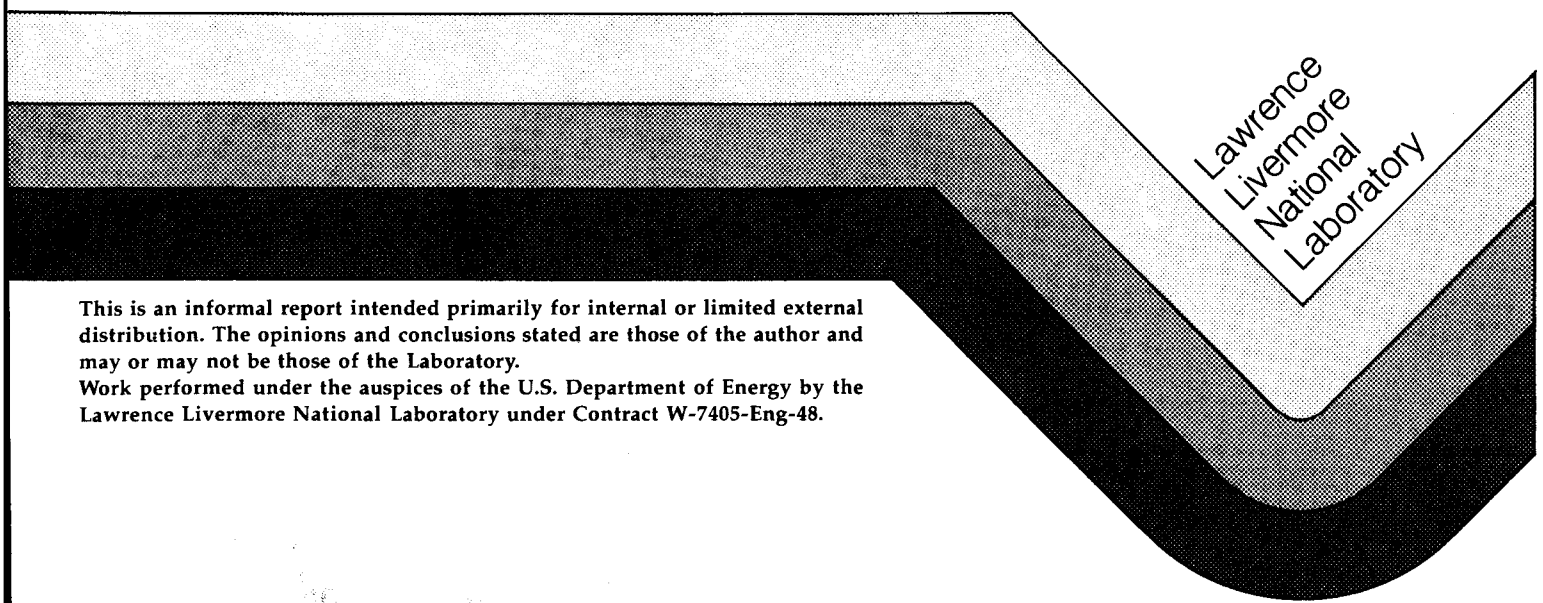
UCID- 21497

Toxicology Study of the High-Energy Plasticizer FEFO

Peter M. Swearengen
James S. Johnson

March 1989



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EXECUTIVE SUMMARY:

This document contains information on the high energy plasticizer FEFO (1,1'-[Methylenebis(oxy)]bis[2-fluoro-2,2-dinitroethane]). It includes interview comments from thirteen known users of the chemical through December, 1987. Included as appendices are other reference documents on FEFO. The first of these, Appendix A, is a survey on worker experiences with FEFO conducted by Horst G. Adolph of the Naval Surface Weapons Center (NSWC). Appendix B is a toxicology screening study of FEFO conducted for LLNL in 1968 by Aerojet General. Appendix C is a material safety data sheet on FEFO from Aerojet Strategic Propulsion Company of Sacramento, California. Appendix D is a Rocketdyne internal memorandum on personnel hazards associated with FEFO. Appendix E is a series of excerpted pages from a formerly classified document at the China Lake Naval Weapons Laboratory. The pages were given to LLNL by Dr. Russell Reed of that facility. Appendix F is a file on medical treatment associated with FEFO exposure that was given to Dr. Milton Finger of LLNL by the Aerojet Corporation in 1972.

The interview comments and the appendices of related information on FEFO were provided to the LLNL Health Services Department along with Industrial Hygiene recommendations from the Safety Science Group. The response of the Health Services Director is included in this document as a preface. Taken together, the document and the medical observations provide a summary of information and recommended guidance for the safe handling of the high energy plasticizer FEFO. The material is believed to be quite biologically active by all observers. It is also believed that by correct use of strict industrial hygiene controls it can be used in large amounts with relative safety.

Interdepartmental letterhead

Mail Station L 423

Ext. 27459

HEALTH SERVICES DEPARTMENT

March 23, 1988

M E M O R A N D U M

TO: Peter Swearengen

FROM: Peter Wald PW

SUBJECT: Review of Toxicology Survey on FEFO

I have reviewed the material that you sent me on FEFO. This material includes:

1. Interviews with lead people at different DOD and DOE facilities who have handled relatively large amounts of FEFO in the past.

2. A toxicologic screening study of FEFO dated September 5, 1968 which was prepared by Aerojet General Corporation.

3. MSDS from Aerojet Strategic Propulsion Company.

4. A document from Dr. Russell Reed at China Lake NWL on toxicity and handling of FEFO.

On reviewing this material, it is obvious that FEFO is a very biologically active compound. Animal experiments and human exposure data support its classification both as a lung and skin sensitizer, and as a skin vesicant. With all the personnel interviewed, it seems apparent that there were problems associated with this compound when workers handled it in an unprotective manner.

Personnel seemed to be able to use and handle large quantities of this compound if appropriate industrial hygiene and personal protective measures are taken.

Based on the material that you provided me, I agree with your impression that "when good work place practices are carried out, FEFO can be manufactured and handled safely." I would add to this recommendation that the following practices be followed when handling FEFO:

FEFO could be thought of as a compound similar to isocyanates, with the same general health effects. Safety glasses or face

shields, gloves and aprons should always be worn when handling FEFO. Whenever possible this material should be handled in the presence of adequate industrial ventilation to minimize worker inhalation exposure. When these compounds cannot be handled in an enclosed setting, it would probably be appropriate to use a respirator with the appropriate cartridge. A full face respirator could certainly be substituted for half face respirator and safety glasses, and may be a more appropriate way to protect workers in light of the experience on accidental instillation of FEFO into the eye. If a worker becomes sensitized to this compound, it may be necessary to completely remove them from exposure. Skin contamination should be treated in usual fashion by flushing the area with water. All exposure, either dermal or inhalation, should be immediately evaluated by medical.

If these above recommendations are followed, I believe that this compound can be used with relative safety in large amounts, provided that strict industrial hygiene controls are utilized.

PW/bjp

Interdepartmental Letterhead

Mail Stop 386

Ext. 2-5230

January 26, 1988

TO: Ken Scribner

FROM: Pete Swearengen

SUBJECT: Toxicology Survey on FEFO

We have completed an investigation on FEFO using the information you provided. Our findings are included in the attached report. We call your attention to Appendix E which was provided by Russ Reed. These are excerpts from an originally classified document. That document described FEFO as "super-toxic." The Aerojet toxicology study of 1968 clearly supersedes that document, but opponents may disagree. As a result, we have attached a list of five recommendations that you can pursue if you see the need.

Peter M. Swearengen

Peter M. Swearengen
Safety Science Group
Hazards Control Department

PMS:beb

Enclosures:

TOXICOLOGY SURVEY ON FEFO

AUTHORS: Peter M. Swearengen and James S. Johnson
Phone: 415-422-5230

The purpose of this investigation was to determine if there is an observable pattern of harmful effects from exposure to FEFO (1,1'-[Methylenebis(oxy)]bis[2-fluoro-2,2-dinitroethane]). We conducted a survey of people who were known to have worked with the chemical. From each person we tried to determine if there had been any occurrence of harmful effects, and if so, what the specific exposure had been, and what the effects were. A similar type of survey done by Horst Adolph at the Naval Surface Weapons Center in March, 1987, is included as Appendix A.

A Material Safety Data Sheet on FEFO from Aerojet Strategic Propulsion Company is included as Appendix B. A toxicology screening study of FEFO done for LLNL in 1968 by Aerojet-General Corporation is included as Appendix C.

We discussed toxicologic effects of FEFO with personnel at several institutions: Aerojet Strategic Propulsion Co., Sacramento, CA; China Lake Naval Weapons Test Station, China Lake, CA; Holston Army Ammunition Plant, Kingsport, TN; Lawrence Livermore National Laboratory, Livermore, CA; Naval Surface Warfare Center, White Oak, MD, and Indian Head, MD; Pantex, Amarillo, TX; and Rocketdyne Division of Rockwell International Corp., Canoga Park, CA.

Rocketdyne has had extensive pilot plant experience with FEFO, having made in excess of 30,000 pounds of the material. Aerojet has used the majority of that material in propellant development and so has had extensive experience in handling FEFO. Holston produced 50 to 100,000 pounds of LX-09 powder containing FEFO. Pantex provided processed raw material for the Holston production. Quantities at the other facilities have been limited to the research and development category.

Conclusion

A wide variety of workers and researchers have been interviewed with reference to FEFO. Reported individual symptoms of exposure vary. Several individuals appear to have been sensitized from exposure to FEFO. Large scale production of FEFO using standard workplace controls has not created any unusual outbreak of sensitization in workers.

Recommendations:

We recommend that an occupational physician (e.g., Dr. David Disher, LLNL) review the findings of this study. That person may choose to contact some of the people interviewed and ask further questions.

At your discretion, additional contacts could be made with personnel identified in this study to further evaluate their manufacturing experience.

Further acute animal toxicology studies should be considered to better characterize the material. You may want to have such information on a carefully purified sample of FEFO.

WE recommend that you carry out a glove permeation study of FEFO and "FEFO-Sol" to determine the best personnel protective equipment.

A final evaluation of the risk in handling FEFO should be made after the occupational physician has reviewed the file. Our initial impression is that when good workplace practices are carried out, FEFO can be manufactured and handled safely.

Aerojet Strategic Propulsion Company, Sacramento, CA.

Product: MX Propellant

Interview:

Ann Houston, Manager, Chemical Products
Phone: 916-355-4559

Ann Houston discussed FEFO with several chemists at Aerojet who told her that they had observed occasional contact dermatitis in some individuals from FEFO. They had also seen dermatitis result from apparent vapor exposure at elevated temperatures. Ann provided a Material Safety Data Sheet on FEFO, and a copy of an Aerojet internal memo on personnel exposure hazards from FEFO. A copy of the memo is included as Appendix D.

China Lake Naval Weapons Test Station, China Lake, CA

Interviews:

May Chan, Chemist, phone conversation 16 Nov., 1987.
Phone: 619-939-3381.

May Chan said that she had experienced no problems associated with FEFO during the time she worked with the material.

Dr. Russell Reed, Chemist, phone conversation, 17 Nov., 1987
Phone: 619-939-7248, 7341.

