J-2984

Copy No. 10

Advisory Center on Toxicology

1972 Toxicological Reports

Prepared Under
Contracts ONR N00014-67-A-0244-0015
and EPA 68-01-0132

NATIONAL ACADEMY OF SCIENCES—NATIONAL RESEARCH COUNCIL

1972 TOXICOLOGICAL REPORTS

1972

TOXICOLOGICAL REPORTS

Prepared under Contracts

ONR N00014-67-A-0244-0015
and
EPA 68-01-0132

ADVISORY CENTER ON TOXICOLOGY

Ralph C. Wands
Ralph C. Wands, Director

NATIONAL ACADEMY OF SCIENCES-NATIONAL RESEARCH COUNCIL
Washington, D. C.

DBZ0018151

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Inquiries on Proprietary Products*

* Reports on these materials are not included in this volume because data involve commercially discreet information.

NATIONAL RESEARCH COUNCIL

NATIONAL ACADEMY OF SCIENCES NATIONAL ACADEMY OF ENGINEERING

2101 CONSTITUTION AVENUE WASHINGTON, D.C. 20418

ADVISORY CENTER ON TOXICOLOGY
DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

4 January 1972

Dr. Walton L. Jones
Deputy NASA Director for
Life Sciences (MM)
National Aeronautics and
Space Administration
Washington, D. C. 20546

Dear Dr. Jones:

As you know, we have two panels considering spacecraft contaminant levels; one for water and one for the atmosphere. Some time ago, Mr. Pecoraro requested that we emphasize wash water standards so that contractors could proceed with the development of equipment used in the wash water cycle. Enclosed you will find the Panel's recommended specifications and rationale for the physical, chemical and microbiological standards of wash water, exclusive of dish water. Also enclosed for your information is a listing of the Panel on Water Quality.

Sincerely yours,

Ralph C. Wands
Director
Advisory Center on Toxicology

Enclosures
1. Recommended Tentative Standards for Wash Water in Manned Spacecraft
2. Water Quality Panel Members

RCW/FGF/lc

Tentative Standards for Wash Water Specifications

Physical Parameters

Color, cobalt units	$\leq$ 15
Conductivity, specific, µmhos-cm^{-1} at 25° C	$\leq$ 2,000
Foaming	Nonpersistent more than 15s
Odor	Nonobjectionable

Chemical Constituents

Carbon, total organic, mg/l	$\leq$ 200
Detergents	Not specified
Lactic acid, mg/l	$\leq$ 50
Nitrogen, ammonia, mg/l	$\leq$ 5.0
Oxygen demand, chemical, mg/l	Not specified
pH	5.0, minimum 7.5, maximum
Sodium chloride, mg/l	$\leq$ 1,000
Solids, dissolved, residue-on-evaporation at 180° C, mg/l	$\leq$ 1,500
Urea, mg/l	$\leq$ 50

Microbiological

Micro-organisms, Number per ml on a standard 48-h plate	$\leq$ 10

Tentative Standards for Wash Water

Discussion

Physical Parameters

Color, cobalt units ________________________________ $\leqq$ 15

This specification meets the requirement for potable water and is considered equally satisfactory for wash water.

Conductivity, specific, μmhos-cm^{-1} at 25° C ___________ $\leqq$ 2,000

This specification is consistent with the limits specified for dissolved ionic material.

Foaming ____________________________________ Nonpersistent more than 15s

This specification approximates the requirement for potable water and is considered satisfactory for wash water.

Odor _____________________________________ Nonobjectionable

This specification meets the requirement for potable water and is considered equally satisfactory for wash water.

Chemical Constituents

Carbon, total organic, mg/l ________________________ $\leqq$ 200

The value for total organic carbon may be an indicator of potentially harmful substances, including nutrients for bacteria, and toxic and irritating organic substances. Until it can be shown that the individual organic components contributing to the total organic carbon value are completely innocuous, it is considered mandatory to limit the concentration of total organic carbon to the specified value.

Detergents, mg/l ______________________________ Not specified

A specification for this constituent cannot be made in the absence of information on the specific detergent formulation and the composition of the degradation products of the detergent materials.

Lactic acid, mg/l ________________________________ $\leqq$ 50

In view of the lack of direct experimental evidence, it is the considered opinion of the panel that this specification provides a safe and reasonable limit.

Nitrogen, ammonia, mg/l ______________________________ $\leq$ 5.0

This specification provides aesthetically acceptable wash water. Ammonia-nitrogen concentrations exceeding the specified value usually cause objectionable odors.

Oxygen demand, chemical, mg/l ___________________ Not specified

This specification is unsatisfactory for designating acceptability of wash water when a limiting concentration of total organic carbon is specified. The latter specification is preferred.

pH ____ 5.0, minimum
7.5, maximum

This specification avoids both excessively acid and excessively alkaline conditions which may prove irritating for extended use.

Sodium chloride, mg/l _________________________________ $\leq$ 1,000

Excessively high concentrations of dissolved salts, including sodium chloride, leave a potentially irritating residue on the skin surface. This specification precludes possible excessive accumulation of salt residue. It is based on a relaxation of a similar specification for potable water and is believed acceptable for wash water.

Solids, dissolved, residue-on-evaporation at 180° C, mg/l ____ $\leq$ 1,500

Excessively high concentrations of dissolved solids in wash water result in the accumulation on the skin surface of a residue of chemical salts and possibly other toxic or irritating substances. This specification, together with other specifications for specific substances, precludes the accumulation of an excessive amount of residue. This specification is based on a relaxation of a similar specification for potable water and is believed acceptable for wash water.

Urea, mg/l ____ $\leq$ 50

In view of the lack of direct experimental evidence, it is the considered opinion of the panel that this specification provides a safe and reasonable limit.

Microbiological

Micro-organisms, Number per ml on a standard 48-h plate ___ $\leq$ 10

An increase in bacterial count directly increases the risk of hazardous infection. This specification adequately minimizes this risk from the use of wash water.

Dr. Riley D. Housewright, Chairman
Microbiological Associates, Inc.
4733 Bethesda Avenue
Bethesda, Maryland 20014

Dr. Marvin W. Skougstad
U. S. Geological Survey
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NATIONAL RESEARCH COUNCIL
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2101 CONSTITUTION AVENUE WASHINGTON, D.C. 20418

ADVISORY CENTER ON TOXICOLOGY
DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

5 January 1972

Ref:BUMED-732-SHB:alj

Chief, Bureau of Medicine and Surgery
Department of the Navy
Washington, D. C. 20390

Dear Sir:

This is in response to your inquiry of 5 August 1971 concerning the toxicity of three hydrazines: 1) Hydrazine, 2) Monomethylhydrazine, and 3) Unsymmetrical dimethylhydrazine. Specific comments on each chemical are furnished in the attachments to this letter.

In general, the hydrazines are highly reactive chemicals which may ignite spontaneously or explosively decompose in the presence of oxidizers or at elevated temperatures. They are all toxic to man by all routes of entry: inhalation, ingestion, skin contact, and skin absorption. Monomethylhydrazine is slightly more toxic, with hydrazine and unsymmetrical dimethylhydrazine being approximately equal in toxicity. Uniformity in toxicity is lacking among these compounds - variations occur by species susceptibility and by route of entry.

