Hydrogen chloride (CASRN 7647-01-0)

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Hydrogen chloride; CASRN 7647-01-0

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

STATUS OF DATA FOR Hydrogen chloride

File First On-Line 06/01/1989

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	no data	
Inhalation RfC Assessment (I.B.)	on-line	07/01/1995
Carcinogenicity Assessment (II.)	no data	

_I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Hydrogen chloride
CASRN — 7647-01-0
Primary Synonym — Hydrocloric acid

Not available at this time.

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

Substance Name — Hydrogen chloride
CASRN — 7647-01-0
Primary Synonym — Hydrocloric acid
Last Revised — 07/01/1995

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

__I.B.1. Inhalation RfC Summary

Critical Effect	Exposures*	UF	MF	RfC
Hyperplasia of nasal mucosa larynx and trachea Rat Chronic Inhalation Study Sellakumar et al., 1994; Albert et al., 1982	NOAEL: None NOAEL(ADJ): None NOAEL(HEC): None LOAEL: 15.0 mg/cu.m (10 ppm) LOAEL(ADJ): 2.7 mg/cu.m LOAEL(HEC): 6.1 mg/cu.m	300	1	2E-2 mg/cu.m

*Conversion Factors and Assumptions — MW = 36.46. Assuming 25 C and 760 mmHg, LOAEL(mg/cu.m) = 10 ppm x 36.67/24.45 = 15 mg/cu.m. LOAEL(ADJ) = 15 x 6 hours/24 hours x 5 days/7 days = 2.7 mg/cu.m. The LOAEL(HEC) was calculated for a gas:respiratory effect in the extrathoracic and tracheobronchial regions. MVa = 0.5 cu.m/day, MVh = 20 cu.m/day, Sa = (15.0 ET + 22.5 TB) = 37.5 sq.cm., Sh = (200 ET + 3200 TB) = 3400 sq.cm. RGDR(ET+TB) = (MVa/Sa)/(MVh/Sh) = 2.27. LOAEL(HEC) = LOAEL(ADJ) x RGDR = 2.7 mg/cu.m x 2.27 = 6.1 mg/cu.m.

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

Sellakumar, A.R., C.A. Snyder, J.J. Solomon and R.E. Albert. 1985. Carcinogenicity for formaldehyde and hydrogen chloride in rats. Toxicol. Appl. Pharmacol. 81: 401-406.

Albert, R.E., A.R. Sellakumar, S. Laskin, M. Kuschner, N. Nelson and C.A. Snyder. 1982. Gaseous formaldehyde and hydrogen chloride induction of nasal cancer in rats. J. Natl. Cancer Inst. 68(4): 597-603.

The Albert et al. (1982) study, discussed in detail by Sellakumar et al. (1985), reported data from a chronic inhalation exposure study in rats. One hundred male Sprague-Dawley rats were exposed to 10 ppm hydrogen chloride (HCl) for 6 hours/day, 5 days/week (duration-adjusted concentration = 2.5 mg/cu.m) for their lifetimes. All animals were observed daily, weighed monthly, and allowed to die naturally or killed when moribund. Complete necropsy was performed on all animals, with particular attention given to the respiratory tract. Histologic sections were prepared from the nasal cavity (one lateral section from each side of the head), lung (one section from each lobe), trachea, larynx, liver, kidneys, testes, and other organs where gross pathological signs were present. However, Sellakumar et al. (1985) did not discuss histopathological events in organs other than the respiratory tract. HCl-exposed animals showed no differences in body weights or survival when compared with air controls. The data indicated 62/99 exposed animals with epithelial or squamous hyperplasia in the nasal mucosa (location not specified) vs. 51/99 in the concurrent control group. Incidence of squamous metaplasia was 9 and 5 in the exposed and control rats, respectively. There was a 24% incidence of hyperplasia of laryngeal-tracheal segments in HCl- exposed rats (larynx 2/22, trachea 6/26) vs. 6% in the controls. The authors did not make any comments concerning the severity of these changes. Based on these results, the 10-ppm (15-mg/cu.m) concentration can be considered a LOAEL [LOAEL(HEC) = 6.1 mg/cu.m].