Dr. Reed said that he had worked with FEFO on a regular basis from 1980 to 1983. During that time he conducted experiments on the average of two days per week. The work then tapered off over the next three years. His function consisted of making small (30g) samples of PBX type material, and curing them in a vacuum oven at 55 C. A typical batch would consist of 30% FEFO, 60% HMX, and 10% polymer (typically CAP or NMMO). He also purified batches of FEFO (200 to 300 g) through silica gel, added carbon black, and would sparge solvent from the purified batch. He considers FEFO to be an excellent ingredient for PBX products. Russell said he experienced no symptoms from FEFO, but added that he was very careful when working with it. He always handled it in a fume hood, and if he got a small drop on his hand he would immediately wash it off. He said that he has allergies, and was aware of reported reactions to FEFO when he began to work with it. On several occasions he handled the plastic material without gloves. He searched his own files on the material and sent an internal document to LLNL (see appendix E).

Dr. Reed suggested we contact Dick Lou (916-355-3257), Adolph Oberth (916-355-3257), and Rolf Bruner (916-355-4708) of Aerojet, Sacramento, and John D. Braun (619-355-3257) of China Lake, for further information on the material. He said he believed that Carl Gotzmer of NSWC, Indian Head, Maryland, had experienced symptoms from handling FEFO (see Gotzmer interview).

Holston Army Ammunition Plant, Kingsport, Tenn.

Product: LX-09

Interviews

J.T. "Buck" Rogers, phone conversation, 7 Dec., 1987.
Phone: 615-247-9111

Buck said he was a chemist by training and worked with this material as a solution in ethyl acetate during a process development period about 1970. He continued the development into the production phase and had responsibility for all aspects of manufacture and chemistry of FEFO at Holston. He described the process as being conventional, where a mixture containing FEFO was added as a lacquer and then solvent was stripped off.

He said that Holston had received a copy of the toxicity study on FEFO prior to production and had conducted medical surveillance throughout the time of use of the material at the plant. Standard protective equipment for factory workers includes coveralls, safety shoes, hats and goggles. For work with FEFO, gloves were added to the required wear. During the drying procedure, respirators were worn by personnel in the immediate area.

He said that the experience at Holston showed no problems with use or manufacture of material containing FEFO. One man had experienced dermatitis during early development of the process, but medical authorities attributed it to heat rash, since it was hot and humid at the time of the rash (summer).

Don Mehaffee, production superintendent, phone conversation, 18 Nov., 1987.
Phone: 615-247-9111

Sam Wright, phone conversation, 12 Nov., 1987.
Phone: 615-247-9111

Both people referred me to Buck Rogers, and both stated their knowledge included one "suspect" case, of a nonclusive nature, out of large numbers of workers with the material.

Lawrence Livermore National Laboratory, Livermore, CA

Interview:

Erica Von Holtz, Chemical engineer, interview, 18 Nov., 1987.
Phone: 415-422-6387.

Erica said she was working with a solution of "FEFO-Sol", which is 30% FEFO in ethyl acetate. She was washing the material with dilute base when it spilled onto the bench top. She cleaned up the spill and then washed her hands. The time until she washed off her hands may have been up to 5 minutes. The following day she developed a rash on her hands and up the length of her arms. She also developed the same rash in the lower waist area. Symptoms lasted for several days before the rash bumps subsided. Prior to that time she had not worn gloves while working with the material. She now wears gloves. Prior to this direct contact exposure, she had experienced no problem with the material while working with it over a period of some months. Erica continues to work with FEFO, and has experienced no subsequent problem. She believes the FEFO she contacted during the spill was quite pure.

Ray McGuire, Chemist, phone interview, 23 Nov., 1987.
Phone: 415-422-7791

Ray said that he has always worn gloves while working with FEFO. He said that 15 or 20 years ago (before he came to LLNL) he was exposed to a mixture of FEFO in methylene chloride when a flask broke and the material went all over his body. A rash followed that exposure about 24 hours later, and lasted for 2 or 3 days. Since then he has been much more sensitive to FEFO. Ray said he develops a rash if he enters a room where FEFO is exposed to the atmosphere. He believes that the FEFO which spilled on him was quite pure.

Naval Surface Warfare Center (NSWC), White Oak, Md

Interviews:

Bob Gill, Explosives Researcher, phone conversation, 17 Nov., 1987.
Phone: 301-743-4853.

Bob said that he had worked with the material in his laboratory at the Naval Ordinance Station in Indian Head, Md. (NOS-IH), for 4 to 5 years without any problem. Then he conducted a vaporization rate study in a fume hood that had poor ventilation. He was near the hood during this study. Since that time his face will get tender and tingle for several hours when he is present in a room with FEFO. Bob said that he had worked with purified material from China Lake prior to the vaporization rate study.

Personal interview, 15 Dec., 1987.

Bob said that the vapor exposure he suffered occurred during the early 1980's. He had not used a respirator prior to that time, but he had used standard issue [sic] gloves, and had conducted his work within a fume hood. The vapor exposure occurred during the vaporization rate study, when the material was heated to 60 C. He did not wear a respirator during the study, which was of one or two days duration. He experienced no contact dermatitis and no chemical burns during his work with FEFO.

Bob listed the following symptoms that he believes were caused by this vapor exposure: A general feeling of weakness and fatigue following exposure to FEFO. This occurs during the course of a day where he has been exposed, and is followed by general feelings of irritability. During the night he will often awake with symptoms of anxiety and mental stress. The symptoms usually clear up by the following morning. Bob stated that this syndrome is a repeatable event. He added that he now feels a tingling around his mouth and lips when he enters a room where FEFO is open to the atmosphere, and that the tiredness will also come over him soon after such exposure.

He went to the medical department for a physical due to these symptoms, and believes that FEFO started a series of physical debilities that he continues to suffer (most notably general weakness and fatigue). He also

believes that FEFO caused him to suffer from anxiety which he continues to experience. Bob has stopped work with FEFO since these problems began, but he believes that the symptoms he experienced are due to cumulative effects which are of an insidious nature. There is no medical record associated with Bob Gill's experience with FEFO. Bob has had a congenital heart valve condition since his youth, but he does not believe this condition to be the cause of his symptoms.

Bill Lawrence, Chemist, phone conversation, 17 Nov., 1987.
Phone: (FTS)8-394-2305.

Bill said that he had done analytical work on FEFO many times. He said that after working with the material over the course of a day, he would experience itching on skin areas such as face, nose and legs. He said that now he experiences an itching skin when present in a room with the material. The material he had worked with was from Aerojet and was quite pure. He had also analyzed material from Rocketdyne that was in a solvent.

Carl Gotzmer, Technical Group Leader, Propellants and Explosives formulation; Personal interview, 15 Dec., 1987.
Phone: 301-743-4853.

Carl said that he has had very limited exposure to FEFO, that he has never worked with it in the laboratory, and that he has never suffered any reaction from exposure to FEFO. He has formed his opinions on the material from observations of the problems of his associate Bob Gill, and from discussions with Leo Asoka, a chemist formerly in his group at NSWC. (Leo had worked extensively with FEFO for several years at a division of Lockheed in Redlands, CA, during the late 60's). Carl has also talked with other explosives researchers about FEFO. He believes that FEFO can affect the nervous system [sic; apparently central nervous system], and that exposure can induce paranoia. Carl is particularly opposed to large scale production of FEFO containing materials. His extensive observations of explosives production at the Naval Ordinance Station (Indian Head, MD) lead him to believe that there would be significant exposure to FEFO for large numbers of personnel.

Leo Asoka, phone conversation, 17 Nov., 1987.
Phone: Was same as Bob Gill, has since left NSWC, contact Carl Gotzmer for further information.

Leo worked with FEFO as a chemist at Lockheed (Redlands, CA) for two or three years during the late 1960's. He said he was doing preparative scale column treatment of the material with solvent to purify it for processing into propellants. He said he handled large amounts of the material and the solvents and that no precautions had been taken or recommended at this facility for use with FEFO. He said he experienced headaches, irritability and allergic problems [sic], which he described as skin irritation or contact dermatitis. He also experienced bleeding gums while he worked with FEFO. He believes his problems came from impurities within the FEFO, because he experienced them during the purification process, and not during the subsequent formulation procedures. Leo left Lockheed in 1973 when the facility closed down. He did not associated his symptoms with FEFO until he came to work at the NSWC-NOS-IH facility where he talked with Bob Gill. He said that he recalled a high absentee rate at Lockheed in his section which he now believes could have been due to symptoms from working with FEFO.

Pantex, Amarillo, Tx.

Interviews:

A.C. Teter, Chemist, Synthesis Section Head, phone conversation, 17 Nov., 1987.
Phone: (FTS) 8-477-3521.

A. C. Teter said that he had worked intermittently with small quantities of FEFO (on the order of several ounces or less) during a development project of about one year. He said that he somehow contacted the material with his hand and then rubbed his eye. As a result he experienced severe eye irritation soon afterwards and his eye nearly swelled shut. Following that experience, he was more cautious when handling the compound. He has experienced no further symptoms, but has used the product very little.

Gordon Osborne, Chemist, phone conversation, 9 December, 1987.
Phone: (FTS) 8-477-3592.

Gordon said that Pantex had made large amounts (55 gallon drum quantities) of LX-09 for the Holston plant during the early 1970's. They had also worked with small quantities infrequently since that time for various development projects. Gordon has experienced no symptoms from working with FEFO. He said there are written safety procedures in the Pantex methods for use of the material and that current practice is to wear gloves and discard them after each day's use.

Gordon also said that one man had irritated his hands while handling FEFO. This man (Nelvin Friday) had experienced clear blisters in several spots on his hands while making an extrudable test explosive on a development project. Gordon added that the Pantex use of FEFO had never been with neat material, but in this case had involved "FEFO-Sol". Other personnel had worked with the material and experienced no problems. (John Short, since retired).

Rockwell International Corp., Rocketdyne Division Canoga Park, CA

Product: FEFO

Interview: at Rocketdyne, FEFO pilot plant, Canoga Park, CA, 1 Dec., 1987.

Dr. Milton Frankel, Chemist.
Phone: 818-710-4803

Dr. Frankel said that his pilot plant has manufactured in excess of 30,000 pounds of FEFO since about 1969. The process is conducted at room temperature, with significant volumes of liquid transfer for column purification and drum loading. During operation of the plant, 4 to 6 people are involved directly with production of FEFO. I spoke with four of these individuals who said that they have no problem with the material when normal precautions are taken.

Current practice is to wear a laboratory coat and two pairs of Pioneer "Stansolv" gloves. (Model A-15 nitrile). The gloves are discarded after each use. The only routine eye protection is corrective eyeglasses. Workers in the pilot plant area may wear a face shield.

When a spill occurs, the lab coat is immediately removed if it contacts FEFO, and also any clothing that touches the material. Any affected skin areas are washed with copious amounts of water.

Dr. Frankel said that in the history of the pilot plant operation (which he started), only one person was sensitized to a precursor of FEFO, i.e. FDNE (Clarence Ackerman, a mechanic working in the pilot plant). This statement appears to conflict with the document received from China Lake (AFRPL, -0047/5/2-786, p.5, April 15, 1971). This document indicates that medical personnel at Rocketdyne at that time were familiar with chemical burn problems associated with FEFO.

Appendix A

Survey of Worker Experiences with FEFO
(Horst G. Adolph, Naval Surface Weapons Center)

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3 Mar 87

MEMORANDUM

From: R10D

Subj: SURVEY OF WORKING EXPERIENCES WITH FEFO-CONTAINING COMPOSITIONS (WITH RESPECT TO HEALTH HAZARDS)

1. FEFO [bis(2,2,2-fluorodinitroethyl)formal], because of its high energy, is a desirable component of high-energy PBX's such as PBXW-119, scheduled for advanced development in the near future. We are in the process of buying several hundred pounds of it, and presumably there will be a significant amount of formulation work with it.

