida, in which a worker drove a forklift under a storage tank of pressurized anhydrous ammonia (60). He severed a downwardly protruding tank nipple, releasing a strong flow of ammonia onto himself.

Table 4: Evaluation of Potchefstroom, South Africa, ammonia incident to estimate human lethality concentrations.

| Time from release (sec) | Concentration range (ppm-v) | Estimated mean concentration range | Concentration range (ppm-v) | Concentration range (ppm-v) | Concentration range (ppm-v) |
|-------------------------|-----------------------------|-----------------------------------|-----------------------------|-----------------------------|-----------------------------|
|                         | 0                           | 0                                 | 0                           | 0                           | 0                           |
|                         | 5                           | 641,000                           | 641,000                     | 641,000                     | 641,000                     |
|                         | 15                          | 365,000                           | 365,000                     | 365,000                     | 365,000                     |
|                         | 30                          | 220,000                           | 220,000                     | 220,000                     | 220,000                     |
|                         | 50                          | 136,000                           | 136,000                     | 136,000                     | 136,000                     |
|                         | 60                          | 109,000                           | 113,000                     | 111,000                     | 110,000                     |
|                         | 80                          | 79,600                            | 85,000                      | 82,500                      | 82,000                      |
|                         | 100                         | 62,200                            | 68,300                      | 65,250                      | 65,000                      |
|                         | 120                         | 49,800                            | 57,300                      | 53,550                      | 53,000                      |
|                         | 180                         | 28,100                            | 37,600                      | 32,850                      | 32,500                      |
|                         | 240                         | 15,800                            | 24,100                      | 19,950                      | 19,500                      |
|                         | 300                         | 7,600                             | 13,700                      | 12,050                      | 11,900                      |
|                         | 360                         | 1,300                             | 7,900                       | 4,600                       | 4,300                       |
|                         | 420                         | 0                                | 2,000                       | 2,000                       | 2,000                       |
|                         | 480                         | 0                                | 251,093                     | 67.5 sec (11.25 min)        | 251,093                     |
|                         | 540                         | 0                                | 50,647                     | 447.5 sec (17.48 min)       | 50,647                     |
|                         | 600                         | 0                                | 63,293                     | 560 sec (9.33 min)          | 63,293                     |
|                         | 720                         | 0                                | 202,354                    | 60 sec (1.00 min)           | 202,354                    |
|                         | 840                         | 0                                | 33,233                     | 560 sec (9.33 min)          | 33,233                     |
|                         | 960                         | 0                                | 202,354                    | 60 sec (1.00 min)           | 202,354                    |
|                         | 1,080                       | 0                                | 33,233                     | 560 sec (9.33 min)          | 33,233                     |
|                         | 1,200                       | 0                                | 202,354                    | 60 sec (1.00 min)           | 202,354                    |

(Continued)
The victim suffered cryogenic ammonia burns to his skin and eyes, as well as lung injury from inhalation of ammonia. However, he was able to extricate himself from the vehicle, run to a telephone, and summon assistance. The incident released an estimated 142 tons of ammonia over 2 hr. Although the victim was hospitalized for 19 days, he survived and eventually returned to work. Five gas dispersion models defined isolines at ground level within which ammonia levels reached \( \geq 900,000 \) ppm-v. Assuming validity of the Ten Berge (33) equation with \( n = 2 \), this incident was reported to indicate a 5-min survivable concentration of 89,400 ppm-v.

Miscellaneous accidents. Several accidents in which ammonia concentrations were inferred by such means are evaluated in Table 3 to discern effect concentrations implied by reported ranges of exposure. Examination of Table 3 reveals an absence of reliable exposure duration data. Nonetheless, the geometric mean of reported lethal exposure ranges is approximately 30,000 ppm. A reasonably conservative exposure would appear to be 5 min based on the amount of time required for dissipation of ammonia, as inferred from the ammonia release accident in Potchefstroom. This accident is evaluated in Tables 4–6 and in supporting text.