Although considerable study of the hydrazines has been accomplished, most of it is applicable to either the TLV recommended by the ACGIH or to an EEL recommended by the NAS/NRC for a special application. In neither instance do the recommended levels apply directly to the confined atmosphere of a submarine. Furthermore, there are no data on any of the three hydrazines to indicate or allow extrapolation to a no-effect 24-hour or 90-day exposure level. However, the Committee has evaluated the available experimental data, and for each of the three hydrazines they have indicated 24-hour and 90-day levels which incorporate a large safety margin that should pose no hazard to health. However, these are not recommended levels, rather, they are "best estimates," derived from available data, that can be used for planning purposes.

The Committee strongly recommends that if the Navy sees a need for setting 24-hour and 90-day hydrazine limits, that support be given to laboratory investigation designed to reveal the no-effect level in several species of animals: rats, dogs, and monkeys. It is particularly important to determine the pathology of low dosage, chronic exposures because of the suggestion of liver, kidney, and enzyme systems damage in earlier studies.

Sincerely yours,

Ralph C. Wands
Director
Advisory Center on Toxicology

RCW/FGF/lc

Enclosures (3)

Hydrazine
($NH_2 NH_2$)

Properties

Hydrazine is a colorless liquid with a specific gravity of 1.011 at 15° C, a melting point of 1.4° C, and a boiling point of 113.5° C. Its vapor pressure is 16.1 mm Hg at 27° C. Its vapors are readily flammable and it may ignite spontaneously or explosively decompose in the presence of oxidizers or at elevated temperatures; The odor detection threshold is 3-4 ppm.

Toxicology

Experimental evidence suggests that hydrazine adversely affects protein and carbohydrate metabolism and interferes with utilization of vitamin B_6. It is an irritant gas that can cause a coughing, wheezing, and a burning sensation in the respiratory tract and, at higher acute dosage, will cause convulsions and death. Chronic poisoning may lead to fatty necrosis of the liver, impairment of kidney functions and blood changes. Hydrazine is readily absorbed through the skin and will cause an alkali-like burn of tissues.

Acute Toxicity

Rats exposed for two to six hours to hydrazine vapors showed 50 to 70% mortality during 14 and 7 day observation periods. The rat LC_{50} for a four-hour exposure is 570 ppm. The mouse oral LD_{50} is 50 mg/kg and the rat oral LD_{50} is 60 mg/kg.

Sub-Acute Toxicity

Inhalation studies in rats at 228 ppm, 58 ppm, and 20 ppm of hydrazine vapors for six hrs/day, five days/wk, over periods as long as six weeks resulted in LT_{50} values of 27, 50, and 144 hours, respectively, indicating a cumulative action.

Chronic Toxicity

Inhalation studies in rats and dogs indicate that 6 mg/m^3 may be the upper limit of tolerance for hydrazine vapors. In one experiment monkeys, rats, and mice were exposed continuously for 90 days to an average concentration of 0.78 ppm of hydrazine vapors, and deaths occurred in all animal groups: 20% of the monkeys, 98% of the rats and 99% of the mice died as a result of the exposures. The rat deaths occurred in the last half of the experiment, again suggesting cumulative action.

Existing Atmospheric Limitations

The ACGIH recommended limit for an eight-hour work day is 1.0 ppm. The NAS/NRC Committee on Toxicology has recommended the following Emergency Exposure Limits (EEL's) for military and space personnel:

10 min	30 ppm
30 min	20 ppm
60 min	10 ppm

Evaluation of Data

Experimental data indicate that hydrazine vapors are hazardous to health, even at low concentrations, when the exposure period extends over a period of several hours. The TLV of 1.0 ppm does not envision the confinement of a submarine where an exposed individual cannot be removed from a contaminated atmosphere. The EEL's are based on the best available data which, however, have not been developed at the most desirable concentrations and time periods. It is possible that experiments at appropriate concentrations of hydrazine vapors for periods of 10, 30, and 60 minutes might provide evidence for an upward revision of the current EEL's.

Recommendations for Submarine Atmospheres

- That the current EEL's for 10, 30, and 60 minutes be adopted.

Planning Guides

- That a 24-hour atmospheric level of 0.25 ppm be used for planning purposes, subject to change from experimental evidence.

- That a 90-day atmospheric level of 0.05 ppm be used for planning purposes, subject to change from experimental evidence.

Monomethylhydrazine
(NH_2NHCH_3)

Properties

Monomethylhydrazine (MMH) is colorless, hygroscopic liquid with a molecular weight of 46.07 and a boiling point of 87° C. Its vapor pressure is 52 mm Hg at 27° C. The ammonia-like odor is detectable at about 1 to 3 ppm.

Toxicology

According to the ACGIH, MMH is the strongest convulsant and the most toxic of the methyl derivatives of hydrazine. In rats it has been shown that MMH inhibits both liver and brain monoamine oxidase. Oxidation of MMH takes place relatively rapidly within the body, reaching a maximum rate within two hours, and is essentially complete by four hours after i.p. injection.

The vapors are irritating to the mucosa and MMH can be absorbed through the skin, producing local burning and contributing to systemic effects.

Chronic exposures can lead to severe hematologic changes, convulsions, and death. Although there is wide species variation in susceptibility to MMH (dogs are much more sensitive than monkeys) lethal exposures consistently produce pulmonary congestion with hemorrhage, hepatic congestion, edema of renal tubular epithelium and subarachnoidal hemorrhage in the brain.

Acute Toxicity

Acute studies in six human subjects revealed MMH to be moderately irritating on exposure to vapor concentrations of 90 ppm for 10 minutes, and the odor less penetrating than was ammonia at 50 ppm/10 minutes. Heinz bodies were detected in the blood of subjects but there were no signs of anemia. Neither was there severe lacrimation nor any suggestion of a bronchospasm.

Acute, non-lethal i.v. dosage of dogs with MMH gives rise to a transient hemolytic anemia from which there is complete recovery in 30 days, whereas monkeys show a lower order of hematologic response. Acute toxicity of MMH by i.v. and oral routes is shown below.

Species	Route of Administration	LD_{50} mg/kg
dog	i. v.	12
mouse	i. v.	33
	i. p.	32
	oral	33
rat	i. v.	33
	i. p.	32
	oral	33

Sub-Acute Toxicity

Sub-acute studies have been limited to daily i. p. administration to monkeys of 2.5 to 5.0 mg/kg of MMH for six weeks. Although no performance decrement was observed at either dosage, clinical signs of toxicity were recorded at both dosages and the number of signs were increased at the higher dosage.

The oral i. v. and i. p. LD_{50} is approximately the same for a given species, with the rat and mouse levels at approximately 32.5 mg/kg. The dog appears more susceptible, having an i. p. LD_{50} of 12 mg/kg.

Liquid MMH in direct contact with the skin will result in local burning and, like the other hydrazines, is readily absorbed through the skin. The percutaneous LD_{50} for rabbits is 110 mm^3/kg and is 56 mm^3 for guinea pigs.