2. During recent work with FEFO containing compositions I encountered a number of people at NSWC who voiced concern about possible health hazards associated with this material. There is, indeed, at least one recent, indisputable case of personnel incompatibility with FEFO at NSWC (Bob Gill). Since more than 25,000 lbs of FEFO were manufactured and processed in industry and DOE facilities in conjunction with LX-09 explosive and MX propellant development, I decided to contact most of the organizations involved in these programs to sample their actual experiences with FEFO during approximately the past 20 years.

3. Rocketdyne Division of Rockwell International produced almost all of the FEFO made in the U.S. According to Dr. M. B. Frankel (818-710-4803), they encountered, over a 20 year period, one case of allergic response to FEFO which necessitated reassignment of the affected person to a FEFO-free area. Aerojet Solid Propulsion Company used the majority of the FEFO produced for MX propellant development. Dr. R. Lou (916-355-5578) stated that they encountered no serious health problems during their work with FEFO other than occasional skin rashes caused by direct contact (personnel not wearing gloves, for example). He expressed the opinion that FEFO could be handled safely with normal safety precautions. He pointed out that they had an explosion when a substantial quantity of neat FEFO was combined with 13A molecular sieves, due to the exotherm generated. In another incident, a plastic bottle containing neat FEFO ruptured after long exposure to sunlight. Holston produced 50-100K lbs of LX-09 molding powder. Mr. S. Wright (615-247-9111) indicated that he was not aware of any health problems caused by FEFO, which they handled only in solution. Pantex personnel pressed and machined LX-09 and were also involved in warhead assembly and demilling. Messrs. G. Osburn and E. Henke (806-381-3592, 3981) did not recall any problems but stated that all personnel wore normal protective clothing. LLNL developed LX-09 and other FEFO-containing formulations. Mr. K. Scribner (415-422-7796) stated that there were no problems during the LX-09 program. However, they had a recent case of accidental exposure to a FEFO solution which resulted in a skin rash extending over much of the body. Apparently this did not result in sensitization, as the person involved is still working with FEFO (wearing two pairs of gloves). R. McGuire, before joining LLNL, accidentally poured FEFO over his legs and feet. This resulted in a serious and widespread skin inflammation. He is very sensitive to direct contact with FEFO since that time, but can still work with it with proper protection.

3 Mar 87

Subj: SURVEY OF WORKING EXPERIENCES WITH FEFO-CONTAINING COMPOSITIONS (WITH RESPECT TO HEALTH HAZARDS)

4. I conclude from this survey that FEFO can be used safely in Navy PBX's provided that certain precautions are taken whenever personnel are exposed to FEFO in the condensed or in the gas phase. Adequate ventilation of the workplace and proper disposal procedures for FEFO-containing materials are essential. Above all, direct skin contact with any FEFO containing material is to be avoided.

HORST G. ADOLPH
Synthesis & Formulations Branch

Distribution:
R10
R101
R10B
R10C
R11
R11 (L. Asaoka, H. Fillman, R. Gill, W. Gilligan, C. Gotzmer, N. Johnson, W. Lawrence, J. Leahy, W. Thomas, K. Wagaman)

DEPARTMENT OF THE NAVY
OFFICER IN CHARGE
WHITE OAK LABORATORY
NAVAL SURFACE WEAPONS CENTER
10901 NEW HAMPSHIRE AVENUE
SILVER SPRING, MD. 20903-5000

Appendix B

Toxicology Screening Study for FEFO
(Aerojet General)

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UCRL-13372

TOXICOLOGY SCREENING STUDY OF FEFO

5 September 1968

UNIVERSITY OF CALIFORNIA
LAWRENCE RADIATION LABORATORY
LIVERMORE, CALIFORNIA

By

B. J. Mechalas and P. H. Allen

(Prepared Under Purchase Order No. 2798307
By The Chemical and Biological Processes Department
Environmental Systems Division, Aerojet-General Corporation
El Monte, California)

AEROJET GENERAL

SPACE DIVISION

I. INTRODUCTION

To establish criteria for the safe handling of the high energy plasticizer FEFO, bis(2, 2-dinitro-2-fluoroethyl)formal, adequate information regarding its toxic properties is necessary. This report presents toxicology data gathered from a series of experiments on the pure compound alone and mixed with its handling solvent, ethyl acetate. Conclusions are reached regarding safe handling procedures for both compounds.

The experiments performed were determinations on intraperitoneal 14 day LD_{50}, reactions to acute and chronic exposures of skin and eyes, and examination of inhalation toxicities. Animals used in experimentation were mice, rats, and guinea pigs. All experiments were conducted according to the "Principles of Laboratory Animal Care" established by the National Society for Medical Research.

A single sample of FEFO produced at Aerojet-General (Environmental Systems Division, Azusa, California) was maintained throughout the course of the experiments as stock. The sample represented a typical production material; its analysis is presented in Table I. The FEFO in ethyl acetate solution was obtained by mixing a portion of this stock with ethyl acetate (Union Carbide, 99. 5%, undenatured) to yield a concentration of 33. 3% FEFO by weight.

II. INTRAPERITONEAL LD_{50}

Determinations of the acute intraperitoneal (IP) LD_{50} levels, or the dose levels which are lethal to 50% of a population, of the two materials yield an overall indication of their systemic toxicities. This allows quantitative comparisons with more familiar hazardous materials.

Injections were performed on adult male mice of the CF-1 strain, weighing 25 to 30 grams. Corn oil was used as a diluent for both compounds, and dilutions of the compounds in corn oil were adjusted to maintain an injection volume of 0.2 to 0.6 cc throughout the dose range examined. Previous intraperitoneal injections of corn oil alone in this volume range had shown no effects on behavior or abdominal viscera. Animals were weighed to the nearest 0.1 gram, and were injected with an appropriate amount of diluted material to give the intended dose exposure. Treated animals were observed for a period of 14 days following injection. Using the method of Litchfield and Wilcoxon[1], LD_{50} values and 95% confidence limits were calculated from percent mortality results.

A. FEFO

Results from the IP injections of diluted neat FEFO are presented in Table II, and are plotted in figure 1. 100 Mice were injected. From these data, an LD_{50} value of 108.5 mg of compound per kg animal weight was calculated, with 95% confidence limits of 107-110 mg/kg. This value coincides reasonably well with a similar determination of 90 mg/kg (95% confidence limits 80-102 mg/kg) previously reported by R. P. Geckler.[2]

An earlier study reports a much lower LD_{50} value for FEFO injected intraperitoneally into male rats of the Charles Rivers[3] CD strain The injection diluent in this study was glycerol. The discrepancy between the earlier study result and those of the later two can be attributed to differences in animal species and injection diluent, and possibly to different levels of impurities in the FEFO samples tested. Average time-to-death and premortem symptoms were also notably different in the earlier study.

With an intraperitoneal LD_{50} toxicity of 108, FEFO can be classed as "very toxic." Probable lethal dose for a 70 kg (150 lb) man would be from a teaspoonful to an ounce. In general, a clinically significant illness may be expected after doses of about one-tenth the probable lethal dose.[4] Mouse intraperitoneal LD_{50} values of more common materials in the same toxicity range are:[5]

Benzedrine	101 mg/kg
Sodium Fluoride	125 mg/kg
Hydrazine	163 mg/kg

Mice injected with lethal doses of FEFO showed mild immediate reactions to the treatment. The injections generally induced lethargy, irregular raising of the fur, and apparent responses to general abdominal discomfort of stretching and licking of the abdomen. Average time-to-death was about two days, with a continuous progression from initial lethargy to immobility and total lack of response to any stimulus immediately prior to death. Terminal stages were usually marked by regurgitation of stomach contents. As shown in figure 2, there was little correlation between dosage leval and time-to-death.

Pathological examination of viscera from mice given lethal intraperitoneal doses disclosed a general contact or chemical peritonitis, as differentiated from a purulent peritonitis caused by a bacterial infection. The inflammation is marked by patchy subcapsular necrobiosis of liver cells and superficial necrosis of peritoneal fat with associated infiltration of neutrophils. Moderate conjestion of the lungs, liver, kidneys, and spleen was also noted. There was no apparent evidence of specific tissue effects of sufficient magnitude to cause death of the animal. In view of the lipid solubility of FEFO and its effect on diffuse peritoneal fat necrosis, some involvement of the central

nervous system, which has high lipid content, may be postulated. Considerably more extended experimentation would be necessary to further examine the specific action of FEFO's toxicity.

B. FEFO IN ETHYL ACETATE

Results from the IP injections of the 33.3% FEFO, 66.7% ethyl acetate mixture in corn oil diluent are presented in table III, and are plotted in figure 3. 120 Mice were injected. From the results, an LD_{50} value of 198 mg/kg was calculated, with upper and lower 95% confidence limits of 288 and 137 mg/kg, respectively. Since these IP exposures were carried out under procedures identical to those used in the diluted neat FEFO tests, the greater scattering of data as illustrated in figure 1 and by the wider 95% confidence limits indicates a greater variation in individual animals' susceptibilities to FEFO in ethyl acetate.

The LD_{50} value of 198 mg/kg for the mixture yields a concentration of 66 mg/kg (95% limits: 96-46 mg/kg) neat FEFO at LD_{50} dosage. This value is significantly lower than the 108 mg/kg toxicity level of FEFO alone. Since ethyl acetate alone is only "slightly toxic," with a reported subcutaneous and oral LD_{50} value of 3000-5000 mg/kg,[5] some synergistic effect of the two components is indicated. At the FEFO proportion tested, however, FEFO in ethyl acetate is slightly less toxic than the neat material. FEFO in ethyl acetate still fits into the "very toxic" classification, and probable lethal dose for a man would be roughly the same as that of FEFO alone, or a teaspoonful to an ounce.

Mice injected intraperitoneally with significant doses of the FEFO-ethyl acetate mixture in corn oil showed immediate responses identical with

those of mice injected with FEFO alone in corn oil. Average time-to-death was two to three days, and as with FEFO alone, there was no correlation between dose level and time-to-death.

Pathological examination of viscera from mice exposed to lethal intraperitoneal levels of the FEFO-ethyl acetate solution yielded much the same results as those obtained from tissues exposed to FEFO alone. Effects were a low grade chemically induced peritonitis associated with diffuse mesenteric fat necrosis and capsular inflammation of the liver and spleen.

III. SKIN AND EYE EXPOSURES

Body surface exposures to hazardous compounds constitute one of the most common modes of exposure in an industrial environment. Information on this route of a compound's toxicity is essential before safe handling procedures can be recommended.

Exposures of skin and eye tissues to the two test compounds were carried out on near-albino* adult female guinea pigs weighing 300 to 375 grams. An individual guinea pig was subjected to one type of exposure only, and tests were carried out in duplicate.

Acute and chronic exposures of a closely clipped flank region were examined, a skin area selected as being suitably sensitive while not subject to extensive physical irritation. Acute exposure was a single direct application of 0.1 cc of undiluted test compound, while chronic exposures of 0.1 cc were made once daily (excepting weekends) for a period of two weeks, hence ten repeated doses. Bandages over affected skin areas were ruled out due to

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*White, pink-eyed, guinea pigs displaying slight pigmentation about the ear tips and feet.

previous experience with their rejection by the animals. Animals were observed for a minimum of two weeks following the single or final application, or as necessary until complete recovery from damage.

