

For Reference Only

AFAMRL-TR-81-136

ADA 111686

12/1/81

Do Not Republish



TOXICOLOGY OF HIGH ENERGY FUELS

MICHAEL G. MACNAUGHTON

DECEMBER 1981

Approved for public release; distribution unlimited

20060630472

AIR FORCE AEROSPACE MEDICAL RESEARCH LABORATORY
AEROSPACE MEDICAL DIVISION
AIR FORCE SYSTEMS COMMAND
WRIGHT-PATTERSON AIR FORCE BASE, OHIO 45433

STINFO COPY

NOTICES

When US Government drawings, specifications, or other data are used for any purpose other than a definitely related Government procurement operation, the Government thereby incurs no responsibility nor any obligation whatsoever, and the fact that the Government may have formulated, furnished, or in any way supplied the said drawings, specifications, or other data, is not to be regarded by implication or otherwise, as in any manner licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use, or sell any patented invention that may in any way be related thereto.

Please do not request copies of this report from Air Force Aerospace Medical Research Laboratory. Additional copies may be purchased from:

National Technical Information Service
5285 Port Royal Road
Springfield, Virginia 22161

Federal Government agencies and their contractors registered with Defense Documentation Center should direct requests for copies of this report to:

Defense Documentation Center
Cameron Station
Alexandria, Virginia 22314

TECHNICAL REVIEW AND APPROVAL

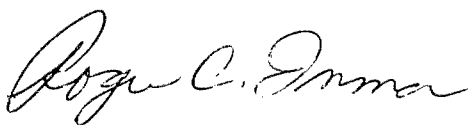
AFAMRL-TR-81-136

The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals, "Institute of Laboratory Animal Resources, National Research Council.

This report has been reviewed by the Office of Public Affairs (PA) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

FOR THE COMMANDER



ROGER C. INMAN, COLONEL, USAF, BSC
Chief
Toxic Hazards Division
Air Force Aerospace Medical Research Laboratory

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER AFAMRL-TR-81 -136	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) TOXICOLOGY OF HIGH ENERGY FUELS		5. TYPE OF REPORT & PERIOD COVERED TECHNICAL REPORT
		6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Michael G. MacNaughton		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS Air Force Aerospace Medical Research Laboratory, Aerospace Medical Division, AFSC, Wright-Patterson Air Force Base, Ohio 45433		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS 62202F; 6302/08/01
11. CONTROLLING OFFICE NAME AND ADDRESS Same as Block 9.		12. REPORT DATE December 1981
		13. NUMBER OF PAGES 16
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)		15. SECURITY CLASS. (of this report) Unclassified
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE
16. DISTRIBUTION STATEMENT (of this Report) Approved for public release; distribution unlimited.		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)		
18. SUPPLEMENTARY NOTES Presented at the Joint Army-Navy-NASA-Air Force Safety and Environmental Protection Subcommittee Annual Meeting, 17-20 November 1981, Kennedy Space Center, Florida.		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) High energy fuels ALCM Cruise missile fuels Toxicology JP-9		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) The development of new weapons systems, high energy fuels, and aerospace materials presents a challenge to the health professional. To avoid health hazards to Air Force personnel these hazards must be identified early in the research phase of development before acquisition decisions are made. This is only possible if the health professional works closely with the design engineers and scientists. (CONTINUED ON REVERSE)		

BLOCK 20 CONTINUED:

The Air Force program to develop high energy cruise missile fuels is a good example of close cooperation between scientists developing these fuels and toxicologists and environmental engineers responsible for research to assess the health and environmental consequences of their deployment throughout the Air Force. A status report is given on the extensive toxicology data base research effort on these fuels. Included are data on acute, chronic, and oncogenic exposures; mutagenic screening tests and emergency exposure limits.

PREFACE

This technical report was an invited oral presentation by Lt Col Michael G. MacNaughton at the Joint Army-Navy-NASA-Air Force (JANNAF) Safety and Environmental Protection Subcommittee Annual Meeting. The meeting was held on 17-20 November 1981 at NASA/Kennedy Space Center, Florida.

INTRODUCTION

As the Air Force moves into the 1980's and 90's new advanced weapons systems, special fuels, and hybrid structural materials will be deployed which could have the potential for creating health hazards for Air Force personnel or for causing unacceptable environmental degradation. The mission of the Air Force toxicology research program is to identify these potential hazards before they are introduced into the field, develop the technology base for establishing safe exposure criteria, and to assist system design engineers in minimizing health and environmental consequences. This paper has two objectives: describe the extensive research effort required to establish the necessary data base for protecting Air Force personnel from toxic chemicals, and illustrate the extent of this research effort by providing a status report on current research to determine safe exposure criteria for a new class of high energy fuels which will be used in ramjet powered cruise missiles.