The Potchefstroom accident. On 13 July 1973 an ammonia bullet tank in Potchefstroom failed, releasing 38 metric tons of anhydrous ammonia. The basis for exposure concentrations in Table 3 was the World Bank Hazard Analysis (WHAZAN; Technica, London) air dispersion model. Higher concentrations in Table 4 were based on the more modern HGSYSTEM model (Shell Research, Ltd., London) (53), which better accounts for the initially heavier-than-air density of cryogenic (adiabatically cooled) ammonia. WHAZAN modeling assumptions used by Pederson and Selig (6) in reconstructing the Potchefstroom accident were applied as inputs to HGSYSTEM (53). Cold, relatively high-density ammonia remains within the breathing zone before equilibrating with ambient outdoor temperature. Consequently, with HGSYSTEM, fatality rates in incident zones correlate with higher ammonia concentrations, and with lower acute toxic potency, of inhaled ammonia.

As Table 4 indicates, the exposure duration in zone 1 was estimated at 448 sec (7.5 min). The time-weighted average exposure over that duration was 58,647 ppm-v (Table 4), with 60% mortality (Table 6). Values for other zones are as follows: zone 2, 9.3 min, 39,293 ppm-v, and 26% mortality; zone 3, 8.8 min, 25,821 ppm-v, and 83% mortality (this value may be considered unreliable because other exposed individuals are presumed to have left the scene uncounted); and zone 4, 9.3 min, 18,073 ppm-v, and 0% mortality (Tables 4 and 6).

A spectrum of predicted ammonia concentration-effect benchmarks is calculated in Table 4 based on observed values, which are also tabulated. Most notably, peak, 1-min, and 5-min human inhalation LC50 and LC0 values are tabulated. These LC50 values are 560,000 ppm-v (peak), 268,832 ppm-v (1 min), and 83,322 ppm-v (5 min); LC0 values are 82,300 ppm-v (peak), 84,883 ppm-v (1 min), and 33,737 ppm-v (5 min).

**Personal communications.** To augment the available database pertaining to ammonia lethality concentrations, a series of telephone inquiries was implemented. Target contacts included representatives of insurance companies that might have experienced losses associated with anhydrous ammonia release, chemical companies manufacturing ammonia, trade associations representing industries facing challenges of handling ammonia, and federal agencies regulating ammonia manufacture, transport, and/or use. No data were found, and no individual indicated that additional human lethality data could be found.

**Discussion and Conclusions: Odor Threshold and Vapor Density**

The reported range of the ammonia odor threshold (0.04–57 ppm-v) corresponds to the range of occupational standards and guidelines for prolonged exposure to ammonia. The odor threshold is also significantly below the ammonia immediately dangerous to life and health (IDLH) value (a National Institute for Occupational Safety and Health (NIOSH) parameter) of 300 ppm-v. This value represents the concentration which, if exceeded for 30 min, may render an exposed individual incapable of escape. Consequently, the distinct odor of ammonia and its relatively low odor threshold constitute excellent warning properties. Individuals would be capable of detecting ammonia nearly simultaneously with the onset of exposure. In circumstances in which ammonia might gradually increase to clinically significant concentrations, the low odor threshold may constitute an early warning system, alerting exposed individuals of the need to take corrective and/or protective actions.

The low odor threshold of ammonia may be regarded as a risk-mitigating factor rather than a risk-enhancing factor, as compared with more difficult-to-detect gases such as carbon monoxide. Nonetheless, the excellent warning properties of ammonia do not constitute a substitute for its routine quantitative monitoring at potential release sites.

The finding that gaseous ammonia exhibits a density of 0.6 relative to air indicates that ammonia releases would tend to rise in tranquil air. However, liquid ammonia may be cryogenically cooled. Its initial density upon release may be heavier than air (53). Equilibration with outdoor ambient temperature would be expected to result in a gradual transition to a lighter-than-air condition.