Chronic Toxicity

Chronic studies have been done on dogs, rats, mice, and monkeys. Animals were exposed to vapor concentrations of 2 and 5 ppm for six hr/day, five days/wk for six months. At the lower concentration there was no effect on rats and monkeys, conjunctivitis was observed in the dogs, but in the mice, ruffed coat, lethargy, and deaths were observed. At 5 ppm hematologic changes were seen in all groups and there were more deaths of mice over the 2 ppm dosage.

Existing Atmospheric Limits

The ACGIH recommended ceiling limit for an eight-hour work day is 0.2 ppm. The NAS/NRC Committee on Toxicology has recommended the following Emergency Exposure Limits (EEL's) for military and space personnel:

10 min	90 ppm
30 min	30 ppm
60 min	15 ppm

Evaluation of Data

A wider range of experimental studies has been done on MMH than on other hydrazines. Sufficient data are available to conclude that man can tolerate as much as 900 ppm/minute without significant injury or residual effect. However, chronic exposures, even at low levels are hazardous to health. The MMH TLV of 0.2 ppm, like hydrazine, does not envision the confinement of a submarine atmosphere. The current EEL's take into consideration the most recent experimental data and appear realistic.

Recommendations for Submarine Atmosphere

- That the current EEL's for 10, 30, and 60 minutes be adopted.

Interim Guide

- That a 24-hour atmospheric limit of 0.2 ppm be used as a guide, subject to change from experimental evidence.

- That a 90-day limit of 0.1 ppm be used as a guide, subject to change from experimental evidence.

Unsymmetrical Dimethylhydrazine
($NH_2N(CH_3)_2$)

Properties

Unsymmetrical dimethylhydrazine (UDMH) has a molecular weight of 60 and a vapor pressure of 156.8 mm Hg at 25° C, approximately 10 times the vapor pressure of hydrazine. The ammoniacal odor of UDMH is detectable at a level of 6 to 14 ppm in about one minute.

Toxicology

Although there are conflicting opinions on some aspects of the toxicity of UDMH in comparison with other hydrazines, it is generally accepted that it is of lower order of toxicity than monomethylhydrazine (MMH) and about equal to hydrazine. The liquid, on contact with the skin, does cause a burn and may be absorbed through the skin like other hydrazines, but its relatively higher vapor pressure results in rapid vaporization so that its main route of entry probably would be inhalation.

The primary effect from UDMH is CNS stimulation proceeding to convulsions at high dosage or prolonged exposure to lower dosage. Chronic exposures lead to hemolytic anemia, possibly fatty necrosis of the liver, and interstitial nephritis. The metabolic fate of UDMH is unknown.

Acute Toxicity

The vapor of UDMH is irritating to the mucosa and causes coughing spasm. Workers who were accidentally exposed to an unknown concentration suffered nose and throat irritations, conjunctivitis and nausea.

Dogs exposed to 50, 200, and 600 ppm of UDMH for single and multiple 60, 15, and 5-minute periods showed no adverse physiological effects.

In one experiment three out of three dogs died on exposure to 111 ppm of UDMH for three hours, one out of three died on exposure at 52 ppm for four hours and one out of three convulsed but recovered from a 24 ppm exposure for four hours.

Chronic Toxicity

Two sets of three dogs each were exposed to UDMH concentrations of 25 ppm or 5 ppm for six hrs/day, five days/wk for 26 weeks. One out of three died at the 25 ppm dosage and hematologic changes were observed in all three. At the 5 ppm dosage no deaths occurred and no pathology was observed on examination, but mild anemia did occur.

Rats and mice proved more susceptible than monkeys to 0.56 ppm of UDMH for 90 days. Chemical laboratory data for all three species was near normal but both rodent species showed a decrement in swim-time performance.

Existing Atmospheric Limits

The ACGIH recommended limit for an eight-hour work day is 0.5 ppm. The NAS/NRC Committee on Toxicology has recommended the following Emergency Exposure Limits (EEL's) for military and space personnel:

10 min	100 ppm
30 min	50 ppm
60 min	30 ppm

Evaluation of Data

Experimental data are adequate to support both the TLV and EEL recommended limits, neither of which envisions the confinement of a submarine atmosphere from which an exposed person could not readily be removed. It does not seem likely that additional experimental studies could result in altering significantly the current recommendations.

Recommendations for Submarine Atmospheres

- That the current EEL's for 10, 30, and 60 minutes be adopted for submarines.

Planning Guides

- That a 24-hour atmospheric limit of 0.25 ppm be used for planning purposes, subject to change from experimental evidence.

- That a 90-day atmospheric limit of 0.1 ppm be used for planning purposes, subject to change from experimental evidence.

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ADVISORY CENTER ON TOXICOLOGY
DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

5 January 1972
Ref:BUMED-7321-DER:jb

Chief, Bureau of Medicine and Surgery
Department of the Navy
Washington, D. C. 20390

Dear Sir:

This is in response to your request for toxicological information on sodium peroxydisulfate (sodium persulfate) when used as a water sanitizer in a wet pot complex.

The enclosures to your request for information have been evaluated and verified with respect to the composition of the sanitizer. Although these enclosures appear to recommend a final sodium persulfate concentration of 50 ppm, the manufacturer's representative indicated that 100 ppm may be necessary to achieve desired germicidal action. At 100 ppm of sodium persulfate it is assumed that ionic copper will stabilize at 200 ppb and ionic silver will stabilize at 20 ppb. These two metallic levels are well below drinking water standards: 1.0 ppm Cu and 0.05 ppm Ag. As suggested in your letter, the germicidal activity of this sanitizer is dependent upon a natural or artificial source of ultraviolet light.

The acute oral LD_{50} of sodium persulfate has not been determined, but for the ammonium salt it is 820 mg/kg in rats. We believe the sodium salt oral LD_{50} would be roughly comparable. The rabbit i.v. MLD of the sodium salt is 178 mg/kg.

Toxicological data on the proposed sanitizer are lacking, but toxicological studies on a closely related formula have been accomplished. Using the data of the closely related formula, the rat oral LD_{50} is approximately 1 g/kg and a low grade rabbit dermal irritation is seen at 2 g/kg. Instillation of 100 mg into rabbit eyes resulted in a mild erythema that persisted for 7 days in several instances even where the eyes had been flushed 2-4 seconds after instillation, and in marked conjunctivitis in unwashed eyes that persisted throughout the test duration of 14 days.

It is reported that some individuals may be sensitive to persulfates, such that allergic response would result in a skin rash that would readily clear if further contact were avoided.

Decomposition of sodium persulfate will take place in the presence of most metals, organic matter, moisture, and temperatures above 100° C. No tendency toward explosive decomposition has been observed. However, this is an oxidizer which might form a combustible mixture with a suitable fuel or reducing agent. Combustible materials that have been wetted with sodium persulfate and then allowed to dry are fire hazards and may spontaneously ignite in the presence of reducers.

It appears to us that the proposed sanitizer is suitable for the intended use, but supervisory personnel should remain alert to the possibility of allergic responses.