Acute eye exposures were made dropwise directly to the corneal surface. A volume of 0.1 cc of undiluted test compound was used, sufficient to slightly overfill the conjunctival sac. Animals were again observed for two weeks or until recovery.

A. FEFO

1. Acute Skin Exposure

Within 24 hours after the single application of 0.1 cc neat FEFO, a distinct erythema or rash, directly corresponding to the application area, had developed in both animals. 48 hours following the application, the erythema was severe (beet red) and accompanied by moderate edema, or swelling of the rash area. One week following exposure, eschar (scab) formation was noted in both animals. By ten days eschar sloughing had begun, and by two weeks hair regeneration was noted on the newly exposed skin. Complete hair regrowth by four weeks indicated a relatively superficial effect of the compound. Daily animal weight records showed a continuous normal gain over the two week post-exposure period, also implying the absence of any major systemic effect.

Two previous reports[2, 6] approximately substantiate these results, while a third study[3] noted no skin effect. Since this same study yielded the previously discussed low intraperitoneal LD_{50} value, it is probable that FEFO concentration and impurity concentrations were different in this earlier material.

2. Chronic Skin Exposure

Initial 48 hour responses to neat FEFO applications mirrored those of the acute exposure animals. By three days, however, a small open wound in the application area became apparent on animal A. Eschar formation was severe in both animals by the fourth day, and sluggish behavior with no stimulus response was noted. By the fifth day, both animals exhibited very labored breathing and considerable mucous drainage from nostrils and mouth. Animal B died on the sixth day. Continuous weight loss by animal A was noted throughout the two week application period and for two subsequent weeks. By two weeks (final application), partial immobility of the left or exposed side limbs was evident, probably due to the severity of the wound, which now encompassed a large area. Recovery of the animal was very slow, involving severe sloughing of damaged skin from the left flank and limbs, and loss of toes from the left side limbs at about five weeks. Weight gain was noted from the fourth to the sixth weeks, at which time the animal was sacrificed for examination.

Pathological examination of animal B (death at six days) disclosed only a marked chronic cellular reaction consistent with response to severe repeated irritation. Extensive edema and large areas of alveoli filled with neutrophils and fibrin, symptoms of pneumonia, were found in the lungs. The conclusion reached was that the animal had been debilitated by the treatment and had succumbed to a complicating pneumonia. Examination of the rib cage and viscera of animal A indicated nonspecific chronic inflammation of the skin, with no significant systemic effects, findings consistent with those of animal B. Results of the repeated applications gave

no evidence of a sensitization or allergic reaction. Instead there appeared to be a cumulative response, with severity proportional to duration of exposure.

3. Acute Eye Exposure

Neat FEFO delivered to one eye of each test animal produced an immediate response of inflammation of the conjunctiva and prolonged lacrymation. The lids of the eyes were visibly swollen by 24 hours, and were completely closed by three days. By the second day, the cornea of one test eye was opalescent, with no details of the iris remaining visible. Swelling began to subside on the fourth day, and by one week the opalescent cornea had begun to clear. Total recovery of both eyes was complete by two weeks, and included loss and regeneration of affected skin and hair surrounding the eyes.

As pointed out in the discussion of acute skin exposure to neat FEFO, variation exists in previously reported effects on eye tissue. These results range from significant eye damage to complete lack of irritant response.[6, 2, 3]

B. FEFO IN ETHYL ACETATE

1. Acute Skin Exposure

Twenty-four hour response of the two test animals to application of 0.1 cc of undiluted FEFO-ethyl acetate solution was similar to that with neat FEFO, but somewhat milder. The erythema formed became severe at two days, with accompanying mild edema. Eschar formation was noted at one week, followed by sloughing at ten days and hair regeneration starting at two weeks. As before, continuous normal weight gain was recorded through the testing period.

2. Chronic Skin Exposure

Initial (two days) inflammation of the application sites on the two animals given FEFO in ethyl acetate was somewhat milder than that noted in animals receiving applications of neat FEFO. By three days, however, the same apparent severity of eschar formation, with small open wounds, was found. Progression of damage was subsequently identical, with sluggish behavior and mucous drainage from nose and mouth at four days, and labored breathing at five days. This condition cleared in one animal by two weeks. The second animal died during the weekend following the second week. Unfortunately, decomposition of the body had too far progressed by the following Monday to allow meaningful pathological examination. Appearance of the animal prior to death would seem to indicate a complicating secondary pneumonia, the evident cause of death of one of the previously discussed guinea pigs given repeated neat FEFO applications. Weight gain by the first guinea pig began at three weeks, and at four weeks regeneration of skin and hair in the application region was progressing well. Again no allergic response was noted to repeated applications of the test compound, but effects appeared to be cumulative.

3. Acute Eye Exposure

Delivery of 0.1 cc of the 33% FEFO-ethyl acetate mixture to the one eye of each test animal produced a response distinctly milder than that to neat FEFO. Immediate lacrymation and mild inflammation of the conjunctiva were apparent, but by two days the eyes were visibly normal. Some slight sloughing of surrounding lid skin was noted in one animal, but by one week no evidence of the exposure remained.

C. GENERAL DISCUSSION OF SKIN AND EYE EXPOSURE RESULTS

Concurrent tests of ethyl acetate alone were run using the same procedures described for FEFO and the FEFO-ethyl acetate solution. These exposures produced no skin response and only brief mild lacrymation of the eye. Repeated skin applications produced no sensitization reaction. Based on this information and that previously discussed, it is apparent that the ethyl acetate in the FEFO-ethyl acetate solution plays a significant role in skin and eye toxicity only as a diluent. No evidence of ethyl acetate acting either as a synergistic agent or as a buffering agent was found. In all cases exposure of surface tissues to FEFO in ethyl acetate produced a similar response to that of neat FEFO exposure, but to a lesser degree. Response seemed proportionate to the amount of FEFO applied. This response can be generally compared with the effects of exposure to a moderately strong inorganic acid or alkali solution.

IV. INHALATION EXPOSURES

Inhalation of vapors from hazardous compounds is another common mode of exposure. No previous reports on the toxicity of FEFO via the inhalation route have been found. Previous investigators relied on the low vapor pressure of the material to minimize the importance of inhalation studies.[3, 6] Since no vapor pressure values at ambient temperature have been reported, inhalation screening was deemed necessary for reliable industrial hygiene recommendations.

Adult male rats, of the Wistar strain weighing 200 to 250 g were selected as test subjects. Exposures of groups of five rats were made in a chamber which consisted of a horizontal glass bell jar measuring 32 x 45 cm, with a median stainless steel mesh floor and a Teflon covered end plate. A flow rate of 10 SLPM air through the chamber was selected. At this rate the CO_2

concentration in the chamber containing five active rats would be maintained below 1%, prohibiting effects which might be attributed to this material. Air flow and chamber temperature (21-23°C), were continuously monitored during test exposures. To minimize reactions with the test compounds, as much as possible of the tubing and equipment which came in contact with the test atmospheres was glass; a few connecting tubes were amber latex. All work was conducted under a fume hood, and due to the explosive nature of the compounds, behind double glass shields.

The air source for the tests was a compressed air purification system designed for Aerojet-General by Western Sales Engineers, Beverly Hills, California. The system passes air successively through a compressor, a water wash process, a refrigeration-drying unit, an activated carbon bed, and 0.65μ pore size Millipore* filter. Up to 10 SCFM purified air is available.

A. FEFO

In view of the evident low vapor pressure of FEFO, exposure to the maximum dose a worker might receive in an eight-hour work day was scheduled first. In the event of marked response to this, dosage would be reduced as necessary to define a threshhold of damage. Conditions were thus defined as an eight-hour continuous exposure to an atmosphere saturated with FEFO at ambient temperature.

Saturation of the 10 SLPM air stream was achieved by passing it through two small impingers in series, each containing 15 cc of neat FEFO, both immersed in a 50°C water bath. This was then passed into an air-cooled condenser coil, and from there directly into the chamber. The temperature

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*Millipore Filter Corp., Bedford, Massachusetts.

of the air exiting the condenser was 22°C, and a fine haze of condensed liquid on the walls of the first few coils of the condenser attested to the success of saturation.

To estimate the concentration of FEFO in this atmosphere, the air stream leaving the exposure chamber was split and bubbled in parallel, (to avoid excessively high gas flow through the trap) through two 300 cc round-bottom flasks, each containing about 150 cc of ethyl acetate. The traps were immersed in a 0°C water bath to minimize volatilization of the ethyl acetate during the eight-hour exposure.

An eight-hour control trial run of the entire system was made, without FEFO in the saturation device, and with five rats in the chamber. No problems were encountered, and the rats remained suitably active, exhibiting no adverse effects.

An eight-hour exposure of five rats to saturation of neat FEFO was then set up. The rats were placed in the chamber and subjected to 10 SLPM air without FEFO, to allow initial observation of behavior. The rats, after several minutes of investigation of the chamber, exhibited typical behavior of preening and squabbling among themselves. The FEFO saturation device was then placed in the system. After a short equilibration period, behavior changes in the animals became evident. At five minutes after the start of FEFO exposure, the rats had ceased squabbling, and were blinking their eyes as if exposed to an irritant atmosphere. At 10 minutes, deeper breathing was evident. The animals were listless and several were sleeping. At 30 minutes all animals were huddled together sleeping, with occasional restless movements. They appeared to be hypersensitive to physical contact. This behavior remained

unchanged throughout the duration of the eight-hour exposure. Intermittently various animals would arise and leave the group temporarily, at which time they exhibited a mildly staggering gait. At the termination of the exposure the rats' responses to transferral to their cages seemed dulled. By twenty-four hours post exposure, all symptoms had disappeared, and the animals appeared normal. All animals survived the two-week post-exposure observation period, at which time two were sacrificed for pathological examination.

The 300 cc of ethyl acetate contained in the two traps were combined, and the ethyl acetate stripped off in a vacuum distillation apparatus, leaving behind a viscous residue which weighed 48 mg. As determined by gas chromatographic analysis, this residue contained only 3.2 mg FEFO, the remainder probably consisting of organic wastes from respiration and perspiration of the animals. The reported ventilation rate of a resting rat is 0.100 liter air/minute.[7] At this rate, at least 95% of the atmosphere passing through the chamber was unaffected by significant contact with the animals. Thus the 3.2 mg of trapped FEFO must represent roughly the input of FEFO into the chamber. In eight hours, 4800 liters of air passed through the chamber, picking up 3.2 mg of FEFO, or the atmosphere was 0.051 parts FEFO by volume per million parts of air (ppm).

Using some of the above evidence, and assuming that 100% of the FEFO passing through an animal's lungs was assimilated by the animal, about 1% of 3.2 mg would have been taken up by each animal, or 0.032 mg. This becomes, at the most, a dose of about 0.13 mg/kg for a 250 g rat, well below any experimentally obtained intraperitoneal lethal levels.

Pathological investigations of lungs of rats exposed to eight hours of a saturated atmosphere of neat FEFO disclosed no marked differences from normal rat lungs which might be attributable to FEFO. Prolonged exposure to FEFO by the inhalation route thus has only a temporary mild narcotic effect, i.e., induces lethargy.