Nonetheless, indoor settings may inhibit effective ammonia dissipation, and both

| Time from | Modeled ammonia concentration range (ppm) | Estimated exposure duration (sec) | Cumulative exposure (sec) | Conc times duration (ppm) | Equiv. mean conc (ppm) |
|-----------|----------------------------------------|----------------------------------|--------------------------|--------------------------|------------------------|
| release (sec) | From (ppm) | To (ppm) | Mean | e | f | g | h | i |
| Column → a b c d e f g h i j (b + c)/2 | a5 = (a15 - a5)/2 | Σ e | d x e | g/50 | g/300 | |
| Zone 4: 250 m from release point | 0 | – | – | – | – | 0 | – | – | – |
| 5 | – | – | – | – | 0 | – | – | – | – |
| 15 | – | – | – | – | 0 | – | – | – | – |
| 30 | – | – | – | – | 0 | – | – | – | – |
| 50 | – | – | – | – | 0 | – | – | – | – |
| 80 | 79,600 | 85,000 | 82,300 | 20 | 20 | 1,646,000 | 27,433 | 5,487 |
| 100 | 62,200 | 68,300 | 65,250 | 20 | 20 | 1,305,000 | 21,750 | 4,350 |
| 120 | 49,800 | 57,300 | 53,550 | 40 | 20 | 2,142,000 | 35,700 | 7,140 |
| 140 | 49,800 | 37,600 | 32,850 | 60 | 140 | 1,971,000 | 32,850 | 6,570 |
| 160 | 15,800 | 24,100 | 19,950 | 60 | 200 | 1,197,000 | 19,950 | 3,990 |
| 180 | 9,100 | 13,700 | 11,400 | 60 | 260 | 884,000 | 11,400 | 2,280 |
| 200 | 5,800 | 8,300 | 7,050 | 60 | 320 | 423,000 | 7,050 | 1,410 |
| 220 | 790 | 5,600 | 4,200 | 60 | 380 | 252,000 | 4,200 | 840 |
| 240 | 4,050 | 4,050 | 4,050 | 60 | 340 | 243,000 | 4,050 | 810 |
| 240 | 2,800 | 2,800 | 2,800 | 60 | 560 | 168,000 | 2,800 | 560 |
| 260 | 51,000 | 51,000 | 51,000 | 1,500 | 1,500 | 90,000 | 1,500 | 300 |
| 280 | 63,863 | 80 sec (1.333 min) | 63,863 | 80 sec (1.333 min) | 18,073 | 560 sec (9.333 min) | 18,073 | 560 sec (9.333 min) | 18,073 |

Conc. concentration. *Based on data reported by Mudan and Mitchell (53).
outdoor and indoor air might be sufficiently turbulent to overcome the density-driven tendency of ammonia to rise out of the personal breathing zone of occupationally exposed individuals. In contrast, environmentally exposed individuals presumably would be situated outdoors, where ammonia typically would not be confined. The low vapor density of ammonia relative to air may therefore be regarded as a risk-mitigating factor rather than a risk-enhancing factor as compared to a heavier-than-air gas such as chlorine.

**Relationship between Concentration and Exposure Duration in Producing Toxic Effect**

An approximation in toxicology (sometimes termed Haber’s rule) is that the product of the dose and duration of exposure to a particular toxic substance equals a constant value \((6,33)\) according to the equation: \(C^* \times t = \text{constant} \), where \(C^*\) is the concentration, \(t\) is the exposure duration, and \(n = \text{unity} = 1\).

This rule is approximate for several reasons \((33)\), the explanation of which is beyond the scope of this report. However, the rule often may be usefully applied to closely spaced exposure durations such as 5 min versus 1 hr. Thus, a 5-min inhalation exposure to a particular concentration in air might be approximately equivalent to a 1-hr exposure to 1/12th of the 5-min concentration. Alternatively, Ten Berge et al. \((33)\) empirically determined that \(n = 2\) for mice and rats, and suggest that \(n = 2\) for humans as well. The relationship elucidated above, with the value of \(n\) chosen from 1 to 2, may be used to adjust ammonia concentrations over varying exposure durations to the equivalent concentration corresponding to any chosen exposure duration from 5 min to 1 hr \((6)\). This report uses both extremes—\(n = 1\) and \(n = 2\).