Sincerely yours,

Ralph C. Wands
Director
Advisory Center on Toxicology

RCW/FGF/lc

NATIONAL RESEARCH COUNCIL
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ADVISORY CENTER ON TOXICOLOGY
DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

12 January 1972

BUMED-731-RAN:alj

Chief, Bureau of Medicine and Surgery
Department of the Navy
Washington, D. C. 20390

Dear Sir:

In response to your letter of 7 October 1971 for toxicological information concerning

a) Federal Mini-streamer Liquid CN Repeater No. 282,
b) Federal Liquid Tear Gas Repeater No. 280,
c) XM 32 CSX Manually Carried Disperser and Riot Control Agent FSN 1365-179-4247 DODAC 1365-K531,

we have the following information.

The contents of the first two items, a) and b), are qualitatively the same, i.e., a tear gas agent in a mixture of two solvents and pressurized with nitrogen. The rate of discharge and the total volume of these two items differ.

The tear gas agent is reported to have an LCt 50 of 3.7 gm.min/m^3 (rats) and 3.5 gm.min/m^3 (guinea pigs) while the "maximum safe inhaled dose for man" is reported to be 350 mg.min/m^3 based on animal data.

We have been informed by the manufacturer that two independent laboratories reported that the solution (tear gas in solvent) was not an eye irritant when tested in accordance with the regulations of the Federal Hazardous Substances Act (Section 191.1 [g] [3] or Section 191.12). However, a third laboratory has reported that a similar amount of the tear gas agent (without the solvents) "produced severe conjunctival congestion" when placed in rabbits' eyes. This condition persisted to a lessening degree and the eyes appeared normal after two weeks.

The solvents (without the tear gas agent) have been reported to cause mild irritation in the eyes of experimental animals.

The third riot control agent (c) contains 1% o-chlorobenzylidene malononitrile (CS) in trioctylphosphate (TOF). The LCt 50 of Cs is estimated to be 61 gm. min/m^3 while the ED 50 for riot control is estimated to be a Ct of 0.1 to 10 mg. min/m^3.

Concentrations of up to 1.0% of CS in TOF were tested in the eyes of human volunteers. Each of the volunteers (male) received one drop or a "brief spray" from a dispenser in one eye. They could not open their eyes for 20 to 85 seconds and only after 70 to 450 seconds were they able to read 20/20 letters. It was concluded that small quantities of up to 1.0% CS in TOF in contact with the eye are extremely irritating and cause transient conjunctivitis but no corneal damage in man.

Injection of 0.5 ml of 1% CS in TOF or TOF alone into the trachea of dogs reportedly caused no discernible clinical damage.

A 1 ml dose of 1% CS in TOF had no effect on the skin of monkeys although 0.025 ml of such a mixture was reported to produce immediate erythema which progressed to necrosis in 8 to 10 days on the skin of rabbits. When 0.025 ml of 1% CS in TOF was placed on the forearm of men, no reactions were reported.

In summary, under experimental conditions where the dose of the riot control agent did not exceed 1 ml of a 1% solution, the cutaneous, respiratory and ocular effects were reported to be reversible and ranged from mild to severe.

Because the conditions under which a tear gas riot control agent might be used are variable, it is difficult to assess the hazards involved with the use of such agents under actual "field" conditions. Exposure to these agents could conceivably range between a transient exposure to a dilute vapor or "overspray" of the material and a repeated injection of milliliter quantities of the agent into the face and eyes of an individual. Such an extreme exposure in conjunction with a potential physical trauma to the eyes (rubbing, wiping, etc.) might lead to sequelae more serious than those observed under experimental conditions.

Sincerely yours,

Ralph C. Wands, Director
Advisory Center on Toxicology

RCW/LMR/eb

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ADVISORY CENTER ON TOXICOLOGY
DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

12 January 1972

Memorandum

To: H. H. Fawcett

From: Ralph C. Wands

Listed below are toxicity ratings recommended by the Committee on Toxicology for the three "high priority" chemicals which you requested via a copy of the Coast Guard letter of November 30, 1971. Information is being sought so that ratings can be applied to the remaining 5 chemicals. We will forward ratings on these as soon as they are available.

As has been done in previous reports of this type the Committee, using a scale of 1-5, has rated the chemicals according to toxicity only and distinct from any hazard consideration.

Chemical	Vapor Irritant	Liquid/Solid Irritant	Chemical Poison	Human Toxicity
Nitroethane	3	2	2	3
Sodium Chlorate	*	3	2	2
t-Butyl hydroperoxide	*	5	3	3

* Insufficient information.

RCW/pf

cc: Dr. Martin A. Paul
Dr. D. L. Katz

NATIONAL RESEARCH COUNCIL

NATIONAL ACADEMY OF SCIENCES NATIONAL ACADEMY OF ENGINEERING

2101 CONSTITUTION AVENUE WASHINGTON, D.C. 20418

ADVISORY CENTER ON TOXICOLOGY

DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

22 February 1972

BUMED-732-SHB:dkh
Otto Fuel II

Chief, Bureau of Medicine and Surgery
Department of the Navy
Washington, D. C. 20390

Dear Sir:

In response to your request of 22 July 1971 for recommendations for Emergency Exposure Limits for the combustion products in submarines of Otto Fuel II, we have the following information.

It is the opinion of the Committee on Toxicology that the exhaust gases of primary toxicological concern are CO, HCN, and possibly NO_2. If the concentrations of the exhaust gases are proportionally reduced so that the levels of CO do not exceed the previously recommended 10, 30, and 60 minute EEL's for CO*, no toxic effects would be expected from the inhalation of the other exhaust products for these time periods. In the event that the contaminant levels exceed those recommended, respiratory isolation by means of the full-face supplied air respirators (mentioned in your letter of 27 August 1971) should prevent intoxication from all the agents with the possible exception of HCN.

Little or no quantitative information is available concerning the reported absorption of HCN vapors through the skin. Therefore, the Committee on Toxicology recommends that appropriate research be conducted to examine the potential toxicity by skin absorption of HCN

*EEL's for CO:	10 min	30 min	60 min
(normal activity)	1500 ppm	800 ppm	400 ppm
(mental acuity)	1000 ppm	500 ppm	200 ppm

vapors, especially at low concentrations, independent of respiratory exposure. The Committee also recommends a 24-hour EEL of 25 ppm for HCN and a tentative 90-day atmospheric concentration of 5 ppm conditional to appropriate research being done to determine any cumulative effects of a 90-day continuous exposure to HCN.

It is possible that many of the exhaust products listed in your initial letter (methane, hydrogen, ethylene, nitrogen oxide, etc.) could undergo further reaction in the presence of ambient oxygen to produce greater volumes of oxidation products, such as CO, CO_2, and NO_2, than are reported in your letter. If NO_2 is produced in significant amounts, the existing EEL's for this agent should be observed*. The exhaust products may also constitute a fire and/or explosion hazard.

It is essential to have human volunteers exposed to these three gases (CO, HCN, NO_2) for the recommended times in order to confirm man's ability to tolerate these levels without suffering untoward effects.