B. FEFO IN ETHYL ACETATE

An atmosphere saturated with FEFO and ethyl acetate would have required, for an eight-hour exposure, use of 4.71 kg or 10.4 lb of mixed compound, due to the high volatility of ethyl acetate. In addition, a concentration in air of 16,000 ppm ethyl acetate by weight, or 57.7 mg/l, has been reported lethal for rats in an eight-hour exposure.[5] In light of this information, conditions for inhalation exposure to FEFO in ethyl acetate were set at saturation of FEFO with sub-lethal concentration of ethyl acetate. The selected ethyl acetate concentration would be sufficient to cause a response by itself, ideally allowing the superimposed or synergistic effects of FEFO saturation to be evaluated.

Precise control of ethyl acetate concentration was established by injecting a metered flow of the liquid alone directly into the airstream, using a Harvard* syringe-type infusion pump. To ascertain a sub-lethal leval which produced adequate effect, two trial exposures of five rats to an atmosphere containing ethyl acetate alone were run. The test levels were 87 mg/liter and 35 mg/liter.

Two of the five rats continuously exposed to 87 mg/liter ethyl acetate died within two hours after start of the experiment, at which time exposure was terminated. Responses exhibited by all five of the rats were immediate

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*Harvard Apparatus Co., Dover, Massachusetts

lacrymation and signs of intoxication. At thirty minutes, the rats were comatose, responding to no external stimulation. Breathing became progressively deeper and more erratic until termination of the experiment. The surviving animals remained comatose for thirty minutes to two hours after being replaced in their cages.

Five rats were placed in the chamber and the infusion pump adjusted to deliver enough ethyl acetate to constitute 35 mg/liter. At fifteen minutes the animals were beginning to look sleepy, and exhibited mild lacrymation. By one hour all animals were sleeping, but responded to noise. At four hours, lung ventilation was noticeably increased, and intoxication was apparent in their responses to noise; at seven hours, panting was moderate. The exposure was carried to eight hours. All five rats awoke on being removed from the chamber, and exhibited no ill effects the following day.

Two weeks after the exposure, two of these animals were sacrificed for pathological examination. Findings were consistent with a pulmonary reaction to an inhaled irritant, including slight intra-alveolar hemorrhage and mild early interstitial pneumonia.

Based on these results, an exposure of five rats to an atmosphere of FEFO vapor saturation and 35 mg/l ethyl acetate was set up by installing the FEFO saturation device in the system, upstream of the injection site of ethyl acetate. Five rats were again placed in the chamber. Their responses to the FEFO-ethyl acetate combination were identical to those of the rats exposed to 35 mg/l ethyl acetate alone, and included hyperventilation and intoxication, as evidenced by their staggering gait. Again the rats had recovered completely by the following day.

Pathological examination of two of these rats sacrificed at two weeks again disclosed pulmonary responses to an inhaled irritant, which were identical to the reactions found with ethyl acetate alone. Prolonged exposure to combined FEFO and ethyl acetate vapors is thus considered only as hazardous as exposure to ethyl acetate alone.

V. AEROJET EXPERIENCE

The experience of Aerojet-General in the industrial hygiene and handling of FEFO has been extensive. In 1961, the Medical Department of the Azusa Facility developed a physician interview technique designed to obtain detailed information on the clinical effects of exposure to toxic materials. These interviews were held in the working area and covered (1) the employee's post occupational history; (2) the work history of the employee with Aerojet-General; (3) the degree of exposure to chemicals; and (4) the route, nature, and duration of exposure to the compounds under study, with observation of the protective equipment used. Six members of the Chemical Division who had greatest contact with FEFO were interviewed. Four of the six workers had experienced dermatitis ascribed to chemical exposure. In three of these four, a probable relationship was established between contact dermatitis and handling of FEFO or its precursor, FDNE. It could not be established whether FDNE or FEFO was implicated, since both compounds were handled concurrently. However, it is known that FDNE is a strong vessicant, while similar reaction to FEFO has not been observed. Rubber gloves were standard protective equipment at the time[8].

Recently, for more than two years, the Chemical Products Division has produced and handled FEFO in up to 250 pound lots, in various solvents. Quantities of up to 5 pounds have been handled as neat material. Approximately 12 employees have been intimately involved in pilot plant operation and in laboratory testing, under a variety of circumstances. Standard protective equipment constitutes lab coats or coveralls, rubber or plastic gloves, safety glasses, and face shield. In areas in which fumes from solvents or stored materials accumulate, air masks are provided and used. Use of protective wear in the production area is rigidly enforced. During this period there have been no known occurrences of dermatitis or intoxication attributable to exposure to FEFO. Semi-annual thorough medical examinations have disclosed no clinical abnormalities in these employees.

VI. SUMMARY AND RECOMMENDED HANDLING PROCEDURES

Neat FEFO has an intraperitoneal LD_{50} value in mice of 108.5 mg/kg. FEFO in ethyl acetate, 33.3% by weight, is only slightly less toxic with an LD_{50} value of 198 mg/kg. These ratings place the two compounds in a "Very toxic" classification, and point out the need for careful handling.

Exposures of guinea pig skin and eyes to FEFO and FEFO in ethyl acetate proved both compounds to be corrosive. There was no evidence that the compounds had penetrated the skin and affected any internal organs. Surface damage to both skin and eye was temporary, and recovery was slow but in most cases complete. Repeated application elicited no sensitized reaction to either compound. Again, the FEFO-ethyl acetate solution proved to be only a slightly less hazardous than the neat material.

Acute inhalation exposure of rats to maximal hazard eight-hour "work day" conditions, or eight-hour exposure to an atmosphere saturated with FEFO vapor, showed the compound to be mildly narcotic by this route. Exposure of rats to an atmosphere both saturated in FEFO and containing a sub-lethal concentration of ethyl acetate proved ethyl acetate to be the primary hazard; no synergistic effect was encountered.

Based on the above evidence and Aerojet-General's experience, safe handling procedures definitely involve the use of protective rubber gloves, goggles, and face shield. In the event of accidental skin spills, the affected surface should be thoroughly and immediately washed. Care should be taken to prevent any situations in which FEFO might be inhaled as an aerosol. Due to its low vapor pressure, occasional inhalation of FEFO vapor appears to be relatively non-hazardous. Inhalation of vapor from the FEFO-ethyl acetate mixture is potentially more hazardous, since ethyl acetate itself is toxic. Limits of industrial exposure to ethyl acetate have been well defined, and must be observed. The reported generally accepted maximum allowable concentration for daily eight-hour exposures is 400 parts ethyl acetate by volume per million parts of air (ppm).[9]

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3. Toxic Hazard Study of Selected Missile Propellants and Fuels,(U) Aerojet General Report No. 0466-01-2, 17 July 1961. (CONFIDENTIAL)

4. Toxic Hazard Study of Selected Missile Propellants and Fuels,(U) Aerojet-General Report No. 0466-01-5, 1 August 1962. (CONFIDENTIAL)

5. W. S. Spector, Handbook of Toxicology, Vol 1: Acute Toxicities, W. B. Saunders Co., 1956

6. New Energetic Binders for Solid Propellant Applications,(U) NOLTR 62-38, 5 April 1962. (CONFIDENTIAL)

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9. M. B. Jacobs, The Analytical Chemistry of Industrial Poisons, Hazards, and Solvents, Interscience Publishers, Inc., 1949.

TABLE I

GAS CHROMATOGRAPHIC ANALYSIS OF FEFO STOCK

Compounds	Peaks	Mole-%
Low Boilers	1	1.7
	2	0.2
	3	1.0
Intermediate Boilers	1	Trace
	2	0.2
	3	<0.1
FEFO	-	96.3
High Boilers	1	0.5
	2	<0.1
	TOTAL:	100.0

TABLE II

RESULTS OF IP INJECTIONS OF FEFO IN CORN OIL

Dose Level of FEFO (mg compound/kg animal wt)	Animals Injected	Mortality Ratio	% Mortality
100	15	6/15	40.0
110	15	8/15	53.3
120	15	9/15	60.0
130	15	10/15	66.7
140	15	11/15	73.3
150	15	13/15	85.6
160	10	9/10	90.0
TOTAL	100		

TABLE III

RESULTS OF IP INJECTION OF 33.3% FEFO/66.7% ETHYL ACETATE IN CORN OIL

Dose Level of FEFO-Ethyl Acetate (mg compound/kg animal wt)	Animals Injected	Mortality Ratio	% Mortality
150	15	5/15	33.3
180	15	6/15	40.0
210	15	11/15	73.3
240	15	14/15	93.4
270	15	9/15	60.0
300	15	12/15	80.0
330	15	9/15	60.0
360	15	14/15	93.4
TOTAL	120		