TOXICOLOGY OF NEW WEAPON SYSTEMS

Enhancement of Air Force mission accomplishment by minimizing delays in weapon system deployment and protecting the health of Air Force workers is the goal of the Air Force toxicology research program conducted by the Toxic Hazards Division of the Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio. The six objectives given in Table 1 form the basis for achieving this goal.

TABLE 1. AIR FORCE TOXICOLOGY TECHNOLOGY BASE OBJECTIVES

1. Determine safe human exposure levels for new fuels, chemicals, and materials.
2. Assist in selecting less toxic alternatives during the concept phase of development.
3. Assist design engineers in reducing human exposures and releases into the environment.
4. Provide medical screening and monitoring strategies for use by field medical personnel.
5. Identify mechanisms of toxic action for use in design of therapeutics.
6. Establish realistic pollution control criteria which protect environmental quality.

Prior to exposing Air Force personnel to a new chemical, it is essential that accurate and realistic safe exposure levels be established. Current OSHA and EPA regulations dictate specific documentation of the health and environmental aspects of a new chemical before it is allowed into the workplace. Of particular importance is the Toxic Substances Control Act of 1976 which requires a full battery of tests including acute, subacute, subchronic, mutagenic effects, teratogenic effects, reproductive effects,

and potential for environmental quality impacts (Back, 1980). Figure 1 illustrates schematically the hierarchy of toxicology research used by the Toxic Hazards Division in quantitating the safe exposure levels for a chemical which may present a potential inhalation and skin adsorption hazard. These range from short term acute LC₅₀ experiments to one year exposures to assess the oncogenic (tumor producing) potential of a chemical or fuel. Completion of a full experimental protocol takes from five to seven years and costs up to 1.5 million dollars, so it is important to select for the full toxicological protocol only those candidate chemicals which have a high probability of actually being deployed.