**Adoption of Acceptable Risk Criteria**

Risk acceptability is a subjective judgment, and cannot be defined scientifically. However, qualitatively different adverse health effects may be proposed as being acceptable, and selection of an acceptable risk might be made from any of a variety of adverse effects. These effects might range from no adverse health effect, to clinically insignificant effects, to reversible injury, to permanent injury, or to lethality. Ammonia benchmarks may be quantified based on holistic consideration of toxicologic data, including human clinical data, animal bioassay data, and reports of industrial ammonia release accidents. Selected acute toxicology benchmarks for ammonia are summarized in Table 7. Ideally, all data sources converge on a single value for each toxicologic benchmark parameter to be quantified. However, Table 7 reveals significant disparity. One source of such disparity is revealed in “Results” that is, a fundamental conflict between contemporary accident reconstruction results versus largely anecdotal data derived from reports of ammonia potency dating back, in some cases, to the years when ammonia competed with mustard gas, chlorine, and other war gases whose primary purpose was to kill enemy soldiers engaged in trench warfare. Potency values reported for lethality in that context have persisted in the contemporary literature, as depicted in Figure 1. Multiple industrial accident reconstruction pointers indicates a lower potency of ammonia than suggested by apparently anecdotal data, and the lower potency suggested by the accident reconstruction data is consistent with animal bioassays using multiple species.

**Fatal Exposure Concentration**

The National Research Council Committee on Toxicology defines three levels of community emergency exposure levels (CEELs, since renamed AEGs). AEG-3 is defined to protect members of the general population, including susceptible but excluding hypersusceptible individuals, against “death or life-threatening effects...for example, pulmonary edema, cardiac failure, or cancer” \((7)\). The benchmark for fatal exposure to ammonia may be derived from American Industrial Hygiene Association (AIHA) emergency response planning guidelines (ERPGs), animal bioassay data, human data, and reports of fatal accidents. These sources should produce consistent results but, in the case of ammonia, they do not. They will be synthesized to produce a conservative but realistic estimate of the ammonia lethality concentration for short exposure durations.

**AIHA ERPG-3.** The AIHA \((61)\) defines ERPG-3 as:

\[ t \]

\[ \text{the maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to one hour without experiencing or developing life-threatening health effects.} \]

The ERPG-3 value for ammonia is 1,000 ppm-v. According to the AIHA,

\[ t \]

\[ \text{this level may cause severe eye and nasal irritation} \]

\((19,26,62)\); however, based on animal toxicology data \((63,64)\) lethality would not be expected.

The 1-hr 1,000-ppm-v ERPG-3 is equivalent to a 5-min value of 12,000 ppm-v using Haber’s rule or 3,464 ppm-v using Ten Berge’s adjustment with \(n = 2\). As indicated in “Results” and in Table 2, higher values are also sublethal. Indeed, the AIHA’s ERPG-3 value is not based on lethality and therefore already incorporates an unquantified safety factor. The actual ammonia lethality level cannot be reconstructed based on the AIHA’s documentation, and the ERPG-3 must be rejected as downwardly adjusted and irrelevant.

**Table 5. Evaluation of the Potchefstroom, South Africa, ammonia incident to estimate human lethality concentrations: summary of fatality rates.**

| Ammonia level | Fatality rate (%) | Peak | 1 min (ppm) | 5 min (ppm) |
|---------------|------------------|------|-------------|-------------|
| Observed      |                  | 0    | 0           | 0           |
|               | 0                | 82,300| 84,883      | 33,737      |
|               | 26               | 365,000| 236,080    | 73,347      |
|               | 60               | 641,000| 262,479   | 87,479      |
| Calculated‡  |                  | 0    | 82,300      | 84,883      |
|               | 10               | 191,341| 143,036    | 48,972      |
|               | 20               | 300,383| 201,188   | 64,207      |
|               | 30               | 398,000| 241,539   | 75,010      |
|               | 40               | 479,000| 255,185   | 79,166      |
|               | 50               | 560,000| 268,832   | 83,322      |
|               | 60               | 641,000| 262,479   | 87,479      |
|               | 70               | 722,000| 296,126   | 91,635      |
|               | 80               | 803,000| 308,773   | 95,791      |
|               | 90               | 884,000| 323,420   | 99,947      |
|               | 100              | 965,000| 337,067  | 104,103     |

*Based on data reported in Mudan and Mitchell \((53)\).  
‡ Adjusted from 7 or 9 min.  
*Interpolating or extrapolating observed values.