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

UF — The uncertainty factor includes a factor of 3 for interspecies differences, 10 for intraspecies extrapolations, and 10 to extrapolate from a LOAEL to a NOAEL. Because of the expected portal-of-entry effect of HCl, an uncertainty factor to account for the lack of both a second-species chronic bioassay and a reproductive bioassay was not considered necessary. It has been suggested that a reasonable estimate of the NOAEL in humans would be between 300 and 3000 micrograms/cu.m (Kamrin, 1992). This estimate resulted from an expert review workshop and is based on examination of the HCl literature, a comparison with sulfuric acid toxicity, and the judgment of those in attendance at the review workshop. However, because the workshop did not address the areas of uncertainty stated above and due to the limited available information, use of uncertainty factors to address these data gaps is considered appropriate.

MF — None

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

Human asthmatics (5/sex) were exposed to 0.8 or 1.8 ppm HCl for 45 minutes, and pulmonary function tests performed immediately after exposure were compared to baseline levels (Stevens et al., 1992). No exposure-related effects were observed in subjective symptoms or in pulmonary function tests, including forced expiratory volume in 1 second, forced vital capacity, maximal flow at 50 and 75% of vital capacity, respiratory resistance, and peak flow. This is the only available controlled human exposure study of HCl.

In a 90-day inhalation study using B6C3F1 mice and Sprague-Dawley and Fisher 344 rats (Toxigenics, Inc., 1984), groups of 31 males and 31 females of each species strain were exposed to HCl at 10, 20, or 50 ppm (15, 30, or mg/cu.m, respectively), 6 hours/day, 5 days/week for 90 days. Several animals died during the study; however, the deaths did not appear to be exposure related. There was a slight but significant decrease in body weight gain in male and female mice

and in male Fischer 344 rats in the high-exposure groups. There was no effect on hematology, clinical chemistry, or urinalysis. Histologic examination showed minimum to mild rhinitis in both strains of rats. Lesions occurred in the anterior portion of the nasal cavity and were concentration and time related. In mice exposed to 50 ppm, there was cheilitis and accumulation of macrophages in the peripheral tissues after 90 days. Mice in all exposure groups developed eosinophilic globules in the epithelial lining of the nasal tissues.

In a short-term study, Kaplan et al. (1988) exposed baboons (3 males/group) to 0, 500, 5000, or 10,000 ppm HCl for 15 minutes and observed them for 3 months. The results indicated dose-related increased frequency of respiratory rate and minute volume following exposure. The higher doses caused decreased arterial PO2, but follow-up measurements at 3 days or 3 months following exposure did not show any abnormalities. The upper airways of the baboon, compared with other mammalian species (rodents), have the greatest similarity to those of the human child, and the complexity of the respiratory tract increases with age. It reasonably can be expected that the more complex structure of the upper airways of the human would remove more of an airborne chemical than those of other mammalian species (rodents). Based on the results of this study, the authors suggested that the human is probably much less sensitive to HCl than is the mouse.

Burleigh-Flayer et al. (1985) exposed male guinea pigs to 0, 320, 680, 1040, and 1380 ppm HCl for 1-6 minutes and measured respiratory rate and induction of sensory or pulmonary irritation. This study indicated sensory irritation at 320 ppm (477 mg/cu.m) with an exposure of 6 minutes, whereas less severe effects were observed at concentrations of 680 ppm or higher during a 1-minute exposure. The concentration of HCl exposure was inversely related to the onset interval of pulmonary irritation.

Buckley et al. (1984) attempted to determine the potential for pathologic damage following exposure to sensory irritants at concentrations eliciting a 50% decrease in respiratory rate in the mouse. The mouse RD50 for HCl was reported to be 309 ppm. The TWA exposure consisted of three exposures (295- 310 ppm) for 5 days (6 hours/day). The lesions noted were confined to the upper respiratory epithelium. No abnormalities were noted in the trachea or lungs.