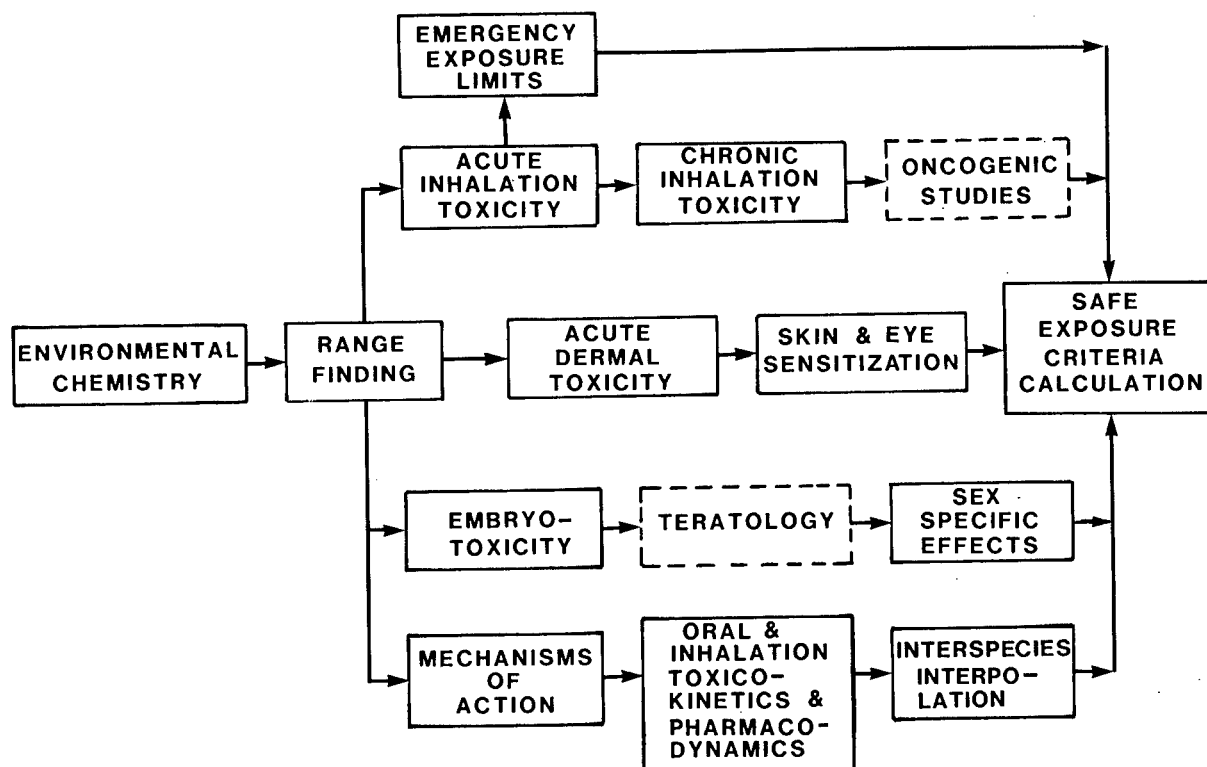


Figure 1. Toxicology Research Protocol

The 5-7 years, extensive manpower, and large expenditure of funds required for full testing of a new compound amplify the importance of toxicologists working closely with the chemists and engineers developing new compounds. Screening candidates during this phase of development allows critical evaluation to determine whether operational benefits of highly toxic materials would be worth the increased support costs imposed by restrictive health or environmental related controls. By making the designer more aware of the life cycle costs associated with using a hazardous material, it is probable he will be more willing to evaluate other alternatives which may have been excluded from preliminary consideration due to higher initial capital costs.

Health and environmental professionals have no alternative but to participate in the design process with other support disciplines (safety, logistics, civil engineering, personnel, etc.). Remaining aloof, as a consultant, will result in exclusion from the decision process and reinforce the feeling of many weapon system engineers that health and environmental professionals do nothing but hinder the timely acquisition of new weapon systems. By actively participating in the development with the other research scientists, health and environmental consequences will be considered along with other costs and benefits in the decision matrix rather than being imposed later after major development or acquisition milestones have already passed.

This will not always be a secure position for health professionals whether they are physicians, toxicologists, industrial hygienists, or environmental engineers. In many cases pressures to meet critical milestones will force health related decisions to be made on less data than normally desired. The alternative is to be totally ignored and to lose the opportunity to make significant positive impacts on the design of a new system. As members of the Air Force our job is to advance the mission of the Air Force by protecting our most important resource, our military and civilian workers. We must realize, however, there is no totally safe chemical and to take an unrealistically conservative approach by requiring zero human exposure in the weapon system design would eliminate the need for our professional participation. No expertise is necessary to create a zero standard.

Many chemicals and fuels used in the military are unique either in their type, quantity used, method of use, or potential for exposing workers. This presents difficult problems to the occupational medicine physician at an operational base. In many cases there are not sufficient data in the literature for him or her to diagnose an overexposure, clinically evaluate laboratory results, or prescribe treatment. A significant portion of the Air Force's occupational medicine program is dedicated to yearly physicals to detect any adverse health consequences resulting from exposure to chemicals or physical agents in the workplace. Without the necessary diagnostic tools, the effectiveness of this physical is severely diminished. The toxicology research program provides the technology base for diagnosing health problems by determining the sites and mechanisms of action of the compound and developing the techniques necessary to analytically determine if the worker has been exposed. Understanding the mechanisms of action and the kinetics of its distribution in the body is also important in extrapolating toxicity data from rodents to humans and in designing the therapeutics for treating overexposures.

Finally, accurate and realistic criteria must be established on the environmental effects caused by release of these chemicals. This includes aquatic and terrestrial animals as well as both natural and agricultural plants. These criteria form the basis for realistic pollution control designs and environmental impact assessments of new weapon systems.

Next the operation of this toxicology program will be illustrated by using, as an example, research to develop a new fuel for the Air Launched Cruise Missile (ALCM).

TOXICOLOGY OF HIGH ENERGY CRUISE MISSILE FUELS

The requirement for a small efficient cruise missile engine capable of generating one pound of thrust for each pound of fuel created the need for a synthetically derived fuel with higher energy content than presently available in the petroleum derived aircraft turbine engine fuels, JP-4, JP-8, and JP-5 (Burdette et al., 1978). Table 2 compares the new synthetic high energy fuel components, RJ-4, RJ-5, and JP-10, with the current turbine engine fuel, JP-4. The higher volumetric energy content of these new fuels is due in large part to their high carbon/hydrogen ratio (C/H), increased density, and lack of carbon-carbon double bonds. The schematics of these synthetic fuels are shown in Fig. 2 and illustrate the bridged ring nature of their structure. In contrast to the conventional petroleum derived turbine engine fuels which are composed of a broad spectrum of paraffinic, polycyclic, and aromatic hydrocarbons, the synthetic high energy fuels are made from relatively pure compounds.