**Table 6. Evaluation of the Potchefstroom, South Africa, ammonia incident to estimate human lethality concentrations: summary by zone.**

| Zone | 1 | 2 | 3 | 4 |
|------|---|---|---|---|
| Individuals | 10 | 27 | 6 | ? |
| Fatalitys (no.) | 6 | 7 | 5 | 0 |
| Survivors (no.) | 4 | 20 | 1 | All |
| Ate rate | 0.60 | 0.26 | 0.83 | 0.00 |
| Survival rate | 0.40 | 0.74 | 0.17 | 1.00 |

? unknown.  
*Based on data reported in Mudan and Mitchell \((53)\).  
† Interpolating or extrapolating observed values.

| Benchmark | Conc (ppm-v) | Duration (min) |
|-----------|--------------|----------------|
| Odor threshold | 0.04–57 | > 0 |
| Standards and guidelines‡ | | |
| ACGIH STEL | 35 | 15 |
| AIHA ERPG-2 (injury) | 200 | 60 |
| NIOSH IDLH | 300 | 30 |
| AIHA ERPG-3 (lethality) | 1,000 | 60 |
| Clinically insignificant effects | 5 | 10 |
| Irreversible effects | 7,051 | 5 |
| 2,035 | 30 |
| 2,035 | 60 |
| Fatal exposure | > 33,737 | > 5,623 |
| > 5,623 | 30 |

*Based on data reported in Mudan and Mitchell \((53)\).  
‡ Interpolating or extrapolating observed values.

**Abbreviations:** ACGIH, American Conference of Governmental Industrial Hygienists; AIHA, American Industrial Hygiene Association; Conc, concentration; ERPGs, Emergency Response Planning Guidelines; IDLH, immediately dangerous to life or health; NIOSH, National Institute for Occupational Safety and Health; STEL, short-term exposure limit.

*National Library of Medicine (13).
Animal studies. Numerous animal bioassay reports were addressed in “Results” (Table 2). They were adjusted to equivalent HECs using parameters for dose conversion among species (7,8) and EPA methodology (8). Although the LC95L Parameter is more conservative than the LC50 Parameter, the death LC95L values resulting in LC50 values that are lower than the LC95L Values (Table 2). Consequently, both parameters will be considered together.

Concentrations of airborne ammonia whose lethality to humans is estimated based on animal bioassay studies produced an arithmetic mean inhalation concentration LC95L or LC50 value of 215,390 ppm-v at 5 min; 35,898 ppm-v at 30 min; and 17,949 ppm-v at 60 min in accordance with Haber’s rule, or 70,508; 28,785; and 20,354 ppm-v, respectively, using Ten Berge’s adjustment with n = 2. Geometric mean values were 108,478; 19,369; and 9,946 ppm-v according to Haber’s rule, and 34,455; 14,559; and 10,433 ppm-v using Ten Berge’s adjustment. The minimum human equivalent LC95L or LC50 value was reported from guinea pig data: 5,956 ppm-v at 5 min; 993 ppm-v at 30 min; and 496 ppm-v at 60 min according to Haber’s rule, and 5,956; 2,431; and 1,719 ppm-v using Ten Berge’s adjustment. These minimum values are outliers, however, and are contradicted by other data on guinea pigs (38): 35,957 ppm-v at 5 min; 14,679 at 30 min; 10,380 ppm-v at 60 min using Haber’s rule, and 8,040; 4,020; and 1,005 ppm-v using Ten Berge’s adjustment with n = 2.

The upper respiratory systems of mammals, including humans, may scrub ammonia, especially during nose breathing. This process affords some protection of the lower respiratory system from injury. This protection, however, tends to be lost quickly at high ammonia concentrations, which saturate the scrubbing capacity of upper respiratory structures. Some lethality values derived from animal bioassays (of rabbits, for example) involved cannulation, and are highly conservative. These values are conservative because cannulation, usually at the windpipe, bypasses the upper respiratory tract, reducing the concentration of ammonia necessary to cause toxic injury to the lower respiratory tract. Animal studies involving cannulation, therefore, tend to reduce ammonia effect levels such as lethality. In contrast, humans exposed to ammonia in accidental releases are unlikely to have been cannulated, and may scrub ammonia by reverting to nose breathing, or even by breathing with mouths covered with wet cloth.