Darmer et al. (1974), in an attempt to determine the HCl hazard at a missile test-firing site, reported 30-minute LC50 values for rats and mice of 4701 and 2644 ppm, respectively; the LC50 values for 5-minute exposures were 40,989 (rat) and 13,745 ppm (mice). Thus, it appeared that mice are 2 to 3 times more sensitive than rats to HCl exposure.

Reproductive and development studies of HCl are limited. Pavlova (1976) exposed two groups of 8-15 female rats to 302 ppm (450 mg/cu.m) HCl for 1 hour. One group was exposed 12 days prior to mating, and the other group on day 9 of gestation. In both groups, signs of severe dyspnea and cyanosis were noted, and mortality occurred in one-third of the animals. Fetal mortality was significantly higher in rats exposed during pregnancy. When the progeny were subjected to an additional exposure of 35 ppm (52 mg/cu.m) at the age of 2-3 months, functional abnormalities in the organs of the progeny were similar to those found in the mothers.

In another study from the same laboratory, female rats were exposed to 302 ppm (450 mg/cu.m) HCl for 1 hour prior to mating. Exposure killed 20-30% of the rats. In rats surviving 6 days after exposure, a decrease in blood oxygen saturation was noted, as was kidney, liver, and spleen damage. In addition, treatment altered the estrus cycles. In rats mated 12-16 days postexposure and killed on day 21 of pregnancy, fewer live fetuses, a decrease in fetal weight, and an increase in relative lung weights of the fetuses were observed (GEOMET Technologies, Inc., 1981).

__I.B.5. Confidence in the Inhalation RfC

Study — Low
Database — Low
RfC — Low

The chronic study used only one dose and limited toxicological measurements. The supporting data consist of two subchronic bioassays; the database does not provide any additional chronic or reproductive studies. Therefore, low confidence was recommended for the study, database, and the RfC.

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

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

This assessment was peer reviewed by external scientists. This review was completed on 05/22/1995. Their comments have been carefully evaluated and considered in the revision and finalization of this IRIS Summary. A record of these comments is included in the IRIS documentation files.

Other EPA Documentation — U.S. EPA, 1988

Agency Work Group Review — 01/19/1989, 02/16/1989, 05/11/1995

Verification Date — 05/11/1995

Screening-Level Literature Review Findings — A screening-level review conducted by an EPA contractor of the more recent toxicology literature pertinent to the RfC for Hydrogen chloride conducted in August 2003 did not identify any critical new studies. IRIS users who know of important new studies may provide that information to the IRIS Hotline at hotline.iris@epa.gov or 202-566-1676.

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

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

_II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Hydrogen chloride
CASRN — 7647-01-0
Primary Synonym — Hydrocloric acid

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

_III. [reserved]
_IV. [reserved]
_V. [reserved]

_VI. Bibliography

Substance Name — Hydrogen chloride
CASRN — 7647-01-0
Primary Synonym — Hydrocloric acid
Last Revised — 07/01/1995

_VI.A. Oral RfD References

None

_VI.B. Inhalation RfC References

Albert, R.E., A.R. Sellakumar, S. Laskin, M. Kuschner, N. Nelson and C.A. Snyder. 1982. Gaseous formaldehyde and hydrogen chloride induction of nasal cancer in rats. J. Natl. Cancer Inst. 68(4): 597-603.

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

Burleigh-Flayer, H., K.L. Wong and Y. Alarie. 1985. Evaluation of the pulmonary effects of hydrochloric-acid using carbon dioxide challenges in guinea-pigs. Fund. Appl. Toxicol. 5(5): 978-985.

Darmer, K.I., E.R. Kinkead and L.C. Dipasquale. 1974. Acute toxicity in rats and mice exposed to hydrogen chloride gas and aerosols. Am. Ind. Hyg. Assoc. J. 35(10): 623-631.

