http://www.epa.gov/iris/subst/0419.htm
Last updated on 8/9/2012

Integrated Risk Information System

Formaldehyde (CASRN 50-00-0)

view QuickView

MAIN CONTENTS

List of IRIS Substances

Search IRIS by Keyword

go

IRIS Summaries/Toxicological Reviews

Entire IRIS Website

Reference Dose for Chronic Oral Exposure (RfD) go

[UPDATE] The (inhaltion) portion of this assessment is currently under development and the latest draft can be found at, IRIS Toxicological Review of Formaldehyde (Inhalation) (External Review Draft)

0419

Formaldehyde; CASRN 50-00-0

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 Formaldehyde

File First On-Line 10/01/1989

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	09/01/1990
Inhalation RfC Assessment (I.B.)	no data	
Carcinogenicity Assessment (II.)	on-line	05/01/1991

_I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

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

Substance Name — Formaldehyde

CASRN — 50-00-0
Last Revised — 09/01/1990

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also 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.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Reduced weight gain, histopathology in rats Rat 2-Year Bioassay Til et al., 1989	NOAEL: 15 mg/kg/day LOAEL: 82 mg/kg/day	100	1	2E-1 mg/kg/day

* Conversion Factors: none

__I.A.2. Principal and Supporting Studies (Oral RfD)

Til, H.P., R.A. Woutersen, V.J. Feron, V.H.M. Hollanders, H.E. Falke and J.J. Clary. 1989. Two-year drinking water study of formaldehyde in rats. Food Chem. Toxicol. 27: 77-87.

Formaldehyde was administered daily in drinking water to Wistar rats (70/sex/dose) for up to 24 months at mean doses of 0, 1.2, 15, or 82 mg/kg/day for males and 0, 1.8, 21, or 109 mg/kg/day for females. Up to 10 rats/sex/dose were sacrificed and examined after 12 months and 18 months of treatment; the remainder was sacrificed and examined at 24 months. Mean body weights of the high-dose group were decreased in males from week 1 and in females from week 24 through termination. Food intake was significantly decreased in all high-dose males with females showing a similar but less consistent decrease in food intake. A 40% decrease in drinking water intake was reported in all high-dose animals while those rats receiving the middle dose showed a slight but generally insignificant decrease in liquid intake. Changes in urinalyses, and hematological and clinical chemistry parameters, were not dose-related, so were not considered to be related to formaldehyde intake. Among the high-dose males, significant decreases were seen in the absolute heart and liver weights at 18 months and at termination; in testes weights at 18 months; and in kidney weights at termination. High-dose females showed significant increases in the relative kidney weights at 12 and 24 months. Relative brain weights were significantly increased in high-dose males at all three examination periods and in females at termination only. Relative testes weights were significantly increased in high-dose males at termination. These relative organ weight increases were generally ascribed to the decreased body weights observed. A significant increase in mortality among males receiving the 15 mg/kg/day dose was not considered toxicologically significant.

Gross examination at 12, 18, and 24 months revealed a raised, thickening of the limiting ridge of the forestomach in most high-dose rats and in some rats of both sexes from other groups. Irregular mucosal thickening of the forestomach and glandular stomach were seen in several rats of the high-dose group and in occasional rats of other groups. The incidence of discoloration and irregularity of the kidney surface and atrophy of the testes was lower in the high-dose group as compared with controls.

Significant histopathological changes of the gastrointestinal tract were found in high-dose males and females and included chronic atrophic gastritis of the glandular stomach from week 53 on, as well as focal ulceration and glandular hyperplasia at the terminal examination. The incidence of focal papillary epithelial hyperplasia and focal hyperkeratosis of the forestomach was significantly increased in both sexes at the terminal examination. These effects of formaldehyde on the gastric mucosa were considered cytotoxic in nature. A significant increase in the incidence of papillary necrosis of the kidneys was reported in both sexes of high-dose rats at the terminal examination. No treatment-related gastric tumors were observed in this study. The incidence and type of tumors observed in other organ systems were common to this strain and similar to those found in aging rats, 30 were not considered toxicologically significant. A NOAEL of 15 mg/kg/day in male rats was indicated in this study.