Finally, because the air-purifying devices on board the submarine will remove some of the contaminants more efficiently than others, it may be necessary to treat each exhaust product on an individual basis for time periods much greater than one hour. Research is recommended to determine the fate of the various exhaust products in the air-purifying devices along with the relative rate of removal of those products from the submarine atmosphere.

*EEL's for NO_2:	10 min	30 min	60 min
	30 ppm	20 ppm	10 ppm

Sincerely yours,

Ralph C. Wands, Director
Advisory Center on Toxicology

RCW/LMR/pf

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DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

22 February 1972

BUMED-732-SHB:alj
Liquid Oxidizers

Chief, Bureau of Medicine and Surgery
Department of the Navy
Washington, D. C. 20390

Dear Sir:

In partial response to your request of 5 August 1971 for emergency inhalation exposure limits (EEL's) for seven liquid propellants which might be used on board submarines, we have the following information for one of these agents, inhibited red fuming nitric acid (IRFNA).

IRFNA is a strong oxidizing agent and more than momentary contact with the liquid can produce a severe chemical burn on exposed tissue. The inhalation hazard is primarily due to nitrogen dioxide, a constituent and decomposition product of IRFNA.

In the event of an accidental release of IRFNA the existing EEL's for NO_2 would apply to the gases generated by such a release.* If the accident were such as to generate an acid mist, the nitric acid droplets would be extremely irritating to the eyes and mucous membranes. Such an exposure would be in addition to the NO_2 exposure and could cause additive or synergistic effects.

The vapors or a mist of nitric acid, free from nitrogen dioxide, act as a primary irritant on the eyes and upper respiratory tract and are expected to be similar to the effects of other strong acids.

Unfortunately there are few data dealing with the toxic effects of nitric acid combined with the effects of NO_2. However, there are reports

* Existing EEL's for NO_2 as previously recommended by the Committee on Toxicology:

10 min	30 min	60 min	24 hr
30 ppm	20 ppm	10 ppm	1 ppm

that "NO_2 is the only toxic constituent" of IRFNA at levels up to the 4 hr LC_{50} for rats (reported to be between 65 and 75 ppm), and "the vapors of IRFNA are approximately 25% more toxic than NO_2" very likely because of "the HNO_3 content of the vapors of IRFNA."

Because of the ambiguity of the existing information concerning the potential toxicity of an exposure to a mixture of NO_2 and HNO_3 it is suggested that appropriate research be conducted to determine the effects of such an exposure. Until such information becomes available, the Committee on Toxicology suggests tentative EEL's for IRFNA of

10 min	30 min	60 min	24 hr
60 mg/m^3	40 mg/m^3	20 mg/m^3	2 mg/m^3

measured as the NO_2 equivalent of the sum of HNO_3, NO, and NO_2.

It is important to note that, in arriving at these tentative EEL's the Committee on Toxicology has assumed the toxicity of HNO_3 and NO_2 to be additive and equal. It is strongly urged that appropriate research be conducted to verify this assumption.

Sincerely yours,

Ralph C. Wands, Director
Advisory Center on Toxicology

RCW/LMR/pf

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ADVISORY CENTER ON TOXICOLOGY

DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

10 March 1972

Ref: DASG-HEP-O

Colonel Alois Peczenik, MC
Chief, Occupational Health Branch
Preventive Medicine Division
Office of the Surgeon General
Department of the Army
Washington, D. C. 20314

Dear Colonel Peczenik:

This is in response to your letter of 27 January 1972 regarding the potential carcinogenicity of Freons 12 and 22.

We have searched our files and find no information indicating carcinogenic potential for these two compounds. However, in 1967 S. Epstein and co-workers published an article indicating an increased evidence of hepatomas and malignant lymphomas following injections of Freon 112 + piperonyl butoxide, and Freon 113 + piperonyl butoxide. There is no suggestion in the literature to date that any of these compounds are carcinogenic alone.

We are enclosing a copy of Epstein's article for your information.

We have also had an opportunity to discuss this situation with the staff of DuPont's Haskell Laboratories who have made a similar literature search recently on this question. They only found the enclosed Epstein article.

We would be most appreciative of being kept informed of the Army Environmental Hygiene Agency researches in this area.

Sincerely yours,

Ralph C. Wands, Director
Advisory Center on Toxicology

Enclosure
RCW/pf

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ADVISORY CENTER ON TOXICOLOGY

DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

30 March 1972

Memorandum

To: Howard H. Fawcett

From: Ralph C. Wands

Listed below are toxicity ratings recommended by the Committee on Toxicology for the remaining five chemicals for which you requested information via a copy of the Coast Guard letter dated November 30, 1971.

As has been done in previous reports of this type the Committee has rated the chemicals according to toxicity only and distinct from any hazard consideration, using a scale of 1-5.

Chemical	Vapor Irritant	Liquid/Solid Irritant	Chemical Poison	Human Toxicity
Dimethyl formamide	3	3	4	3
2-Hydroxyethyl-acrylate	5	5	4-5	4
a-methyl styrene mixture with cumene	No new information since letter of 10/14/71 to H. H. Fawcett			
1, 3 pentadiene	*	*	*	*
Nitrobenzene	1	2	4-5	3

* Insufficient Information

RCW:LMR/pf

cc: Dr. Martin A. Paul
Dr. D. L. Katz

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ADVISORY CENTER ON TOXICOLOGY

DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

6 April 1972

Ref:BUMED-7321-DER:phc
Dimethylaniline

Chief, Bureau of Medicine and Surgery
Department of the Navy
Washington, D. C. 20390

Dear Sir:

Reference is made to your letter of January 24, 1972 requesting tolerance limits (applicable to continuous ingestion) for dimethylaniline (DMA) in potable water.

The Committee on Toxicology considered this request at its February 2, 1972 meeting. Their position remains essentially as expressed in our response of November 22, 1971. In the absence of analytical, organoleptic and toxicological data, the Committee on Toxicology is unable to suggest a tolerance limit for DMA in drinking water. However, if an estimate of the upper limit of acceptability is needed, an emergency drinking water standard (for 2 or 3 days without regard to taste or odor) of 2. 5 ppm of DMA might possibly be adopted.

Further discussion and evaluation of related problems suggest that the odor and taste of the catchment basin water might regulate acceptability. Chlorination of water containing significant quantities of DMA will probably leave an objectionable taste and odor and, furthermore, the toxicity of the chloramines formed from DMA is unknown.

The Committee reiterates its recommendation that for a long-term supply of potable water the chemical quality of water held in the catchment basin liner should be demonstrated so that there is no question about the absence of DMA. The initial steps are envisioned as successive leachings of a catchment basin with concomitant chemical analysis so that quantitative data are available for evaluation.

Sincerely yours,

Ralph C. Wands, Director
Advisory Center on Toxicology

RCW/FGF/eb

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AREA CODE 202, 961-1751

7 April 1972

Ref:BUMED-7321:DER:phc
Polyurethane coatings

Chief, Bureau of Medicine and Surgery
Department of the Navy
Washington, D. C. 20390

Dear Sir:

This is in response to your request for toxicological evaluation of additional polyurethane coatings, dated 20 October 1971 and 19 January 1972.