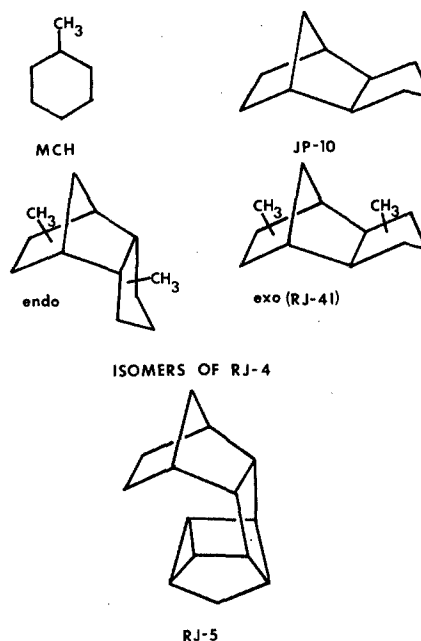
TABLE 2. HIGH DENSITY FUEL CHARACTERISTICS*

FUEL	RJ-4	RJ-5	JP-10	MCH	JP-4
FORMULA	$C_{12}H_{20}$	$C_{14}H_{18}$	$C_{10}H_{16}$	C_7H_{14}	$C_{9.5}H_{19}$
MOLECULAR WEIGHT	164	188	136	98	133
KBTU/GALLON	141	161	142	120	118
SPECIFIC GRAVITY	0.94	1.08	0.94	0.77	0.75
FLASH POINT, °C	60	66	52	-4	-29
VAPOR PRESSURE, MM HG	0.35	0.25	0.50	43	91

*MIL-P-87107B, 1977 and MIL-F-82522A, 1967.

While RJ-4 is usable for the Navy Tomahawk Submarine Launched Cruise Missile (SLCM), its high freezing point and low volatility make it unusable for the Air Launched Cruise Missile (ALCM). The ALCM was designed to be carried externally on the B-52 and required a fuel with the high volatility and low freezing point of JP-4. JP-10 meets all the requirements for an ALCM fuel except for its low volatility which was overcome by adding methylcyclohexane (MCH) (Burdette et al., 1978). This commercially available solvent provided the needed volatility but its low volumetric energy (120,000 BTU/gal) significantly reduced available thrust. Adding RJ-5, with the highest energy content of the synthetic fuels, returned the combined ALCM fuel, called JP-9 (65-70% JP-10, 20-25% RJ-5, 10-12% MCH), to the original 141,000 BTU/gal of JP-10.

Figure 2
Structures of High Energy Cruise
Missile Fuels



RJ-4 AND RJ-5 TOXICITY

A list of completed or ongoing studies on the toxicity of high energy fuels is given in Table 3. It was because of a close working relationship between the Aero Propulsion Laboratory and the Toxic Hazards Division that acute exposure experiments documented the low toxicity of RJ-4 and RJ-5 during early research on various candidate fuels in 1974. The acute oral LD₅₀ in rats was determined to be greater than 16 g/kg for both RJ-4 and RJ-5 (Haun et al., 1978).

TABLE 3. HIGH DENSITY FUEL TOXICOLOGY

<u>FUEL</u>	<u>TYPE</u>	<u>EXPOSURE</u>	<u>CONCENTRATION</u>	<u>DURATION</u>	<u>ANIMALS</u>
RJ-4	Chronic	Inhalation	298 ppm	6 mos int	Dogs, Rats, Mice, Monkeys
RJ-5	Chronic	Inhalation	20 ppm	6 mos	Dogs, Rats, Mice, Monkeys
	Chronic	Inhalation	20 ppm	12 mos int	Dogs, Rats, Mice, Hamsters
	Chronic	Inhalation	4 ppm	12 mos int	Dogs, Rats, Mice, Hamsters
JP-10	Acute	Inhalation	950-1440 ppm	2 hrs	Rats, Mice, Hamsters
	Acute	Injection			Rats, Mice, Hamsters
	Sensit.	Skin, Eye			Rabbits, Guinea Pigs
	EEL	Inhalation	150-1005 ppm	1 hr	Dogs, Rats, Mice
	Chronic	Inhalation	100 ppm	12 mos int	Dogs, Rats, Mice, Hamsters
	Acute	Dermal		24 hr	Rats
	Teratology	Oral	250-1000 mg/kg	6 days	Rats
	Teratology	Inhalation	572 ppm	6 days int	Rats
	Toxicokin.	Inhalation			Rats
MCH	EEL	Inhalation	4071-6564 ppm	1 hr	Dogs, Rats, Mice
	Chronic	Inhalation	400 ppm	12 mos int	Dogs, Rats, Mice, Hamsters
	Chronic	Inhalation	2000 ppm	12 mos int	Dogs, Rats, Mice, Hamsters