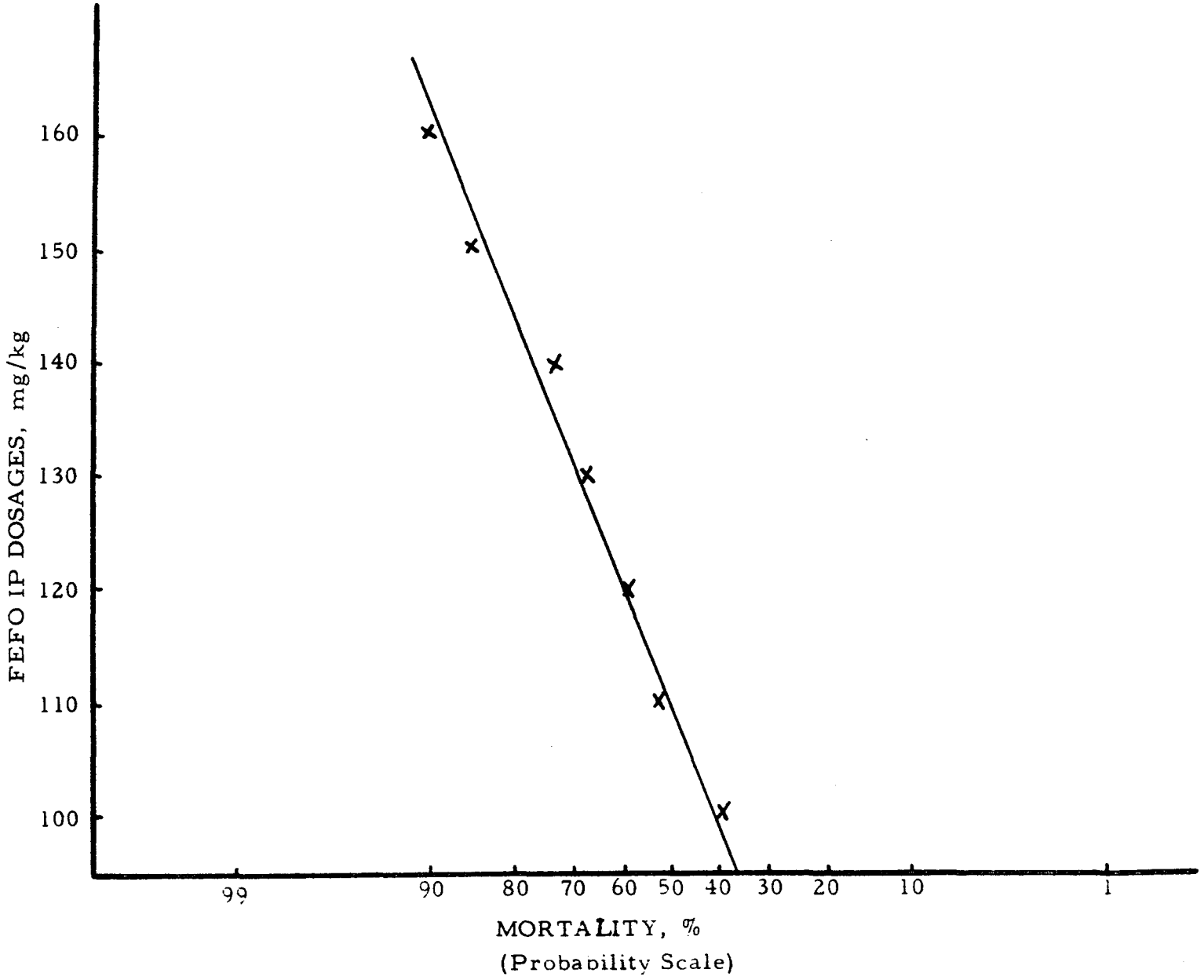

Figure 1

INTRAPERITONEAL FEFO RESULTS

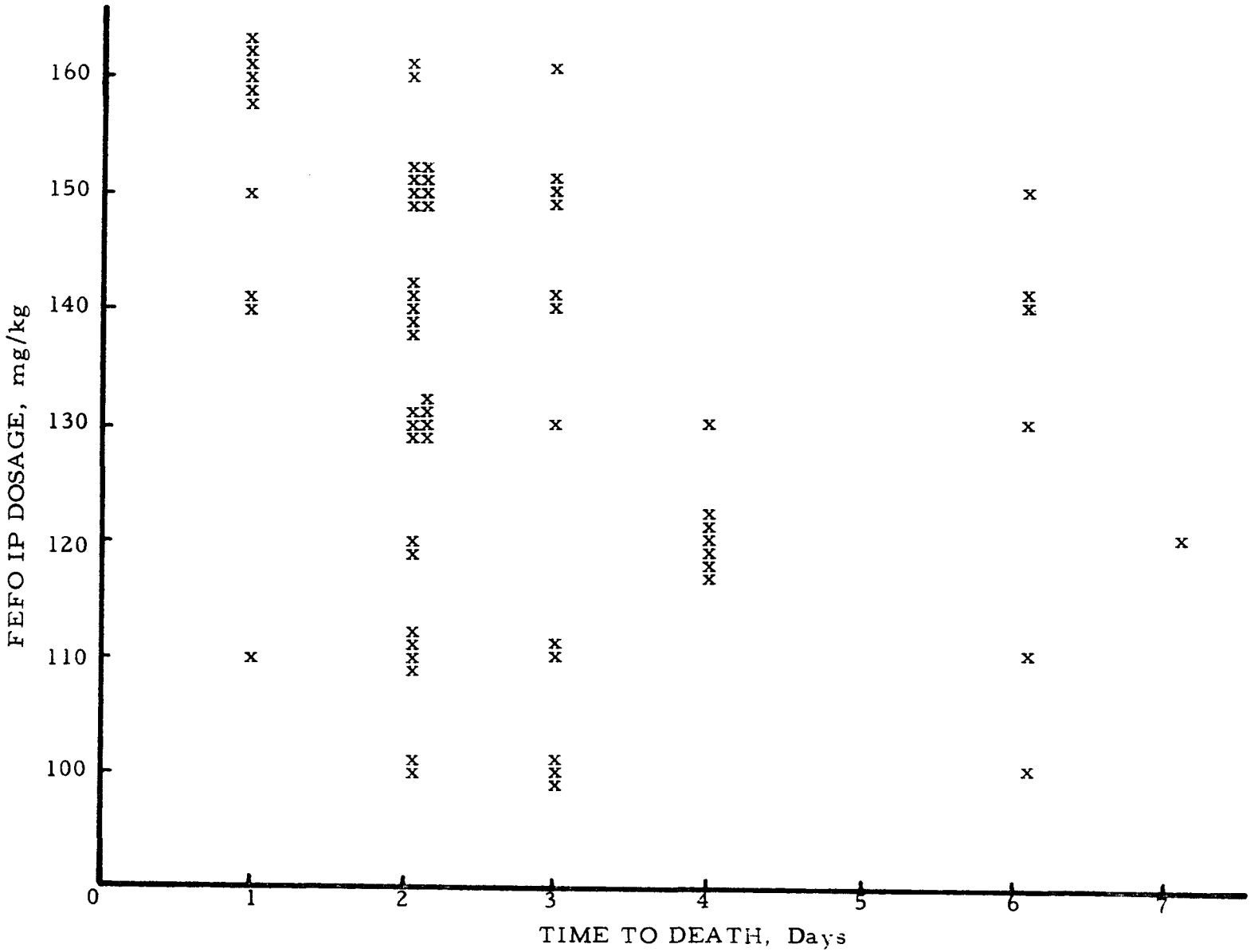

Figure 2

TIME TO DEATH AS A FUNCTION OF FEFO IP DOSAGE

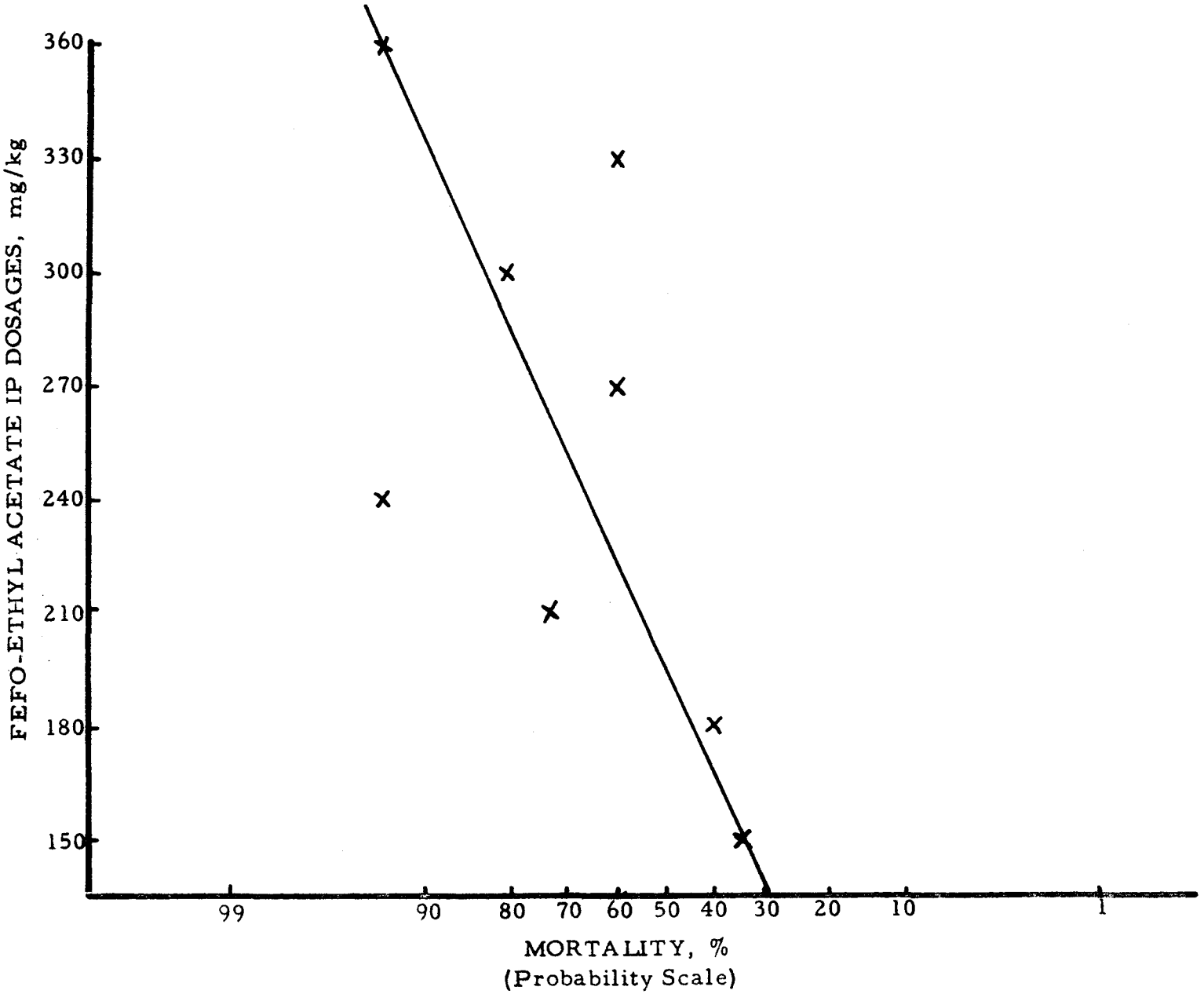

Figure 3

INTRAPERITONEAL FEFO & ETHYL ACETATE RESULTS

Appendix C

Material Safety Data Sheet on FEFO
(Aerojet Strategic Propulsion Company)

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AEROJET STRATEGIC PROPULSION COMPANY
AEROJET TACTICAL SYSTEMS COMPANY
MATERIAL SAFETY DATA SHEET

I PRODUCT IDENTIFICATION

DATE: 5/82
REV. NO.: 3

MANUFACTURER'S NAME: North Amer. Rockwell or Aerojet Solid Prop.C.
REGULAR TELEPHONE NO. / EMERGENCY TELEPHONE NO: 5-4321

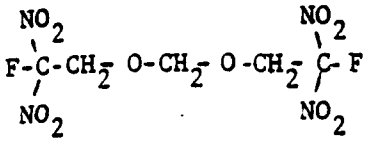
ADDRESS: Nimbus, CA

NAME: Bis(2,2-Dinitro-2-Fluoro Ethyl)Formal

SYNONYMS: FEFO

FORMULA: $C_5H_6N_4O_{10}F_2$

II HAZARDOUS INGREDIENTS AND GENERAL COMMENTS



Class A explosive

NOL impact: 37 to 54cm 2.5kg.wt.
DTA: 195°C (Exo)
225°C (Peak)

FEFOSOL (30-35% FEFO in Ethyl Acetate): Treat same as neat FEFO for toxicity. Less sensitive to shock or impact than neat FEFO.

FEFO/$MeCl_2$(20/80): Treat same as FEFOSOL.

See MSDS 115 for methylene chloride.

CRITICAL DIAMETER is 3/8-1/2". Contact EH&S PRIOR TO USE

III PHYSICAL DATA

BOILING POINT, °C (°F) TORR (mm Hg)	120°C @ 3mm 250°C @ 760mm	MELTING POINT, °C (°F)	14°C
SPECIFIC GRAVITY (H_2O = 1)	1.60 @ 25°C	VAPOR PRESSURE AT TEMP.	NA 2.19×10^{-4} torr
VAPOR DENSITY (AIR = 1)	NA	SOLUBILITY IN H_2O BY WT.	Low
% VOLATILES BY VOLUME	NA	EVAPORATION RATE (= 1)	NA
APPEARANCE AND ODOR	Clear yellow liquid		

25°C, 760 mm Hg

IV FIRE AND EXPLOSION DATA

FLASH POINT (TEST METHOD)	NA	AUTOIGNITION TEMPERATURE	NA
FLAMMABLE LIMITS IN AIR, % BY VOLUME	LOWER: NA	UPPER: NA	
EXTINGUISHING MEDIA	Explosive - use deluge or sprinkler systems.		
SPECIAL FIRE FIGHTING PROCEDURES	Do not fight fires involving FEFO		
UNUSUAL FIRE AND EXPLOSION HAZARD	Explosion hazard when shocked or exposed to water or flame. Do not fight fires.		

V HEALTH HAZARD INFORMATION

THRESHOLD LIMIT VALUE (TLV): Not established.