The Deft Chemical Coatings (Defthane Enamel 03 series) are formulated from Desmodur N, using a variety of solvents in different proportions. Among the solvents used are toluene, methyl ethyl ketone, cellosolve acetate, and butyl acetate. The irritant effect of the polyurethane coatings are, in the main, associated with the solvent carriers. Each of these solvents was treated in detail in our reply to you on this same subject, dated 9 December 1971. The known toxicology of Desmodur N was also presented in detail by Enclosure 2 to our 9 December 1971 response. Summarizing our earlier responses with regard to the Defthane Enamel 03 Series, we conclude that the entire series would be classified as mild irritants and potential sensitizers requiring respiratory, eye, and skin protection when they are used.

The Dexter Corporation's Laminar® X-500 Light Stable 4W-70 and 4W-89 coatings are similar to the other products we have discussed, i.e., they are formulated by combining a polyisocyanate with certain hydroxyl-bearing resins in a solvent system.

A commercial laboratory has investigated some toxicological aspects of the X-500 catalyst. The results of these investigations show that no deaths are produced in rats from multiple oral doses of 67 mg/kg. Rabbit dermal tests were negative at a dose of 6.5 g/kg. Rabbit eye tests reveal a mild erythema after one hour and a score of 6.6 out of a possible 110. No residual damage is reported.

The specific coatings, 4W-70 and 4W-89, employ X-500 dissolved in about four organic solvents in varying proportions. The solvents are toluol, butyl acetate, methyl ethyl ketone, cellosolve acetate, cyclohexanone, and ethyl acetate. These coatings, similar to others in this same category with related organic solvents, are eye, skin, and respiratory irritants. The degree of protection required varies with the type of use but, in general, protection from irritation is achieved through adequate ventilation and eye and skin barriers. If used in enclosed spaces, respiratory protection would be necessary. In the event of a fire, pyrolysis products would include CO, CO_2, NO_2, aldehydes, and HCN.

This completes our replies on polyurethane coatings, initiated by your request of 9 August 1971.

Sincerely yours,

Ralph C. Wands, Director
Advisory Center on Toxicology

RCW/FGF/eb

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ADVISORY CENTER ON TOXICOLOGY

DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

25 April 1972

Chief, Aerospace Medicine Division
Office of the Surgeon General
Department of the Air Force
Washington, D. C. 20314

Dear Sir:

Our report to you dated 14 January 1971, dealt with the toxicology of four herbicides, some of which incorporated sodium chlorate. We have subsequently received the following unpublished data on the latter which we are pleased to share with you as an up-dating of our earlier report.

Rat Oral LD50	4100 mg/kg
Mouse Intraperitoneal LD50	308 mg/kg

In addition to the foregoing acute studies a 60-day drinking water (ad libitum) test was carried out using cats and mice. Concentrations ranging from 0 to 4000 ppm produced no methemoglobin or blood destruction even though these are highly susceptible species. Rats, guinea pigs, mice, and cats were also observed at those water levels and no effects were found in water consumption, urinary output, behavior, appearance, weight, food consumption, hematology, organ/body weight ratios, or gross and microscopic pathology including bone-marrow smears.

Sincerely yours,

Ralph C. Wands, Director
Advisory Center on Toxicology

RCW/pf

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ADVISORY CENTER ON TOXICOLOGY

DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

2 May 1972

5050/NAS/2

Commandant (MHM)
U. S. Coast Guard
Washington, D. C. 20591

Dear Sir:

As you requested on April 10, 1972, we transmit herewith information concerning the effects of chlorine on experimental animals, vegetation, materials, and man. This information was compiled from the literature holdings of the Advisory Center on Toxicology by the staff of the Center.

We call your attention to the enclosed sections taken from the "Basis for Establishing Guides for Short-Term Exposure of the Public to Air Pollutants," which was prepared by the Committee on Toxicology for the Environmental Protection Agency (EPA). These sections refer to the philosophy of recommending limits for exposures that are predictable as well as for exposures that are accidental (unpredictable).

The sections of the information on Cl_2 referring to odor threshold and levels of Cl_2 at which irritation is first noticed may be significant in light of national primary air-quality standards. Primary standards define levels of air quality necessary to protect the public health with adequate margins of safety.

The sections of the enclosed information referring to effects on plants may be significant for national secondary air-quality standards that are judged necessary to protect the public welfare.

As of this date the EPA has not yet set primary or secondary air standards for chlorine. Since the legal responsibility of setting air standards for the protection of the public health and welfare belongs to the EPA, it is inappropiate for the Committee to recommend such standards to you. However, we anticipate a request from EPA for recommendations for short-term exposure of the public to chlorine. In the event that such a request is made to us by EPA we will endeavor to coordinate these requests so as to respond to both as soon as possible.

Sincerely yours,

Ralph C. Wands, Director
Advisory Center on Toxicology

RCW/eb
Enclosure

Chlorine

Chlorine is a greenish yellow gas at ambient temperatures and pressure having a molecular weight of 70.9, a boiling point of -34° C, and a specific gravity 2.47 times that of air. It is readily liquefied and is normally shipped in the liquid state in steel containers (cylinders, tank cars, etc.)

As a liquid, chlorine exerts a vapor pressure of 3.66 atmospheres at 0°C, 6.62 atmospheres at 20° C, 8.75 atmospheres at 30° C, and 41.7 atmospheres at 100° C. (1-3)

Chlorine is slightly soluble in water, 2.26 liters of gas dissolving in one liter of water at 20° C. (For comparative purposes the solubility of ammonia, hydrogen chloride, and chlorine at 0° C is 53 moles/l, 23 moles/l, and 0.2 moles/l respectively.)

The odor threshold of chlorine has been reported to be about 5 ppm (1), 3.5 ppm (4), and 0.3 ppm (5) in this country. Russian scientists report odor threshold levels of 0.2 ppm to 0.4 ppm. (6,7)

Effects on Animals

Chlorine, as a gas, is classified as a primary irritant on the respiratory tract, affecting both the upper respiratory passages and the deeper structures of the lung, i.e., the bronchi (3).

A probable theory of the action of chlorine on moist tissue is that chlorine abstracts the hydrogen from the water present in the tissue, allowing the formation of nascent oxygen and hydrogen chloride. This oxidation together with the formation of HCl is believed to result in the tissue irritation and/or damage observed upon excessive exposure.(3)

"Brief exposure to air containing 1000 ppm Cl_2 kills even large animals." (1) If the animal is not killed rapidly, death usually ensues from pulmonary edema.

Cralley (8) examined the effects of chlorine on mucociliary activity of sections of excised rabbit trachea. The chlorine was generated by the action of hydrochloric acid on potassium permanganate. The excised tracheal tissue was maintained in a constant temperature-humidity chamber and observed microscopically.

Thirty ppm of Cl_2 for 5 minutes and 18-20 ppm for 10 minutes caused cessation of ciliary activity without recovery. Cralley reports that the concentration necessary to produce ciliostasis is of the same order that produces immediate irritation of the throat, i.e., 15 ppm. Concentrations ranging from 200 ppm for less than one minute to 20 ppm for about 2-1/2 minutes caused reversible ciliostasis.