Human data, apparently anecdotal. Human lethality values derived from animal data were significantly higher than lethality values derived from apparently anecdotal reports of lethality following human exposure. The latter produced an arithmetic mean inhalation lethality value of 95,000 ppm-v at 5 min; 15,833 ppm-v at 30 min; and 7,917 ppm-v at 60 min in accordance with Haber’s rule; or 20,000; 8,165; and 5,774 ppm-v, respectively, using Ten Berge’s adjustment with n = 2. Geometric mean values were 39,482; 6,580; and 3,290 ppm-v according to Haber’s rule, and 16,119; 6,580; and 4,653 ppm-v using Ten Berge’s adjustment. Thus, a disparity exists between lethality data derived from animal versus human studies, and this disparity is approximately 3-fold when arithmetic mean lethality values are considered (215,390 ppm-v/95,000 ppm-v = 2.3 at 5 min using Haber’s rule; 70,508 ppm-v/20,000 ppm-v = 3.5 (also at 5 min) using Ten Berge’s adjustment).

Accident reports. The toxicologic findings discussed above and presented in Table 2 are quantitatively complex but qualitatively simple: predictions of ammonia concentrations that would be lethal to humans tend to be significantly lower than lethal concentrations inferred from animal studies. This is true under Haber’s rule (C′n = constant, with n = 1) or Ten Berge’s adjustment with n = 2 (based on data on mice and rats).

Considered alone, the human data are questionable, as explained previously. Considered in the context of the animal data, the human data are further questionable: no obvious basis is evident for the apparently greater sensitivity of humans than animals. This disparity between human lethality values inferred from human data versus animal data motivated reconstruction of the 1973 industrial accident in Potchefstroom, which killed 18 people, as described and tabulated in Tables 4-6 and depicted in Figure 2.

Figure 2 illustrates the effect of increasing peak, 1 min, and 5-min time-weighted average anhydrous ammonia concentrations in air on the human fatality rate. The LC950 values are estimated to be a peak of 560,000 ppm-v, a 1-min mean of 268,832 ppm-v, and a 5-min mean of 83,322 ppm-v. Longer term values were not generated because the air modeling addressed an exposure period of under 10 min.

The Potchefstroom accident reconstruction indicates ammonia lethality levels significantly higher than both the human data and animal bioassay data. However, the accident reconstruction is complicated because the plant contained a control room and other structures that were at least partially enclosed. These potential refuges would tend to elevate the apparent resistance of individuals to ammonia. A conservative interpretation of the accident reconstruction, therefore, is appropriate. For example, the 5-min concentration producing 0% mortality (LC95) determined from zone 4, where no fatalities occurred, was 33,737 ppm-v (Table 6). This value is consistent with human lethality levels derived from the animal bioassay data, but is still higher than lethality levels inferred from the human data. It is also consistent with the Mulder and Van der Zalm report (47), in which an individual died, possibly unnecessarily, following exposure to a sizable but unknown fraction of 330,000-ppm-v saturated ammonia vapor. A reasonable inference from analysis of available accident data is that they validate adjustment of animal lethality concentrations to human equivalent values.

Irreversible Injury Concentration

AEGI-2 is defined by the National Research Council Committee on Toxicology to protect members of the general population, including susceptible but excluding hypersusceptible individuals, against permanent or long-lasting effects, impairment of the ability to escape, or disablement; for example, as a result of “severe eye or respiratory irritation, disorientation, and organ damage” (1). The IDLH and the ERPG-2 parameters are candidates for the irreversible injury (AEGI-2) benchmark, but the values assigned these parameters in the case of ammonia are flawed. However, the IDLH or the ERPG-2 methodology might be adopted, rather than the IDLH or ERPG-2 value for ammonia. Appropriate use of these parameters is addressed below.

AIHA ERPG-2. A reasonable candidate value for the benchmark for irreversible injury is 200 ppm-v, which corresponds to the AIHA ERPG-2 value (65). The AIHA (65) defines ERPG-2 as

[t]he maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to one hour without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual’s ability to take protective action.

The ERPG-2 for ammonia is 200 ppm-v. According to the AIHA (65),

[t]here is likely to be strong odor and some eye irritation at this level (20,66,67), but serious health effects are unlikely. Rats continuously exposed to 180 ppm for 90 days showed no adverse effects (66), and humans repeatedly exposed to 100 ppm for six weeks developed only slight eye irritation (66).