Knowledge of the apparent low acute toxicity of these fuels was important to fuel chemists and engineers working with the candidate compounds and minimized any actions which may have been required to protect researchers or provide personal protection for fuel handlers. By performing the acute toxicity studies at this stage of development, if initial results had indicated these fuels were acutely toxic, cost/benefit tradeoffs could have been made to determine whether the advantages of each high energy fuel were worth the increased supportability costs involved with handling a hazardous chemical.

With the data that these hydrocarbons could be classed as minimally toxic and were not skin or eye irritants, experiments were begun to assess the effect of occupational exposures to inhaled vapors. The low volatility of RJ-4 and RJ-5 made the possibility of high inhalation exposures unlikely, so six month intermittent exposures (6 hours per day, 5 days per week) to atmospheres saturated with the fuels were performed to evaluate a worst case situation. These maximal exposures (298 ppm RJ-4, 20 ppm RJ-5) produced only mild respiratory tract irritation and some weight depression in the exposed animals. Odors of RJ-4 and RJ-5 are particularly objectionable making it doubtful that respiratory irritation would be a problem considering the low volatility of the compounds. Some mice held for one year post-exposure after exposure to RJ-5 did produce more tumors than the controls indicating RJ-5 might be a weak tumor producer (MacEwen and Vernot, 1979; 1980). Mutagenic potential studies using the Ames, mouse lymphoma, and dominant lethal assay were all negative. Unscheduled DNA synthesis was positive which indicates DNA toxicity, not lesions, which lead to mutations. This assay is not a measure of mutagenic activity but many mutagens are positive (Brusick and Matheson, 1978).

To further define the oncogenic (tumor producing) potential of RJ-5, mice, rats, hamsters, and dogs were exposed to 4 and 20 ppm (0.03 and 0.15 mg/liter) for one year using the same intermittent exposure scheme. The magnitude of this type of exposure protocol is illustrated in Table 4. Large numbers of rodents are required to statistically determine tumor production caused by the test chemical with a background of natural and toxicologic attrition.

This protocol involved 1314 animals which were maintained during the exposure and for one year postexposure. The animals were observed hourly during the exposure and daily thereafter until the experiment was terminated. Individual rats, hamsters, and dogs were weighed biweekly while being exposed and then every four weeks during postexposure observation. Mice were weighed as groups on a monthly basis. Animal tissues (42,048) must be necropsied, made into slides, and microscopically analyzed by a pathologist.

The animals exposed to RJ-5 completed their one year postexposure period this month, and the pathology will consume another year before results are known. Very few signs of stress were observed; however, there was some depression of body weight in the exposed male rats and hamsters.

TABLE 4. ANIMAL DISTRIBUTION IN RJ-5 EXPOSURES*

	CONCENTRATION, MG/LITER		
	<u>0.03</u>	<u>0.15</u>	<u>0</u>
RATS, male	65	65	65
RATS, female	65	65	65
MICE, female	200	200	200
HAMSTERS, male	100	100	100
DOGS, male	4	4	4
DOGS, female	4	4	4

*MacEwen and Vernot, 1980.

JP-10 TOXICOLOGY

The acute oral LD₅₀ of JP-10 was greater than 20 ml/kg and an inhalation LC₅₀ for the rat was calculated to be approximately 1200 ppm (6.7 mg/liter). Skin and eye irritation tests were negative with a moderate potential for sensitization (MacEwen and Vernot, 1979). The exposure protocol to determine a safe exposure limit for JP-10 is similar to that described for RJ-5. The required four species of animals were exposed to 100 ppm (0.56 mg/liter) of JP-10 for one year using an occupational chronic exposure scheme. Exposure and postexposure have been completed and tissues from the rodent organs are now being examined for evidence of significant changes. Dogs used in the study will be held until June 1984. The only effects of exposure to 100 ppm noted during the exposure or postexposure observation were some weight depression in male rats and hamsters. There were no observed differences between mice and dog exposure and control groups (MacEwen and Vernot, 1981). Establishing a safe exposure level must await final evaluation of tissue from animals sacrificed after one year postexposure.