EFFECTS OF OVEREXPOSURE

ACUTE: Highly toxic from skin contact, eye contact or vapor inhalation. A strong vesicant.

CHRONIC: Unknown.

EMERGENCY AND FIRST AID PROCEDURES

EYES: Flush with water for 15 minutes. Report to Medical.

SKIN: Wash with water. Apply Zephrin solution (1/1000). Report to Medical.

INHALATION: Remove to fresh air. Report to Medical.

INGESTION: Report to Medical.

VI REACTIVITY DATA

CONDITIONS CONTRIBUTING TO INSTABILITY

Heat, impact, friction (thin film) shock may cause ignition. Neat FEFO will detonate with #8 cap.

INCOMPATIBILITY (MATERIALS TO AVOID)

Basic materials.

HAZARDOUS DECOMPOSITION PRODUCTS

HF, oxides of nitrogen and carbon.

CONDITIONS CONTRIBUTING TO HAZARDOUS POLYMERIZATION

Will not occur.

VII SPILL OR LEAK PROCEDURES

STEPS TO BE TAKEN IF MATERIAL IS RELEASED OR SPILLED

Keep ignition sources away. Use rubber gloves. Pick up using inert absorbent.

NEUTRALIZING CHEMICALS

Destroy residues with methanolic solution of Na_2S.

WASTE DISPOSAL METHOD Small quantities may be placed in gusset trays and anti-static poly bag. Large quantities to be packed in vendor shipping containers. Send all material to thermal treatment facility.

VIII SPECIAL PROTECTION INFORMATION

VENTILATION REQUIREMENTS

For small quantities, general room ventilation is adequate. For larger quantities or confined areas, use local exhaust.

SPECIFIC PERSONAL PROTECTIVE EQUIPMENT	
RESPIRATORY (SPECIFY IN DETAIL)	For small quantities in well ventilated areas no respirator is required. For larger quantities or in confined areas use cartridge respirator such as MSA GMA or AO type R-51).
EYES	Safety glasses.
GLOVES	Rubber. (Neoprene)

OTHER CLOTHING AND EQUIPMENT

Flameproof coveralls, suitable to avoid skin contact.

IX SPECIAL PRECAUTIONS

PRECAUTIONARY STATEMENTS

Comply with compatibility and quantity/distance requirements during storage.

OTHER HANDLING AND STORAGE REQUIREMENTS

Store in original container. Keep tightly sealed. Store in cool place. Must be monitored during storage to prevent degraded (and more hazardous) material from accumulating.

Appendix D

Personnel Hazards Associated with FEFO
(Internal Memorandum, Rocketdyne)

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11 January 1972

TO: Chemists and Technicians, C4 Propellant Program

FROM: A. O. Dekker

SUBJECT: Hazard of Personnel Contact with FEFO

COPIES TO: D. L. Conklin, C. J. Rogers

ENCLOSURE: Excerpt from Hercules Report No. AFRPL-0047/5/2786 (April 15, 1971) pages 4-6

The available data on FEFO in the enclosure and our own experience show that skin contact should be prevented and that any contact however trivial should be reported to Medical at once.

FEFO may (1) produce severe contact dermatitis in some individuals, (2) produce reactions which are delayed several days after the contact, and (3) sensitize an individual so that he can no longer work with it.

You will recall our experience that TDI sensitized certain individuals so that they could no longer work with TDI propellants. A similar experience with FEFO would mean a serious loss of experienced personnel from the program. We think we can avoid it by not handling the propellant with bare hands, by wearing long gloves and goggles when working with FEFO, by good general housekeeping practices, by prompt flushing of the contacted skin area as outlined in the reference, and by reporting any contact at once to Medical for treatment to minimize injury.

The two different Zephiran solutions described in the enclosure will be available at Medical for placing in each laboratory or work station for immediate flushing of the skin or irrigating eyes. Note that the solution for use on the skin is never to be used on the eyes.

A great deal will depend on the alertness of the individual if we are to succeed in preventing inadvertent exposure. Not only must care be I.

used in removing gloves and not re-using them, but spills must be carefully cleaned up, contaminated equipment must be clearly marked, and care taken, for example, not to grasp doorknobs with contaminated gloves.

Appendix E

Declassified Excerpts on Toxicology of FEFO
(China Lake Naval Weapons Laboratory)

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(U) g_o = gravitational constant

t_z = burn time

A = propellant surface area

m = propellant mass

subscript 1 = motor No. 1

subscript 2 = motor No. 2

By selecting two pairs, one with different propellant surface areas and one with different throat sizes, an intersect occurs in the q-N curves which corresponds to the effective values. This is shown in Figure 3 with one curve calculated for .75C.50-1.5 (approximately 10 gram) and 2C1.5-4 (approximately one pound) motors and the other for .75C.50-1.5 and .75C.50-3.5 (approximately 25 gram) motors. The previously mentioned computer program uses a power series extrapolation of the q-N coordinates to determine the intersection.

(U) Knowing the effective heat flux and particle size for a given propellant, the previous equation can be used to predict the specific impulse in the large motor. This is accomplished by selecting one micromotor and the large motor as the pair to be considered and then calculating the velocity lag of the effective particle size in these motors. Assuming t_z,A, and m are known for the large motor, the specific impulse can be calculated.

(U) The Rohm & Haas specific impulse scaling technique has been adapted to operate successfully at Hercules with a minimum of effort required by the user. This analysis will be extended to a parametric study of the 17 candidate propellants upon completion of the micromotor and OPC motor firings.

Toxicity of FEFO

The fluorodinitro plasticizer (bis-(2-fluoro-2, 2-dinitroethyl) formal, FEFO) presently used in candidate formulations A-III, B-IV, C-IV, and D-11 has been found to have the potential of causing serious latent contact dermatitis to personnel upon direct contact. As a matter of standard operating procedure, the degree of toxicity of FEFO was researched at the proposal stage of this contract (approximately 1-1/2 years ago) and found to be unknown. This toxicological problem has only become apparent to the manufacturer (Rocketdyne Division of North American Rockwell) in the past year. This was brought to our attention when one of our people suffered severe contact dermatitis about the hands and forearms after cleaning up a FEFO/solvent (ethyl acetate) solution and apparently coming in direct contact with the FEFO. His response to this exposure did not become apparent until nearly 48 hours later and then only the appearance of a blotchy red rash on his hands and wrists was apparent. This condition progressed to extensive dermatitis over most of his hands and forearms. The FEFO apparently penetrated deep into the subepidermal layer causing considerable inflammation of both arms and lymphodermia. This caused the condition to spread to otherwise unexposed areas.

(U) At this point (some 4 days after the initial exposure), Dr. Milt Frankel, propellant specialist of Rocketdyne, Canoga Park, California, where the FEFO was manufactured, was contacted. He confirmed that they have had some people who did respond to FEFO (after direct contact), resulting in a red itching rash.
(U) However, the following day the condition had worsened, Dr. T. C. Weggeland, M. D., Medical Director, Bacchus, then contacted Dr. W. K. Shulte, M. D., Medical Director at Canoga Park, and it was learned that they are quite familiar with this problem. In fact, emergency procedures and supplies at onsite locations for administration in the event of an accidental exposure have been made available. Dr. Shulte instructed Dr. Weggeland to administer a shot of Kenalog (active ingredient triamcinolone acetonide) intermuscularly and also to use Kenalog lotion topically. This treatment was very effective, as the patient's inflammation began to decrease and no additional area were affected.

(U) Dr. Shulte was contacted by the principal investigator to learn what could be done to prevent exposure, what to do in the event of exposure, extent of condition, and any other pertinent information. Standard operating procedure is to always wear long rubber gloves when working with FEFO. Dr. Shulte also suggested that goggles be worn. In the event someone has come in direct contact with FEFO (which is necessary for any problem to occur), the affected region is to be flushed immediately with a tincture of Zephiran (1/1000 dilution), then apply ice cold compresses containing the Zephiran solution on, above, and below the affected area for 15 minutes every two hours for a minimum of 24 hours. This procedure has been found to be very effective in minimizing injury.

(U) After this first aid, the patient is given an intermuscular shot of Kenalog and also is to administer topically Kenalog lotion twice daily. Relief from the itching can be obtained by dabbing onto the affected areas a solution of baking soda and water and using cold compresses. Further relief from the general discomfort is received by continuing the cold compresses of the tincture of Zephiran. Continued injections of the Kenalog can be given at dosages and intervals prescribed by the attending physician until the inflammation has essentially eased to exist.

(U) In the event of exposure to the eyes, immediate copious irrigation for 15 minutes with a 1/30,000 aqueous solution of Zephiran is to be used. This procedure is to be repeated every hour for at least 4 hours. The patient should be taken to an ophtalmologist after the first Zephiran irrigation, If possible. If not, continue as discussed above and after each irrigation add 1 to 2 drops of Pentocaine to the eye (this deadens the eye ball and thus reduces the pain). An eye pad should be used to prevent any foreign matter from getting into the eye.

(U) Vapors of FEFO are apparently not a problem at room temperature; however, very serious pulmonary conditions have occurred upon exposure from vapors of the precursors and is a likely problem with FEFO if it were heated to a point where significant quantities (which are probably not much more than a few parts per million or less) would be made available. Again, these conditions are latent and do not appear until several hours later.

Dr. Shulte hospitalizes anyone who has been exposed to these vapors for 48 hours with appropriate tracheotomy equipment readily available.

(U) With this recently discovered toxicological problem with FEFO, the Stanford Research Institute (SRI), Menlo Park, California, has started an extensive investigation at the request of Rocketdyne. The NASA-Lewis Research Center in Cleveland, Ohio and SRI have conducted texicololgical studies with the precursors FTM (fluoro trinitro methane) and FDNE (fluoro dinitro ethanol).

(U) Two other aspects concerned with FEFO exposure are: (1) It affects different people to varying degrees. That is, some people who have been exposed will not show any affect while others upon the same exposure may receive serious contact dermatitis. In other words, it has an allergenic affect. In fact, a technician who also had direct contact with FEFO showed no response whatsoever. (2) It was also asked of Dr. Shulte if once a person is exposed to FEFO if they can be sensitized. He stated that although their data is limited and they've been able to minimize the extent of injury by their emergency procedures, he is of the opinion that one can be sensitized. He did state, however, that direct contact will still necessary before an individual could be affected.

(U) It is recommended that the amount of the nonflammable volatile solvent (Freon TAO presently used for clean up (or any similar solvent) be kept to a minimum, as it may well serve as a vehicle to transport the FEFO into the skin.

3 Eye Contact

The corrosive action of tentranitromethane on protein material resembles that of nitrous acid, which causes conjunctival inflammation, ulceration, and, in more severe contacts, pupillary changes and paralysis of the eye muscles, as well as severe burns.

4 Ingestion

Accidental ingestion of the material is unlikely except through lack of assiduous cleanliness; however, ingestion toxicity is considered to be extremely high.

(c) FDNE

Limited data are available describing the toxicity of FDNE. Based on limited skin test results with rabbits it would appear that FDNE is extremely toxic on contact. Seven out of seven rabbits died within several hours following one application of FDNE to exposed skin[32b]. Dose levels were as low as 1 ml of FDNE per kg of body weight.

(d) FEFO[33]

1 Animal Data

Five rats injected with 1 or more mg FEFO/kg of body weight died within 2.4 to 88 hours. Glycerol was used as a diluent. One rat that received a 0.1-mg/kg dose serviced with minor transient

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[32b]Private communication from W. E. McQuistion, NOS, Indian Head, Maryland, to H. J. Marcus, Aerojet-General Corporation, Azusa, California, 21 August 1967.