The ERPG-2 value does not represent an irreversible injury level, but an eye irritation level—and not the highest tolerable. Silverman et al. (19) reported that all seven individuals voluntarily exposed to ammonia at 500 ppm-v for 30 min tolerated the exposure without adverse effect or inability to escape. A fundamental problem with ERPG-2 is that eye irritation and associated lacrimation occur over a wide range of concentrations,
with effects varying from annoyance to clinical significance. Impairment of vision may reduce escape ability, but escape ability is reduced routinely by factors such as darkness during industrial emergencies, either because they may occur at night or because power may be lost during daytime emergencies in structures not illuminated internally by sunlight.

**NIOSH IDLH.** Another reasonable candidate value for the benchmark for irreversible injury is 300 ppm-v for 30 min, which corresponds to the NIOSH IDLH value (68) (Table 7). Preference of this regulatory criterion over toxicologic data would seem desirable, given the apparent unavailability of detailed dose–response human toxicology data documenting irreversible injury from ammonia inhalation. However, use of the IDLH value is undesirable. The IDLH value is based on secondary literature (68), and NIOSH indicated that the primary literature was not examined. NIOSH investigators indicate that

[...]

However, AIHA (65) is superseded by AIHA (61), which states that 300–500 ppm-v is a maximum 1-hr exposure, irritating the eyes, nose, and throat. The AIHA (61) does not state that 300–500 ppm-v is the maximum tolerable, nor that the time frame over which its effects might become intolerable is 30 min. The AIHA also does not state that 300–500 ppm-v might render an exposed individual incapable of escape within 30 min. Indeed, the AIHA (61) further states that 1,000 ppm-v represents

[...]

The 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.... This level may cause severe eye and nasal irritation; however, based on animal toxicology data lethality would not be expected.

In supporting an IDLH value of 300 ppm-v, NIOSH (68) indicates that “AIHA (1971) also reports that 5,000 to 10,000 ppm are reported to be fatal (Mulder and Van der Zalm 1967).” However, Mulder and Van der Zalm (47) do not say this. Indeed, they cite the 5,000- to 10,000-ppm-v lethality range, but primarily for the purpose of refuting it. They indicate that the deceased was exposed to many times 10,000 ppm-v, that he ignored instructions to report to the infirmary for timely medical attention, and that he was able to resume work for 3 hr despite his injuries.

NIOSH (68) also states that “exposures for 30 min to 2,500 to 6,000 ppm are considered dangerous to life (Smyth 1956) [69].” However, Smyth (69) is a secondary source that compiled suggested “hygienic standards for daily inhalation” (emphasis added).

The NIOSH report fails to indicate how the lethality values it cites might be related to its selection of an IDLH. However, one might surmise that NIOSH regards these lethality values as LC₉₀ values, which might be equated to 10 times a preliminary IDLH value (70):

...LC₉₀ values (after “adjusting” if necessary to 30 min) were divided by a safety factor of 10 to determine a ‘preliminary’ IDLH for comparison purposes.

Thus, the presumed lethality values of 5,000–10,000 ppm-v would support IDLH values of 500–1,000 ppm-v, and 2,500–6,000 ppm-v would support an IDLH of 250–600 ppm-v. However, the lethality values cited by NIOSH appear to be unreliable based on analyses presented herein.

**Potchefstroom accident reconstruction.** The irreversible injury concentration may be derived in a manner consistent with derivation of the IDLH value. The IDLH is initially estimated as one-tenth the (animal) LC₉₀ value. Subsequent adjustment may be necessary based on examination of other types of data, such as explosivity limits and the concentrations at which respiration is reduced 50% in mice or rats exposed for 10 min. The mean 5-min LC₉₀ value derived earlier from animal bioassay data is 70,508 ppm-v using the Ten Berge adjustment, which in this case is more conservative than the Haber’s rule value (215,390 ppm-v). The 5-min LC₉₀ value derived earlier from the Potchefstroom accident reconstruction is 83,322 ppm-v, but this may represent an upper limit, as discussed previously. Using the mean 5 min LC₉₀ value from animal bioassays produces an irreversible injury concentration of 7,051 ppm-v at 5 min; 1,175 ppm-v at 30 min; and 588 ppm-v at 1 hr using Haber’s rule; and 7,051; 2,879; and 2,035 ppm-v, respectively, using Ten Berge’s adjustment with n = 2. These values are approximately one-fifth the 5-min lethality value of 33,737 ppm-v.

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