Formaldehyde was administered daily in the drinking water of Sprague-Dawley rats (15/sex/dose) at doses equivalent to 0, 50, 100, or 150 mg/kg/day for 90 days (Johannsen et al., 1986). Male and female high-dose rats (150 mg/kg/day) and male rats receiving the 100 mg/kg/day dose showed a significant decrease in body weight gain. A dose-related decrease in the intake of drinking water was reported in both sexes of treated rats. Food intake and feed efficiency was comparable among all groups. No statistically significant differences were seen in urinalyses, or hematological and blood chemistry parameters. No treatment-related histopathological findings were observed. A NOAEL of 50 mg/kg/day was indicated for rats.

Similarly, formaldehyde was administered in the diet of pure-bred beagle dogs (4/sex/dose) at doses of 0, 50, 75, or 100 mg/kg/day for 90 days. A significant decrease in body weight gain was reported in the high-dose dogs of both sexes with no effect on weight gain at the two lower dose levels. A reduced food consumption and feed efficiency was observed in dogs at all treatment levels. No treatment-related effects were seen on hematological, blood chemistry, or urinalysis parameters, nor were any treatment-related lesions observed. The gastrointestinal mucosa was not affected by formaldehyde intake. A NOAEL of 75 mg/kg/day was indicated.

Marks et al. (1980) administered formaldehyde as an aqueous solution to pregnant CD-1 mice at oral doses of 74, 148, and 185 mg/kg on days 6 to 15 of gestation. The high dose was lethal to most of the treated mice by day 18. Mortality was 1/35 and 22/34 among dams treated at 148 and 185 mg/kg/day, respectively. In the high-dose group, the number of resorption sites was increased and mean litter size was slightly decreased. No effects on fetus size, and no gross or microscopic skeletal or soft tissue abnormalities were observed.

Hurni and Ohder (1973) exposed pregnant beagle dogs (9 to 11/group) to formaldehyde in the diet at levels of 125 or 375 ppm from 4 days after mating through day 56. Assuming that 1 ppm in the diet of a 10-kg dog consuming 250 g of dry chow/day equals 0.025 mg/kg/day (Lehman, 1959), this would correspond to doses of 3 or 9 mg/kg/day. The dogs were weighed weekly, and the pups were weighed at birth and twice weekly thereafter. Feeding of formaldehyde had no effect on pregnancy rate, maternal body weight, or duration of gestation. Mean litter sizes were within normal ranges. No effects were reported on growth or mortality. All pups were inspected for defects at birth and at 8 weeks postpartum. Stillborns, as well as pups dying before weaning, were autopsied and examined for internal and skeletal anomalies. Normal behavior, appearance, mobility and muscular coordination were reported for all dogs observed for up to 9 months.

Seidenberg et al. (1987) evaluated formaldehyde in the Chernoff/Kavlock developmental toxicity screen. Formaldehyde was administered by gavage at 540 mg/kg/day to pregnant ICR/SIM mice on gestation days 8 through 12. The mice were allowed to deliver, then several neonatal growth and viability parameters were measured in the offspring. Comparative statistical analysis of these parameters between treated animals and concurrent (vehicle-treated) controls revealed no significant effect on any perinatal parameter examined.

__I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF — An uncertainty factor of 100 was used to account for the inter- and intraspecies differences.

MF — None

__I.A.4. Additional Studies/Comments (Oral RfD)

Based on this 2-year study in rats in which a NOAEL is identified, the uncertainty factor of 100 is considered appropriate for extrapolating results to humans. This study consisted of adequate numbers of animals of both sexes as well as a thorough examination of toxicological and histological parameters.