GEOMET Technologies, Inc. 1981. Hydrogen chloride: Report 4, Occupational Hazard Assessment. U.S. Department of Health and Human Services, NIOSH, Cincinnati, OH. NTIS PB83-105296.

Kamrin, M.A. 1992. Workshop on the health effects of HCl in ambient air. Reg. Pharm. Toxicol. 15: 73-82.

Kaplan, H.L., A. Anzueto, W.G. Switzer and R.K. Hinderer. 1988. Effects of hydrogen chloride on respiratory response and pulmonary function of the baboon. J. Toxicol. Environ. Health. 23(4): 473-493.

Pavlova, T.E. 1976. Disturbance of development of the progeny of rats exposed to hydrogen chloride. Bull. Exp. Biol. Med. 82: 1078-1081.

Sellakumar, A.R., C.A. Snyder, J.J. Solomon and R.E. Albert. 1985. Carcinogenicity of formaldehyde and hydrogen chloride in rats. Toxicol. Appl. Pharmacol. 81: 401-406.

Stevens, B., J.Q. Koenig, V. Rebolledo, Q.S. Hanley, and D.S. Covert. 1992. Respiratory effects from the inhalation of hydrogen chloride in young adult asthmatics. J. Occup. Med. 34: 923-929.

Toxigenics, Inc. 1984. 90-Day inhalation study of hydrogen chloride gas in B6C3F1 mice, Sprague-Dawley rats, and Fischer-344 rats. Study conducted for CIIT, Research Triangle Park, NC. CIIT Docket No. 20915.

U.S. EPA. 1988. Health Assessment Document for Chlorine and Hydrogen Chloride. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC. EPA-600/8-87- 041A. (External Review Draft)

_VI.C. Carcinogenicity Assessment References

None

_VII. Revision History

Substance Name — Hydrogen chloride
CASRN — 7647-01-0
Primary Synonym — Hydrocloric acid

Date	Section	Description
01/01/1991	I.B.	Inhalation RfC summary on-line
01/01/1991	VI.	Bibliography on-line
01/01/1992	IV.	Regulatory Action section on-line
06/01/1995	I.B.	Inhalation RfC noted as pending change
06/01/1995	I.B.6.	Work group review date added
07/01/1995	I.B.	Inhalation RfC replaced; new RfC
07/01/1995	VI.B.	Inhalation RfC references replaced
04/01/1997	III., IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.
10/28/2003	I.B.6.	Screening-Level Literature Review Findings message has been added.

_VIII. Synonyms

Substance Name — Hydrogen chloride
CASRN — 7647-01-0
Primary Synonym — Hydrocloric acid
Last Revised — 01/01/1991

- 7647-01-0
- ACIDE CHLORHYDRIQUE (French)
- ACIDO CLORIDRICO (Italian) 362
- CHLOORWATERSTOF (Dutch)
- CHLOROHYDRIC ACID
- CHLOROWODOR (Polish)
- CHLORWASSERSTOFF (German)
- HYDROCHLORIC ACID
- HYDROCHLORIDE
- HYDROGEN CHLORIDE

- MURIATIC ACID
- SPIRITS of SALT
- UN 1050
- UN 1789
- UN 2186

IRIS Home

Chronic Health Hazards for Non-Carcinogenic Effects

Reference Dose for Chronic Oral Exposure (RfD)

- Oral RfD Summary
- Principal and Supporting Studies
- Uncertainty and Modifying Factors
- Additional Studies/Comments
- Confidence in the Oral RfD
- EPA Documentation and Review

Reference Concentration for Chronic Inhalation Exposure (RfC)

- Inhalation RfC Summary
- Principal and Supporting Studies
- Uncertainty and Modifying Factors
- Additional Studies/Comments
- Confidence in the Inhalation RfC
- EPA Documentation and Review

Carcinogenicity Assessment for Lifetime Exposure

Evidence for Human Carcinogenicity

- Weight-of-Evidence Characterization
- Human Carcinogenicity Data
- Animal Carcinogenicity Data