[33]Most of the data presented in this section was generated by Wright-Patterson AFB and Aerojet-General Corporation and is documentated in A Toxic Hazard Study of Selected Missile Propellants, Technical Documentary Report No. MRL-TDR-62-41, May 1962, Contract No. AF 33(616)-7836.

irregularities in respiration. For the animals that died, there was low correlation between time-to-death, convulsions, and doses received; this suggested a large variation in individual susceptibility. The affected animals had partial loss of hind-limb coordination and irregular respiration, followed by a series of tonic convulsions.

No effects were noted in guinea pigs used for skin and eye tests in which glycerol solutions and pure material were administered.

Considering the high toxicity observed in intraperitoneal tests and the lack of systemic effects resulting from topical application, the materials is probably not readily absorbed in a form that will produce readily observable systemic effects such as were seen after intraperitoneal injection.

When placed in the eyes of test animals, FEFO caused damage to the eye tissue[34]. It was also found that FEFO was adsorbed through the skin causing a sluggish effect in test animals. This effect wore off with time but there is no knowledge of the cumulative effects. Since the vapor pressure of FEFO is low at ambient temperature, the use of rubber gloves, goggles and a hood or well-ventilated room should be adequate protection. FEFO has been used extensively by NOL personnel for several years with no evidence of any toxic effects.

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[34]B. Burke, H. Heller, J. C. Hoffsommer, M. J. Kamlet, R. Rich and M. Stosz, New Energetic Binders for Solid Propellant Applications, NOLTR 62-38, 5 April 1962, U.S. Naval Ordinance Laboratory, White Oak, Maryland.

2 Clinical Data

Of six persons observed after having worked with FEFO, one suffered skin rash and one had an uncertain relationship between exposure and urinary frequency and headaches. Because these workers were also in contact with other compounds, there is a large degree of uncertainty in attribution the symptoms to FEFO. In unrelated observations, other chemists have reported that accidental skin spills, washed off immediately, produce no toxic symptoms.

3 Industrial Hygiene

a Methods for Decreasing Toxic Hazards

Although intraperitoneal tests on animals indicate that FEFO is super toxic (LD_{50} <1 mg/kg), the physical properties and low or absent skin penetration reduce the handling hazard. Operations that might lead to oral or aerosol exposures should be under industrial-hygiene control. Exposure to vapors does not appear to present health hazards because the material has a low vapor pressure, as indicated by an inability to distill appreciable quantities at 50°C at low pressure.

Body surfaces should be decontaminated with large quantities of soap and water. Organic solvents may be used to decontaminate equipment. Decontamination involving actual destruction of FEFO (or FDNE) can be accomplished with a methanolic solution of sodium sulfide which effectively reduces the material to nonhazardous inorganic products.

Disposal may be accomplished by dilution with organic solvents or burning in areas of good ventilation.

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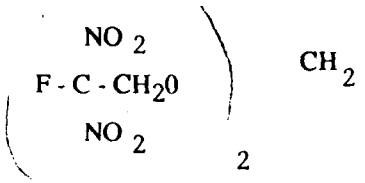
AEROJET-GENERAL Toxic Hazard Evaluation INDUSTRIAL HYGIENE PRECAUTION GUIDE			BIS (2,2 DINITRO-E-FLUOROETHYL-) Synonyms and/or Code Designation BDNFEF BIS-(2,2-DINTRO-2 FLUORETHYL-FORMAL Structural Formula 
Orig. Issue Date	Rev. No.	Rev. Date	
Destroy all Superseded Issues			

Route/Rating	Toxicity Rating*	Class of Toxicity	Intraperitoneal Single Lethal Dose mg/kg for Rats	Probable Lethal Dose for 70 kg (150 lb) man
Intraperitoneal	6	Super Toxic	Less than 5	A taste (less than 7 drops)
	5	Extremely Toxic	5 - 50	Between 7 drops and 1 teaspoonful
6	4	Very Toxic	50 - 500	Between 1 teaspoonful and 1 ounce
	3	Moderately Toxic	500 - 5 g/kg	Between 1 ounce and 1 pint (Less than 1 lb)
	2	Slightly Toxic	5 - 15 g/kg	Between 1 pint and 1 quart
	1	Practically Non-Toxic	Above 15 g/kg	More than 1 quart
	Toxicity Rating*	Class of Toxicity	Vapor Exposure 4 hr Lethal Conc. ppm for Rats	
Inhalation	6	Super Toxic	Less than 10	
	5	Extremely Toxic	10 - 100	
Test pending	4	Very Toxic	100 - 1000	
	3	Moderately Toxic	1000 - 10,000 (10,000=1% by vol.)	
	2	Slightly	1% - 10% by vol.	
	1	Practically Non-Toxic	Above 10% by vol.	
Skin (morbidity)		Practically non-toxic	See reverse side	
Eye (morbidity)		"	"	

* The toxicity rating is based on mortality, not morbidity, i.e., it is really a lethality rating. In general a clinically significant illness may be expected after doses of about one-tenth the probable lethal dose. The above data from animal studies do not mean that damage will not be produced by exposure of humans at lower dosages.

This information is not to be released through speech or written material to anyone not authorized to receive such information and especially outside the company and permission to release or transmit this information must be obtained from the Medical Director.

STAMP THIS FORM WITH SECURITY CLASSIFICATION IF APPROPRIATE

EXPERIMENTAL DATA SUMMARY ON REVERSE SIDE

TOXICITY RANGE-FINDING	References: AGC-Department of Life Science
Summary of Experimental Animal Studies	Toxic Hazard Evaluation Report, 61-02-RDNFEF
ROUTE/SPECIES/STRAIN	COMMENTS
Intraperitoneal Rats	0.1 mg/kg: no effects, survived 1 mg/kg: 1 rat-death in 23 hrs; 1 rat death in 24 hours 10 mg/kg: death in 26 hrs 50 mg/kg: death in 15 hrs 100 mg/kg: death in 44-88 hrs
Skin, Saturated 2 x 2 Cm Patch Repeated After 2 Weeks Guinea Pigs	1,10 , and 100% solutions produced no irritation or allergic effects
Eye, 0.1 ml Guinea Pigs	1,10, and 100% solutions produced no allergic effects
Inhalation, 4 hr Exposure, Rats	test pending

Miscellaneous Comments (Including Outstanding Properties)

Partial loss of hind limb coordination and irregular respiration was followed by a series of tonic convulsions of varying intensity. Termination occurred while gasping in a postconvulsive state. Low correlation between time-to-death, severity of convulsions, and doses received suggests a large variation in individual susceptibility. Postmortem findings essentially normal except for hemorrhagic lungs. Possible synergistic effects with the diluent glycerol, cannot be ruled out but are probably of second order importance.

Absence of skin or ocular effects may be due to either a lack of absorption or possibly ported absorption but non-toxicity of the compound at the dose levels used.

Note: Interpretation or use of this information should be restricted to qualified medical personnel familiar with the usual limitations of range-finding data.

Appendix F

Medical Treatment File Associated with FEFO
(Aerojet Corporation)

DO NOT MICROFILM
THIS PAGE

aerojet solid propulsion company
P. O. BOX 13400 SACRAMENTO, CALIFORNIA 95813 • TELEPHONE (916) 355-4000

1 February 1972

Dr. Milton Finger
Lawrence Livermore Laboratory
Livermore, California

Dear Dr. Finger:

Dr. Hamel, of our laboratory, told me that you had mentioned that you were working to obtain government funding for an investigation of the toxicology of FEFO and would appreciate a description of any incidents which have occurred at Aerojet. The enclosure describes the only incident that we have had in our recent program which was initiated last July.

Sincerely,

A. O. Dekker, Manager
C4 Propellants

CC: D. L. Conklin
E. E. Hamel

Encl: Dermatitis attributed to FEFO

26 January 1972

DERMATITIS ATTRIBUTED TO FEFO

An employee, one of a group of 6 employees who had been working with FEFO in the laboratory for 3 months, noticed a slight burn on the back of his hand. About a month later he noticed a puffiness around the eyes which seemed to be worse some days than others. Finally, after another six weeks he reported to Medical with dermatitis on his face, back of hands, and both wrists. He was removed from work with FEFO for one week during which the dermatitis disappeared. He was then cleared for work with FEFO, but was intentionally assigned to a part of the program in which less FEFO is handled. He has now been working on this new assignment for 5-1/2 weeks without trouble until today (1/26/72) when he noticed a red swollen spot on his arm.

Rocketdyne
North American Rockwell

6633 Canoga Avenue
Canoga Park, California 91304

August 31, 1971

Max W. Biggs, M.D.
University of California
Lawrence Radiation Laboratory
P. O. Box 808
Livermore, California

Dear Dr. Biggs:

Thank you for your letter of August 24, 1971, regarding the treatment of "FeFo" skin contamination used at our Rocketdyne Division. Please excuse the delay in my response as I have been out of town for several days.

Enclosed you will find a fairly complete dissertation on the techniques that we use on skin contamination, eye contamination and on inhalation of "FeFo". As you will note, this is a mighty potent material on contact and I cannot stress enough the urgency of immediate medical care.

If I can be of any further assistance please do not hesitate to call or write at any time.

Sincerely,

ROCKETDYNE

Bill Shulte

W. K. Shulte, M.D.
Medical Director

WKS:jk

Enclosure

TECHNIQUE USED IN TREATING "FeFo" CONTAMINATION
(Skin - Eyes - Inhalation)

In our experience, immediate medical attention is of utmost importance. Delayed reporting of an exposure has resulted in extremely painful penetrating wounds that tend to ulcerate and cause marked lymphodema.

Skin: Flush skin immediately with large quantities of cold water (safety shower if available) removing any contaminated clothing. Give special attention to skin folds and areas around and under the nails. Following the initial skin flush, all areas of exposure are treated with iced solution of Benzalkonium Chloride (solution of Zephiran) 1:1000 (0.1%) in the form of compresses from 1 to 4 hours, depending upon the severity of the burn.

Eyes: First attention should be given to flushing with cool water for 5 to 10 minutes, followed by irrigation of Benzalkonium Chloride Solution (1:30,000). The irrigations should be carried out every 5 minutes for at least 1 hour. Corneal injury, in delayed treatment, may occur. This may be very painful and can result in loss of vision. It has been our practice to have consultation by an ophthalmologist, following our initial first aid treatment.

Inhalation: "FeFo" inhalation is extremely irritating to the lungs. Prompt removal from exposure is the first order. Rest should be enforced and humidified 100% oxygen should be given at atmospheric pressure to relieve cyanosis or dyspnea. Hospitalization is essential (for observation) for a period of 24-48 hours in order to detect the possible onset of respiratory complications after a symptom-free latent period.

Addendum: Delayed treatment, due to delayed reporting of a skin exposure, in one case, resulted in an extensive dermatitis of both hands and forearms. The "FeFo" penetrated deeply into the subcutaneous tissue causing marked inflammation with extensive lymphedema of one arm. In this instance, the patient was given an I.M. injection of "kenalog-40". Also ice cold compresses

Benzalkonium Chloride were applied for 30 minutes every three hours during the day and Kenalog Cream was applied topically, three times daily. The patient responded dramatically to this treatment.

I strongly recommend the use of long rubber gloves and goggles to all personnel working with "FeFo".