Takahashi et al. (1986) conducted a two-stage carcinogenesis bioassay in male Wistar rats. The animals were administered N-methyl-N'-nitro-N- nitrosoguanidine (MNNG) at 100 mg/L in the drinking water for the first 8 weeks of the study, followed by administration of 0.5% formalin (dose not specified) in the drinking water during weeks 8 through 40. Other groups of animals received just MNNG or formalin (dose not specified). The animals were sacrificed at the termination of dosing and the stomachs were examined grossly and microscopically. The actual doses of formaldehyde received by the test animals is not known, because dose concentrations were not reported, and drinking water consumption was not measured. Formalin did not produce malignant tumors when given alone. In animals receiving just formalin, forestomach papillomas occurred in 8/10 animals. In rats given MNNG alone, adenocarcinoma of the pylorus occurred in 1/30 rats, preneoplastic hyperplasia of the pylorus occurred in 7/30 rats, and adenocarcinoma of the duodenum occurred in 3/30 rats. In the group administered both MNG and formalin, forestomach papillomas occurred in 15/17 animals, adenocarcinoma of the pylorus in 4/17, preneoplastic hyperplasia of the pylorus in 7/17, and adenocarcinoma of the duodenum in 1/17.

__I.A.5. Confidence in the Oral RfD

Study — High
Database — Medium
RfD — Medium

Confidence in the critical study is high since it consisted of adequate numbers of animals of both sexes, as well as a thorough examination of toxicological and histological parameters. Confidence in the database is medium as several additional chronic bioassays and reproductive and developmental stuides support the critical effect and study. Medium confidence in the RfD follows.

__I.A.6. EPA Documentation and Review of the Oral RfD

Source Document — U.S. EPA, 1989

Other EPA Documentation — None

Agency Work Group Review — 11/17/1989, 05/17/1990, 06/20/1990

Verification Date — 06/20/1990

__I.A.7. EPA Contacts (Oral RfD)

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).

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

Substance Name — Formaldehyde
CASRN — 50-00-0

Not available at this time.

_II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name — Formaldehyde
CASRN — 50-00-0
Last Revised — 05/01/1991

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

_II.A. Evidence for Human Carcinogenicity

__II.A.1. Weight-of-Evidence Characterization

Classification — B1; probable human carcinogen, based on limited evidence in humans, and sufficient evidence in animals. Human data include nine studies that show statistically significant associations between site-specific respiratory neoplasms and exposure to formaldehyde or formaldehyde-containing products. An increased incidence of nasal squamous cell carcinomas was observed in long-term inhalation studies in rats and in mice. The classification is supported by in vitro genotoxicity data and formaldehyde's structural relationships to other carcinogenic aldehydes such as acetaldehyde.

__II.A.2. Human Carcinogenicity Data

Limited. At least 28 relevant epidemiologic studies have been conducted. Among these, two cohort studies (Blair et al., 1986, 1987; Stayner et al., 1988) and one case-control study (Vaughan et al., 1986a,b) were well-conducted and specifically designed to detect small to moderate increases in formaldehyde-associated human risks. Blair et al. studied workers at 10 plants who were in some way exposed to formaldehyde (largely through resin formation) and observed significant excesses in lung and nasopharyngeal cancer deaths. Despite a lack of significant trends with increasing concentration or cumulative formaldehyde exposure, lung cancer mortality was significantly elevated in analyses with or without a 20-year latency allowance. No explicit control was made for smoking status. Stayner et al. reported statistically significant excesses in mortality from buccal cavity tumors among formaldehyde-exposed garment workers. The highest SMR was for workers with long employment duration (exposure) and follow-up period (latency). The Vaughan et al. nasal and pharyngeal cancer case-control study examined occupational and residential exposures, controlling for smoking and alcohol consumption. It showed a significant association between nasopharyngeal cancer and having lived 10 or more years in a mobile home, especially for mobile homes built in the 1950s to 1970s, a period of increasing formaldehyde- resin usage. No exposure measurements were available.