METHYLCYCLOHEXANE TOXICITY

Of the three JP-9 compounds, methylcyclohexane (MCH) is the most volatile and would present the greatest exposure to fuel handlers. Saturated vapor over JP-9 would contain 9400 ppm MCH (37.0 mg/liter), 660 ppm JP-10 (3.7 mg/liter), and 160 ppm RJ-5 (1.2 mg/liter) (MacEwen and Vernot, 1979). The American Conference of Governmental Industrial Hygienists has established a MCH Threshold Limit Value (TLV) of 400 ppm (1.6 mg/liter) and a Short Term Exposure Limit (STEL) of 500 ppm (2.0 mg/liter). Workers can be exposed continuously to the STEL for 15 minutes without irreversible damage and significant loss of coordination. These levels are based on the TLV for heptane which also exhibits a narcotic effect similar to MCH.

Basing a TLV on a compound's similarity to another chemical is tenuous and even though at high concentrations the analogy between heptane and MCH may be appropriate, there are insufficient data on the central nervous system effects to feel confident about long term exposures (MacEwen and Vernot, 1979). This scarcity of chronic data on MCH prompted the initiation of a one year exposure to the current TLV, 400 ppm, and the highest tolerable dose, 2000 ppm (8.0 mg/liter). Evidence from observation during and following exposure to these concentrations and examination of tissues from animals sacrificed at the end of the exposure revealed no significant differences between control and exposed animals. Final determination of the safe exposure level must await histopathology results.

EMERGENCY EXPOSURE LIMITS

The research described above was designed to produce safe exposure levels to which Air Force workers can be occupationally exposed with confidence that there will be no health impairment. There are, however, instances during which personnel are exposed to levels greatly exceeding the TLV for short periods of time. These occur during accidents and emergency operations. To permit accurate planning for storage limits, hazard zones, emergency response procedures, personal protective equipment, and system safety design, it is necessary to have an Emergency Exposure Limit (EEL). EEL's are defined as "concentrations of contaminants that can be tolerated without adversely affecting health but not necessarily without acute discomfort or other evidence of irritation or intoxication. They are intended to give guidance in the management of single, brief exposures to air-borne contaminants in the working environment." (Frawley, 1964).

Experiments were conducted to permit calculation of EEL's for MCH and JP-10 which would not produce toxic stress or coordination difficulties. These experiments were designed to determine physiological responses to these higher exposures and to allow measurement of effects on the central nervous system (CNS) which would hinder a worker's self rescue. To quantitatively determine neurological effects, dogs were trained to perform four basic tasks. The dogs were trained to fetch, come, stay, and lead. Approximately six weeks of training was required, and the dog's ability to perform the above tasks was compared before and after exposure.

Animals were placed in atmospheres containing MCH concentrations from 4071 to 6564 ppm for one hour and were observed for signs of hyperactivity during the exposures and for gross pathological changes 28 days post-exposure. Behavioral and neurological function were determined using the trained dogs who performed their trained tasks immediately postexposure.

Exposure to 6564 ppm (26.0 mg/liter) caused immediate hyperactivity in the rats followed by loss of coordination and eventual prostration. During the postexposure observation there were no signs of stress; weight gain was comparable to controls, and gross pathology examinations revealed no exposure related lesions. Exposure of rats to 4172 ppm (16.7 mg/liter) and mice to 4758 ppm (19.1 mg/liter) still produced some hyperactivity but with no lack of coordination. Four dogs exposed to a concentration of 4071 ppm (16.3 mg/liter) acted normally during the exposure and performed their

trained tasks up to the standards established during training. Based on the effects observed in rodents and dogs, it is believed that a one-hour exposure to a concentration of 4000 ppm (16.0 mg/liter) would not hamper self rescue or result in irreversible damage to man. This same EEL should apply for shorter periods since a 6564 ppm exposure resulted in significant changes in coordination and neurological function (MacEwen and Vernot, 1979).

To develop an EEL for JP-10 the same method used for MCH was employed. Rodents were first exposed to varying concentrations of JP-10 to establish a dose which produced no observable effect and then dogs were exposed to evaluate changes in CNS function. Rodents and dogs were exposed to concentration-time doses shown in Table 5 (MacEwen and Vernot, 1979).