Heyroth (1) reported that the repiratory rate of animals was increased upon exposure to 200-1000 ppm Cl_2. The exposure of cats to a concentration of 300 ppm for one hour caused deaths after a period during which the conjunctiva were inflamed and there was coughing and dyspnea.

Effects on Humans

The sensitivity of men to chlorine varies greatly. Men may work without interruption in air containing 1 or 2 ppm, while 3-6 ppm may cause a stinging or burning sensation in the eyes, nose, or throat, and sometimes headache. There may be redness or watering of the eyes, sneezing, coughing and huskiness, or loss of the voice. Exposure for one-half to one hour to 14-21 ppm is dangerous, and 100 ppm is intolerable after one minute. (1)

Zielhuis (9) derived the following dose-response relationship based on a literature review of the effects of Cl_2:

> "At 1-3 ppm there may be slight irritation; 4 ppm cannot be exceeded for more than one hour without discomfort; above 5 ppm there is severe irritation of the eyes, nose and respiratory tract which becomes intolerable for more than a few minutes; more than 30 ppm is dangerous and possibly lethal after 30 minutes. This information suggests that the concentration should be kept below 10 ppm to prevent pulmonary oedema while for exposure of 30-60 minutes the concentrations should be low enough to prevent disabling discomfort."

Kowitz et al. (10) studied the effects of Cl_2 on men accidentally exposed to this gas in a transportation accident. Of approximately 150 men exposed, 59 were included in the analysis by the author. Eleven subjects who were hospitalized were evaluated serially with respiratory-function tests on four occasions during the following two to three years.

The mean acute respiratory-function changes of the 11 subjects were compatible with an alveolocapillary injury. This was followed by repair over the following 2-3 year period. Increased airway resistance, and a decrease in lung volume and diffusing capacity remained at the end of the study period. Decreased vital capacity, increased elastic work of breathing, and a decreased diffusing capacity resulted from the exposure in the 59 subjects as reported by the authors.

Kaufman and Burkons (11) studied 18 subjects accidentally exposed to Cl_2. The subjects were observed during the initial 24 to 48 hours after their exposure and then examined serially during the next 14 months. Physiological tests included vital capacity, forced expiratory volume, residual volume, airway resistance, diffusing capacity, and arterial oxygen tension. X-rays were taken during these examinations, which were done 1, 2, 4, 12, and 14 months after the Cl_2 exposure.

From the results of this study the authors conclude that, within hours following a single but rather severe chlorine gas exposure, acute evidence of obstructive airway disease was observed. Within 30 to 90 days following the exposure the physiologic disturbance was not evident. Clinical signs and symptoms as well as roentgenograms returned to normal within 30 days and remained so. Two of the subjects showed severe pulmonary edema after exposure and were cyanotic for several days but showed no permanent sequelae during the next 14 months.

In high concentrations Cl_2 irritates the skin, causing burning and irritation with the possibility of blister formation. (1) However, such irritations would be expected to occur only when the exposure to the high concentrations is rendered tolerable by the use of respiratory protective devices. (3)

Table I lists various concentrations of Cl_2 along with findings or remarks concerning these concentrations.

Effects on Materials

Chlorine has a very strong chemical affinity for many substances. It will react with almost all the elements and with many organic and inorganic compounds. At elevated temperatures it reacts vigorously with most metals. At ordinary temperatures dry, liquid, or gaseous Cl_2 does not corrode steel. In the presence of moisture, highly corrosive conditions exist due to the formation of hydrochloric acid and hypochlorous acid. (12)

A detailed discussion of the conditions and effects of Cl_2 on materials is beyond the scope of this report. For information concerning specific materials, engineering references such as Metals Handbook (22) should be consulted.

Effects on Plants

Chlorine is capable of causing marginal and tip necrosis in plants; younger leaves being less susceptible than middle-aged or older leaves. (13)

Brennan *et al.* (14) exposed a variety of plants to Cl_2 gas at concentrations ranging from 0.1 to 1.5 ppm for 2 to 4 hours. They report that bleaching of the foliage at low levels and necrosis at somewhat higher levels were the most common effects observed.

Radish and alfalfa were the two most sensitive species tested, showing injury at 0.1 ppm for two hours. Tobacco, zinnia, gomphrema, onion, corn, mustard, and sunflower were damaged by 0.1 to 0.25 ppm for 4 hours. Tomato, cucumber, dahlia, nasturtium, petunia, pinto bean, squash, corn-pea, geranium, and azalea were damaged at levels of 0.5 to 0.8 ppm for four hours. Polygonum, oxalis, and pepper were uninjured at levels of 1.5 ppm Cl_2 for three hours.

Chloride accumulation in the exposed plants exhibited no correlation with the degree of Cl_2 exposure, nor was the damage to wet leaf surfaces significantly different from that observed on dry leaf surfaces.

Tomato plants kept in darkness following a Cl_2 exposure exhibited less damage than plants exposed and held under greenhouse lighting conditions.

Benedict and Breen (15) exposed a variety of weeds to Cl_2 at concentrations ranging from 0.5 to 2.5 ppm for four hours and reported that mustard, chickweed, and sunflower were the most susceptible to Cl_2 fumigation, while Kentucky bluegrass, Lamb's-quarters, and pigweed were the most resistant. Those weeds grown under conditions of low soil moisture were reported to be more resistant to Cl_2 injury than plants grown under conditions of high soil moisture.

Table I

Concentration	Remarks	Ref.
0.3 - 3.5 ppm	Range of reported odor thresholds	16
1 ppm	TLV	1
1 - 2 ppm	Men can work without interruption	9
1 - 3 ppm	There may be slight irritation	19
3 ppm	Pennsylvania short-term limit for 5 min	
3 ppm	Permissible excursion for 15 minutes based on TLV	16
3 ppm	Recommended as 60 min EEL	9
3 - 4 ppm (0.01 mg/l)	Can be breathed for several hours without serious effect	23
3 - 6 ppm	Stinging or burning in the eyes, nose and throat and perhaps headache due to sinus irritation. Maybe watering of eyes, sneezing, coughing and bloody nose and/or blood-tinged sputum.	1
4 ppm	Cannot be exceeded for more than 1 hour without discomfort	9
4 ppm	Recommended 30 min EEL	9
Above 5 ppm	Severe irritation of the eyes, nose, and respiratory tract which becomes intolerable for more than a few minutes	9
5 ppm	Recommended 15 min EEL	9
7 ppm	Recommended 5 min EEL	9
14 - 21 ppm	Dangerous for 1/2 to 1 hour	1
20 ppm	Ciliary activity (in vitro) ceases in two minutes	8
20 ppm	Ciliary activity (in vitro) ceases without recovery	8
34 - 51 ppm	Lethal in 1 - 1-1/2 hours	23

APPENDIX

Established Limits:

TLV: 1 ppm (3 mg/m^3) (15 minute excursion: 3 ppm)[16]

Russian Maximum Allowable Concentration (industrial): 0.001 mg/l (1 mg/m^3) [17]

Recommended EEL for submarine crews: 3 ppm for 60 minutes [18]