The 25 other reviewed studies had limited ability to detect small to moderate increases in formaldehyde risks owing to small sample sizes, small numbers of observed site-specific deaths, and insufficient follow-up. Even with these potential limitations, 6 of the 25 studies (Acheson et al., 1984; Hardell et al., 1982; Hayes et al., 1986; Liebling et al., 1984; Olsen et al., 1984; Stayner et al., 1985) reported significant associations between excess site-specific respiratory (lung, buccal cavity, and pharyngeal) cancers and exposure to formaldehyde. Some of these studies looked at potential confounders (such as wood-dust exposure) in greater detail; they did not discern sinonasal cancer incidence excesses of the size predicted. Others (Liebling et al., 1984; Stayner et al., 1985) overlapped the Acheson et al. (1984), Hardell et al. (1982) and Hayes et al. (1986) studies; the improved design and nonoverlapping portions of the later studies (Blair et al., 1986; Stayner et al., 1988) reinforce the conclusions of the earlier studies. Analysis of the remaining 19 studies indicate that leukemia and neoplasms of the brain and colon may be associated with formaldehyde exposure. The biological support for such postulates, however, has not yet been demonstrated. Although the common exposure in all of these studies was formaldehyde, the epidemiologic evidence is categorized as "limited" primarily because of the possible exposures to other agents. Such exposures could have contributed to the findings of excess cancers.

__II.A.3. Animal Carcinogenicity Data

Sufficient. Consequences of inhalation exposure to formaldehyde have been studied in rats, mice, hamsters and monkeys. The principal evidence comes from positive studies in both sexes of two strains of rats (Kerns et al., 1983; Albert et al., 1982; Tobe et al., 1985) and males of one strain of mice (Kerns et al., 1983), all showing squamous cell carcinomas.

For the CIIT, Kerns et al. (1983) exposed about 120 animals/sex/species (Fischer 344 rats and B6C3F1 mice) to 0, 2, 5.6 or 14.3 ppm, 6 hours/day, 5 days/week for 24 months. Five animals per group were sacrificed at 6 and 12 months and 20 per group were killed at 18 months. At 24 and 27 months the number sacrificed is unclear. The studies were terminated at 30 months. From the 12th month on, male and female rats in the highest dose group (14.3 ppm) showed significantly increased mortality compared with controls. In the 5.6- ppm group, male rats showed a significant increase in mortality from 17 months on. Female mice showed generally comparable survival across dose groups, as did male mice, but the male mice as a whole showed increased mortality because of housing problems. Squamous cell carcinomas were seen in the nasal cavities of 51/117 male rats and 52/115 female rats at 14.3 ppm (HDT) by experiment's end (as many as 35 carcinomas had been identified in males by month 18 based on EPA analysis notes and Kerns

(Chart 8). At 5.6 ppm, 1/119 male rats and 1/116 female rats showed squamous cell carcinomas of the nasal cavity. No such tumors were seen at 0 or 2 ppm. Polypoid adenomas of the nasal mucosa were seen in rats at all doses (0 ppm: 1/118 M, 0/114 F; 2 ppm: 4/118 M, 4/118 F; 5.6 ppm: 6/119 M, 0/116 F; 14.3 ppm: 4/117 M, 1/115 F) in a significant dose-related trend, albeit one that falls off after a peak. Among the mice, squamous cell carcinomas were seen in two males at 14.3 ppm. No other lesions were noteworthy.

Sellakumar et al. (1985) exposed male Sprague-Dawley rats, 100/group, 6 hours/day, 5 days/week for lifetime to 10 ppm HCl and to 14 ppm formaldehyde. This was a combined exposure HCl and formaldehyde were administered simultaneously, and each was administered separately. An equal number of rats received an air control. HCl was administered to determine if tumor response was enhanced by an additional irritant effect or by the combining of formaldehyde and HCl to form bis-(chloromethyl)ether (BCME). Groups receiving formaldehyde alone or with HCl showed an increase in nasal squamous cell carcinomas; those without formaldehyde were free of carcinomas and other tumors (0/99 in each group), although rhinitis and hyperplasia were of comparable incidence.

Tobe et al. (1985) conducted a 28-month study of male Fischer 344 rats (about 2 weeks younger than those in Kerns et al., 1983). Groups of 32 rats were exposed 6 hours/day, 5 days/week to 0, 0.3, 2.0, 3,3, or 15 ppm formaldehyde in aqueous solution methanol; another group of 32 was exposed to methanol only (vehicle control). Animals were sacrificed at 12, 18, and 24 months. Exposure to 15 ppm ended at 24 months; at that point, mortality was 88%. At 28 months mortality was 60% in the control group and 32% in the 0.3 dose group. Squamous cell carcinomas were seen at 15 ppm in 14/27 rats surviving past 12 months, compared with 0/27 in the controls. No polypoid adenomas were observed; the increased incidences of rhinitis and hyperplasia were dose-related.