TABLE 5. ANIMAL EXPOSURES TO JP-10 TO ESTABLISH AN EEL

<u>SPECIES</u>	<u>CONCENTRATION, PPM</u>	<u>TIME</u>
RATS	150	1 hr
	254	1 hr
	723	30 min
	823	30 min
	1015	10 min
MICE	150	1 hr
	254	1 hr
	723	30 min
	823	30 min
	1218	30 min
	1311	10 min
DOGS	151	1 hr
	718	30 min
	1000	10 min

Dogs were able to perform their trained tasks at all exposures. They did experience coughing and slight lacrimation at 718 ppm (4.0 mg/liter) and displayed fine tremors and lack of activity at the conclusion of the 1000 ppm (5.6 mg/liter) tests. Gross and histopathology revealed no exposure related lesions. Based on the above exposures preliminary EELs were determined to be 150 ppm (0.84 mg/liter) for one hour, 600 ppm (3.4 mg/liter) for 30 minutes, and 1000 ppm for 10 minutes. The selection of 600 ppm was based on observed lacrimation and coughing in dogs at 718 ppm.

SUMMARY

This description of high energy fuel toxicology illustrates the extensive research and long lead times required to develop an accurate health data base for a new Air Force chemical or fuel. It is fortuitous that the high energy fuels have a low toxicity, an objectionable odor, and low volatility, all of which reduce the possibility of adverse health

effects. Based on a TLV of 400 for MCH and the measured concentrations of 9400 ppm MCH (37.0 mg/liter), 600 ppm JP-10 (3.7 mg/liter), and 160 ppm RJ-5 (1.2 mg/liter) in saturated JP-9 vapor, the TLVs for JP-10 and RJ-5 would have to be below 7 ppm and 1 ppm before they would be the significant components. Preliminary results indicate that if the MCH TLV is used to control exposures to JP-9, the worker would be protected.

By cooperating closely with the Air Force fuels scientists, initial acute toxicity range-finding experiments were begun early in the research phase of the high energy fuel development program. These early experiments provided the data necessary to protect researchers and established the toxicology foundation for planning chronic and oncogenic studies as development decisions were made on the candidate fuels.

The lead time provided by this symbiotic relationship between the production laboratory and the toxicology researchers has assured that when the Air Launched Cruise Missile is deployed there will be a solid health effects data base to go with it. This accurate human toxicology base will form the basis for a complete and effective preventive occupational medicine program. By establishing a prospective toxicology program, we can eliminate much of the worker's fear associated with introduction of a new chemical into the workplace and assure the health professionals have the information to protect them.

REFERENCES

Back, K.C., 1980; The Impact on DoD of the Toxic Substances Control Act, AFAMRL-TR-80-69 (AD A088-525), Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio.

Brusick, D.J. and D.W. Matheson, 1978, Mutagen and Oncogen Study on RJ-5 Final Report, AMRL-TR-78-23 (AD A064-951), Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio.

Brusick, D.J. and D.W. Matheson, 1978, Mutagen and Oncogen Study on RJ-4, AMRL-TR-78-45 (AD A064-955), Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio.

Burdette, G.W., H.R. Lander, and J.R. McCoy, 1978, "High Energy Fuels for Cruise Missiles", Proceedings AIAA 16th Aerospace Sciences Meeting, Huntsville AL.

Frawley, J.P., 1964, "Emergency Exposure Limits," Amer. Ind. Hyg. Assoc. J. 25:578.

Haun, C.C., J.D. MacEwen, and E.H. Vernot, 1978, Toxicity of High Density Jet Fuel Components, AMRL-TR-78-16 (AD A068-596), Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio.

MacEwen, J.D. and E.H. Vernot, 1979, Toxic Hazards Research Unit Annual Technical Report: 1979, AMRL-TR-79-56 (AD A075-976), Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio.

MacEwen, J.D. and E.H. Vernot, 1980, Toxic Hazards Research Unit Annual Technical Report: 1980, AFAMRL-TR-80-79 (AD A091-617), Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio.

MacEwen, J.D. and E.H. Vernot, 1981, Toxic Hazards Research Unit Annual Technical Report: 1981, AFAMRL-TR-81-126, Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio.

MIL-F-82522A, 1967, Fuel, Ramjet Engine, T-H Dimer, Grade RJ-4.