Pennsylvania Short-Term Limits: 3 ppm for 5 minutes [19]

Maximum allowable concentration in populated areas: average 24-hr

concentration: 0.03 mg/m^3
maximal single concentration: 0.1 mg/m^3 (Russian figures)[20]

Recommended EEL's for occupational exposure:[9]

60 minutes: 3 ppm
30 minutes: 4 ppm
15 minutes: 5 ppm
5 minutes: 7 ppm

International MAC's in the workplace: [21]

German Federal Republic: 2 mg/m^3 [1968]
German Democratic Republic: 1 mg/m^3 [1963]
Great Britain: 3 mg/m^3 [1955]
Hungary: 1 mg/m^3 [1956]
Poland: 1 mg/m^3 [1959]
Yugoslavia: 3 mg/m^3 [1957]
Czechoslovakia: mean MAC: 3 mg/m^3; peak MAC: 6 mg/m^3 [1969]

Chlorine Bibliography

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ADVISORY CENTER ON TOXICOLOGY
DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

3 May 1972

Ref: BUMED-7321-DER:dkh
"Leak Lock"joint sealing
compound

Chief, Bureau of Medicine and Surgery
Department of the Navy
Washington, D. C. 20390

Dear Sir:

In response to your request of March 17, 1972 for toxicological information concerning the use of "Leak Lock" joint sealing compound aboard nuclear submarines, we have the following information.

The manufacturer has informed us that ethyl alcohol is the only agent that will volatilize into the atmosphere during the application of "Leak Lock." For maintenance, the joints may be cleaned of the sealant with any solvent alcohol or strong caustic solution.

The manufacturer also reports that the material does not contain any curing agents and does not produce dermatitis. The pigments in the sealant are primarily kaolins and their use in this product would not be expected to cause any toxicological hazards.

We have no information on any analyses of this material by independent analytical and testing laboratories.

In conclusion, the use of "Leak Lock" aboard submarines in the quantities mentioned in your letter of March 17 (3 pounds) would not be expected to produce any significant health problems when good industrial hygiene is practiced, i.e., the TLV's for ethyl alcohol and any solvent alcohols are observed and skin and eye protection are adequate if caustic solutions are used in cleaning the joints.

The Committee on Toxicology has previously recommended for submarines a 24-hour emergency limit for ethyl alcohol of 500 ppm and a 90-day limit of 100 ppm.

Sincerely yours,

Ralph C. Wands
Director
Advisory Center on Toxicology

RCW/LMR/lc

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ADVISORY CENTER ON TOXICOLOGY

DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

8 May 1972

Ref:BUMED-732-SHB:dkh
Liquid Oxygen(LOX)

Chief, Bureau of Medicine and Surgery
Department of the Navy
Washington, D. C. 20390

Dear Sir:

In accordance with your request of 13 September 1971, the Committee on Toxicology has examined the specifications for aviator's breathing oxygen. The Committee's conclusions, comments, and recommendations are as follows:

1. The present standards and the associated 2, 3, and 5-fold allowances for contaminant concentration during storage of LOX provide ample protection against systemic toxicity and respiratory irritation. "Present standards" are understood to mean those contained in the following references, which you provided: (a) Canadian Military Specifications and (b) the Bureau of Weapons 1961 speed letter described in the July 23, 1961 Medical News Letter.

2. Good manufacturing and handling practices appear capable of meeting these standards easily.

3. The difficulties experienced seem to be related to odor problems with their associated psychological complications.

4. The Committee concurs with previous recommendations that analytical procedures and equipment be developed for on-board monitoring of aviator's breathing oxygen at all stages of production and use.

5. The attention of the Navy is called to the current research and development program at the Air Force School of Aerospace Medicine (Dr. Billy Welch), leading to a portable analyzer for aviator's breathing oxygen.

6. The Committee concurs with previous suggestions that the initiation of odor problems may be controlled by filtration of LOX to remove liquid and solid particulates developing during all stages of storage and transfer. Research and development effort should be directed to this end.

7. The Navy may wish to consider an orientation program for aviators dealing with breathing oxygen and its possible odors.

Sincerely yours,

Ralph C. Wands, Director
Advisory Center on Toxicology

RCW/pf

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2101 CONSTITUTION AVENUE WASHINGTON, D.C. 20418

ADVISORY CENTER ON TOXICOLOGY

DIVISION OF CHEMISTRY AND CHEMICAL TECHNOLOGY

AREA CODE 202, 961-1751

6 June 1972

Marcus M. Key, M.D.
Assistant Surgeon General
Director
National Institute for Occupational
Safety and Health
5600 Fishers Lane
Rockville, Maryland 20852

Dear Dr. Key:

Thank you for your letter of May 15 and the opportunity to review the draft of "Criteria for Recommended Standard for Carbon Monoxide." It has been reviewed by Dr. L. M. Roslinski of our staff and myself. Enclosed are our composite personal comments which do not constitute a formal review by the Academy or any of its committees.

Sincerely yours,

Ralph C. Wands
Director
Advisory Center on Toxicology

RCW/pf

Enclosures

NATIONAL RESEARCH COUNCIL

NATIONAL ACADEMY OF SCIENCES NATIONAL ACADEMY OF ENGINEERING

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28 June 1972

Dr. Charles A. Berry
NASA Director for Life Sciences
Code MM
National Aeronautics and Space
Administration
Washington, D. C. 20546

Dear Dr. Berry:

Attached you will find the report of the Academy's Committee on Toxicology on "Air Quality in Manned Spacecraft," in response to your request of December 21, 1970. A special sub-committee and panel were convened to study the problems and to prepare the report, which in turn was thoroughly reviewed within the Committee on Toxicology. The membership of the Panel is shown in the introduction of the report. (A report on wash water standards was submitted to you on January 4, 1972, and a report on potable water standards is in preparation).

As a result of staff communications during this study, some elaboration of your original request took place. You will note, for instance, that permissible limits have been recommended for 60 minutes, 90 days, and 6 months. Also, some chemicals might be present in the confined commode area of a spacecraft where a 10-minute limit would be applicable. Where this is so, a limit has been recommended.

The Panel, with the concurrence of the Committee and NASA, decided not to give any consideration at this time to the question of air quality for 3-year (1000-day) space flights. Some of the factors involved in this decision were that (a) it would permit the Panel to focus its attention on the more immediate needs of NASA for guidance related to design requirements of current active projects; (b) there are not sufficient data presently available to set standards; (c) special consideration will be needed to determine if new protocols for toxicity testing are required and, if so, to develop them. If you would like the Committee to continue these studies with a view to recommending permissible limits for continuous 3-year exposures, or the research efforts necessary to provide the essential data, would you please advise us.

Dr. Charles A. Berry

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This has been a very interesting study on our part and we thank you for all the cooperation we have received from NASA during the course of the study, particularly from Mr. Joseph Pecoraro.

Sincerely yours

Ralph C. Wands
Director
Advisory Center on Toxicology

RCW/FGF/eb
Enclosure

cc: Dr. Jones w/1 copy enclosure
Mr. Pecoraro w/50 copies enclosure