While these three rodent studies are principal in the weight-of-evidence, inhalation studies have been carried out in other strains and species. Dalbey (1982), as part of a promotion experiment, exposed male Syrian golden hamsters to 10 ppm formaldehyde 5 times/week, 5 hours/day throughout their lifetimes, 132 animals were untreated controls. Although survival time was significantly reduced in the treated group, no tumors were observed in either treated or control groups. Rusch et al. (1983) carried out a 6-month toxicity study in 6 male cynomolgus monkeys, 40 F344 rats (20M, 20F), and 20 Syrian golden hamsters (10M, 10F) with 22 hours/day, 7 days/week exposure to three levels of formaldehyde with corresponding controls. The highest dose tested was 2.95 ppm. The short duration of the assay, the small sample sizes, and, possibly, the low concentrations tested, limited the sensitivity of the assay to detect tumors. In the highest dose group in both rats and monkeys, incidences of squamous metaplasia/hyperplasia of the nasal turbinates were significantly elevated.

__II.A.4. Supporting Data for Carcinogenicity

Mutagenic activity of formaldehyde has been demonstrated in viruses, Escherichia coli, Pseudomonas fluorescens, Salmonella typhimurium and certain strains of yeast, fungi, Drosophila, grasshopper and mammalian cells (Ulsamer et al., 1984). Formaldehyde has been shown to cause gene mutations, single strand breaks in DNA, DNA-protein crosslinks, sister chromatid exchanges and chromosomal aberrations. Formaldehyde produces in vitro transformation in BALB/c 3T3 mouse cells, BHK21 hamster cells and C3H-10TI/2 mouse cells, enhances the transformation of Syrian hamster embryo cells by SA7 adenovirus, and inhibits DNA repair (Consensus Workshop on Formaldehyde, 1984).

When inhaled, acetaldehyde, the closest aldehyde to formaldehyde in structure, causes cancers in the nose and trachea of hamsters, and nasal cancers in rats.

_II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

None.

_II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

Inhalation Unit Risk — 1.3E-5 per (ug/cu.m)

Extrapolation Method — Linearized multistage procedure, additional risk

Air Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	8E+0 ug/cu.m
E-5 (1 in 100,000)	8E-1 ug/cu.m
E-6 (1 in 1,000,000)	8E-2 ug/cu.m

__II.C.2. Dose-Response Data for Carcinogenicity, Inhalation Exposure

Tumor Type — squamous cell carcinoma
Test Animals — Rat/F344, males
Route — inhalation
Reference — Kerns et al., 1983

---------- Dose ----------		
Administered (ppm)	Human Equivalent (mg/kg)/day	Tumor Incidence
0	0	0/156
2	2	0/159
5.6	5.6	2/153
14.3	14.3	94/140

__II.C.3. Additional Comments (Carcinogenicity, Inhalation Exposure)

In the Kerns et al. (1983) study, rats that died at 11 months (prior to appearance of the first squamous cell carcinoma) were not considered at risk. Those sacrificed at 12 and 18 months were treated as though they would have responded in the same proportion as rats remaining alive at the respective sacrifice times and those living beyond 24 months were included with animals sacrificed at 24 months. From the estimates of the probability of death with tumor within 24 months and its variance, the number of animals at risk and the number with tumors were derived for a 24-month study with no 12- or 18-month kills. These rounded numbers are shown above and were used for significance tests and modeling.

The unit risk should not be used if the air concentration exceeds 8E+2 ug/cu.m, since above this concentration the unit risk may not be appropriate.

__II.C.4. Discussion of Confidence (Carcinogenicity, Inhalation Exposure)

The experimental range is close to expected human exposures. Estimated lifetime excess risks from six epidemiologic studies are close to upper bound risks based on animal data (usually within 1 order of magnitude for four types of estimated occupational and residential exposure). Animal-based estimates derived using time in the model were similar but would have required the use of more assumptions in the calculations. Three non-zero doses were used in addition to controls in the study on which calculations are based, with a large number of animals per group. Male and female incidences were close throughout the exposure groups.

_II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

__II.D.1. EPA Documentation

Source Document — U.S. EPA, 1987

The OTS Assessment of Health Risk has received wide internal and external review.

__II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Work Group Review — 02/03/1988

Verification Date — 02/03/1988

__II.D.3. EPA Contacts (Carcinogenicity Assessment)

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).

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

_VI. Bibliography

Substance Name — Formaldehyde
CASRN — 50-00-0
Last Revised — 08/01/1991

_VI.A. Oral RfD References

Hurni, H. and H. Ohder. 1973. Reproduction study with formaldehyde and hexamethylenetetramine in beagle dogs. Food Cosmet. Toxicol. 11: 459-462.

Johannsen, F.R., G.J. Levinskas and A.S. Tegeris. 1986. Effects of formaldehyde in the rat and dog following oral exposure. Toxicol. Lett. 30: 1-6.

Marks, T.A., W.C. Worthy and R.E. Staples. 1980. Influence of formaldehyde and sonacide (potentiated acid glutaraldehyde) on embryo and fetal development in mice. Teratology. 22: 51-58.

Seidenberg, J.M., D.G. Anderson and R.A. Becker. 1986. Validation of an in vivo developmental toxicity screen in the mouse. Teratol. Carcinogen. Mutagen. 6: 361-374.

Takahashi, M., R. Hasegawa, F. Furukawa, K. Toyoda, H. Sato and Y. Hayashi. 1986. Effects of ethanol, potassium metabisulfite, formaldehyde and hydrogen peroxide on gastric carcinogenesis in rats after initiation with N-methyl- N'nitro-N'nitrosoguanidine. Jap. J. Cancer Res. 77: 118-124.

Til, H.P., R.A. Woutersen, V.J. Feron, V.H.M. Hollanders, H.E. Falke and J.J. Clary. 1989. Two-year drinking water study of formaldehyde in rats. Food Chem. Toxicol. 27(2): 77-87.

U.S. EPA. 1989. Draft Drinking Water Health Advisory for Formaldehyde. Office of Drinking Water, Washington, DC.

_VI.B. Inhalation RfC References

None

_VI.C. Carcinogenicity Assessment References

Acheson, E.D., M.J. Gardner, B. Pannett, H.R. Barnes, C. Osmond and C.P. Taylor. 1984. Formaldehyde in the British Chemical Industry. The Lancet. p. 611-615.

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

Blair, A., P.A. Stewart, R.N. Hoover, et al. 1986. Mortality among industrial workers exposed to formaldehyde. J. Natl. Cancer Inst. 76(6): 1071-1084.

Blair, A., P. Stewart, P.A. Hoover, et al. 1987. Cancers of the nasopharynx and oropharynx and formaldehyde exposure. J. Natl. Cancer Inst. 78(1): 191-193.

Consensus Workshop on Formaldehyde. 1984. Deliberations of the Consensus Workshop on Formaldehyde, October 3-6, 1983. Little Rock, AK. (Final report)

Dalbey, W.E. 1982. Formaldehyde and tumors in hamster respiratory tract. Toxicology. 24: 9-14.

Hardell, L., B. Johansson and O. Axelson. 1982. Epidemiological study of nasal and nasopharyngeal cancer and their relation to phenoxy acid or chlorophenol exposure. Am. J. Ind. Med. 3: 247-257.

Hayes, R.B., J.W. Raatgever, A. de Bruyn and M. Gerin. 1986. Cancer of the nasal cavity and paranasal sinuses, and formaldehyde exposure. Int. J. Cancer. 37: 487-492.

Kerns, W.D., K.L. Pavkov, D.J. Donofrio, E.J. Gralla and J.A. Swenberg. 1983. Carcinogenicity of formaldehyde in rats and mice after long-term inhalation exposure. Cancer Res. 43: 4382-4392.

Liebling, T., K.D. Rosenman, H. Pastides, R.G. Griffith and S. Lemeshow. 1984. Cancer mortality among workers exposed to formaldehyde. Am. J. Ind. Med. 5: 423-428.

Olsen, J.H., S.P. Jensen, M. Hink, K. Faurbo, N.O. Breum and O.M. Jensen. 1984. Occupational formaldehyde exposure and increased nasal cancer risk in man. Int. J. Cancer. 34: 639-644.

Rusch, G.M., J.J. Clary, W.E. Rinehart and H.F. Bolte. 1983. A 26-week inhalation toxicity study with formaldehyde in the monkey, rat and hamster. Toxicol. Appl. Pharmacol. 68: 329-343.

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

Stayner, L.S., A.B. Smith, G. Reeve, et al. 1985. Proportionate mortality study of workers in the garment industry exposed to formaldehyde. Am. J. Ind. Med. 7: 229-240.

Stayner, L.T., L. Elliott, L. Blade, R. Keenlyside and W. Halperin. 1988. A retrospective cohort mortality study of workers exposed to formaldehyde in the garment industry. Am. J. Ind. Med. 13(6): 667-682.

Tobe, M., T. Kaneko, Y. Uchida, et al. 1985. Studies of the inhalation toxicity of formaldehyde. National Sanitary and Medical Laboratory Service (Japan). p. 1-94.

Ulsamer, A.G., K.C. Gupta, M.S. Cohn and P.W. Preuss. 1982. Formaldehyde in indoor air: Toxicity and risk. In: Proceed. 75th Ann. Meet. Air Pollut. Control Assoc. 16 p.

U.S. EPA. 1987. Assessment of Health Risk to Garment Workers and Certain Home Residents from Exposure to Formaldehyde. Office of Toxic Substances, Washington, DC.

Vaughn, T.L., C. Strader, S. Davis and J.R. Daling. 1986a. Formaldehyde and cancers of the pharynx, sinus and nasal cavity: I. Occupational exposures. Int. J. Cancer. 38: 677-683.

Vaughn, T.L., C. Strader, S. Davis and J.R. Daling. 1986b. Formaldehyde and cancers of the pharynx, sinus and nasal cavity: II. Residential exposures. Int. J. Cancer. 38: 685-688.

_VII. Revision History

Substance Name — Formaldehyde
CASRN — 50-00-0

Date	Section	Description
10/01/1989	II.	Carcinogen summary on-line
10/01/1989	VI.	Bibliography on-line
12/01/1989	I.A.	Oral RfD now under review
02/01/1990	VI.	Supplementary data on-line
09/01/1990	I.A.	Oral RfD summary on-line
09/01/1990	II.	Text edited
09/01/1990	VI.A.	Oral RfD references added
01/01/1991	II.	Text edited
01/01/1991	II.C.1.	Inhalation slope factor removed (global change)
05/01/1991	II.C.1.	Corrected units in risk level concentrations
08/01/1991	VI.A.&C.	Citations clarified
01/01/1992	IV.	Regulatory Action section on-line

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.
01/02/1998	I., II.	This chemical is being reassessed under the IRIS Program.

_VIII. Synonyms

Substance Name — Formaldehyde
CASRN — 50-00-0
Last Revised — 10/01/1989

- 50-00-0
- ALDEHYDE FORMIQUE (FRENCH)
- ALDEHYD MRAVENCI (CZECH)
- ALDEIDE FORMICA (ITALIAN)
- BFV
- FA
- FORMALDEHYD (CZECH, POLISH)
- FORMALDEHYDE
- FORMALDEHYDE SOLUTION (DOT)
- FORMALIN
- FORMALITH
- FORMIC ALDEHYDE
- FORMOL
- FYDE
- HOCH
- IVALON
- KARSAN
- LYSOFORM
- METHANAL
- METHYL ALDEHYDE
- METHYLENE GLYCOL
- METHYLENE OXIDE
- MORBICID
- NCI-C02799
- OPLOSSINGEN (DUTCH)
- OXOMETHANE
- OXYMETHYLENE
- PARAFORM
- POLYOXYMETHYLENE GLYCOLS
- RCRA WASTE NUMBER U122
- SUPERLYSOFORM
- UN 1198 (DOT)
- UN 2209 (DOT)

IRIS Home

Chronic Health Hazards for Non-Carcinogenic Effects

Reference Dose for Chronic Oral Exposure (RfD)

- Oral RfD Summary
- Principal and