MIL-P-87107B, 1977, Propellant, High Density Synthetic Hydrocarbon Type, Grades JP-9 and JP-10.



DEPARTMENT OF THE AIR FORCE
AIR FORCE AEROSPACE MEDICAL RESEARCH LABORATORY (AFSC)
WRIGHT-PATTERSON AIR FORCE BASE, OHIO 45433

REPLY TO
ATTN OF: TH

12 October 1983

SUBJECT: Changes and Updates to AFAMRL-TR-81-136, Toxicology of High Energy Fuels

TO: TR Distribution List

1. JP-10, the fuel for the Air Launched Cruise Missile (ALCM), is new in the AF inventory and there have been numerous inquiries concerning its health hazards. AFAMRL-TR-81-136 summarized toxicological data on JP-10 as of December 1981; however, results of long-term oncogenic studies were not available at that time. This letter provides an update on AFAMRL JP-10 toxicology studies and corrects some minor errors in the original document.
2. The vapor pressure of JP-10 (Table 2, pg 5, AFAMRL-TR-81-136) should read 14.2 mm Hg rather than 0.50 mm Hg.
3. The paragraph on JP-10 (pg 8, AFAMRL-TR-81-136) should now read as follows:

JP-10 Toxicology

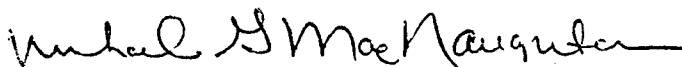
As with RJ-5, the synthetic fuel JP-10 was also found to be relatively nontoxic with an oral LD50 of greater than 18.8 g/kg and an LC50 of 6840 mg/m³ (MacEwen and Vernot, 1979). Skin and eye irritation tests were negative with a moderate potential for some sensitization. JP-10 produced marginal clastogenic effects in the CHO/chromosome aberration assay but was negative in the other mutagenic assays (Sivak, 1983). It was not embryotoxic in rats after inhalation of 600 ppm vapors or oral doses up to 1 g/kg (Keller et al., 1983).

Following these range-finding studies, a concentration of 562 mg/m³ JP-10 was selected as the level for a one-year intermittent study in dogs, rats, mice, and hamsters to assess oncogenic response. During the exposure, there was a slight weight depression in the exposed rats and hamsters, but no observable weight difference between exposed and control mice and dogs (MacEwen and Vernot, 1981). Female mice displayed liver cell vacuolization in 50% of control and 75% of exposed animals. The most significant histopathologic finding in exposed male rats held for one-year postexposure was the presence of 9 renal cell carcinomas and 1 poorly differentiated malignant renal neoplasm compared with only 1 in the controls. Accentuated renal tubular degeneration was also more prevalent in 87% of exposed male rats. No significant lesions were noted in female rats. Although there was only one exposure concentration, toxic nephropathy and renal cell tumors in male rats appear to result from extended exposure to JP-10.

CY TO: UCI/THRU

The human significance of the observed toxic nephropathy and renal cancer in male rats exposed to JP-10 is unknown; however, these same effects have also been observed in male rats exposed to gasoline. Further research is ongoing to assess the applicability of the male rat as an animal model in hydrocarbon caused nephrotoxicity.

4. The decision has been made to use JP-10 rather than JP-9 in the ALCM. This should cause no significant change in health hazards associated with this weapon system, and we feel a 25 ppm TWA interim exposure limit for JP-10 will protect workers. Direct analysis of JP-10 will be required in workplace industrial hygiene surveys instead of indirectly measuring the more volatile methylcyclohexane as was possible with JP-9 (Hossain, 1982).



MICHAEL G. MACNAUGHTON, LT COL, USAF, BSC
Deputy Director, Toxic Hazards Division

1 Atch
References

REFERENCES

Hossain, M.A., 1982, Evaluation of Portable Instruments for JP-9 and JP-10 Detection, USAF OEHL Report 82-013EH111GSA, USAF Occupational and Environmental Health Laboratory, Brooks Air Force Base, Texas.

Keller, W.C., R.C. Inman, K.O. Yu, and K.C. Back, 1983, "Evaluation of the Embryotoxicity of JP-10 in the Rat," Drug and Chemical Toxicology 6(2):181-190.

Sivak, A., 1983, Evaluation of Dimethyl Methylphosphonate and Exo-Tetrahydrodi-(Cyclopentadiene) in a Battery of in vitro Short Term Assays, AFAMRL-TR-82-95 (AD A124 785), Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio.