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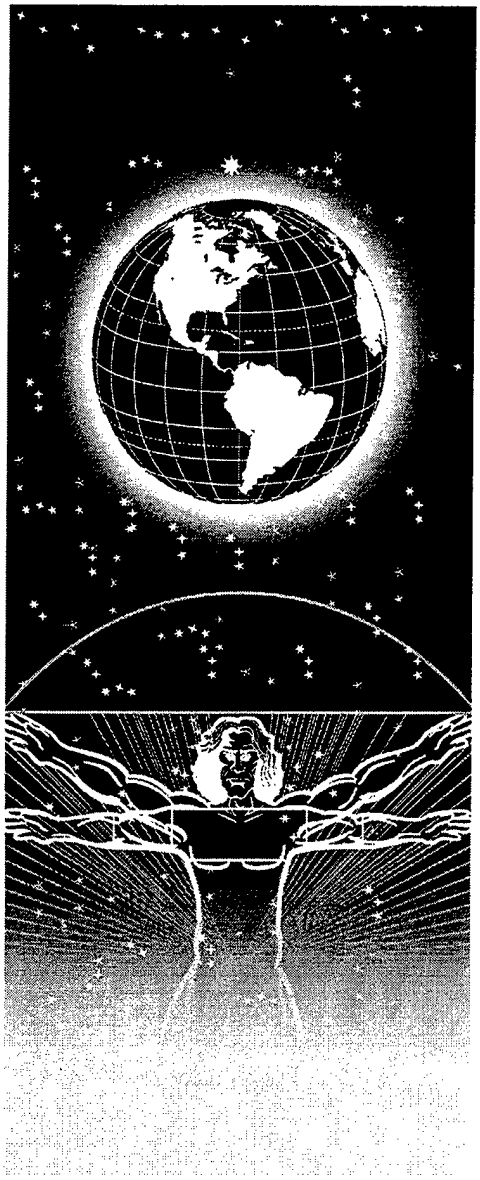

UNITED STATES AIR FORCE ARMSTRONG LABORATORY

Acute Toxicity Evaluation of a New Noncorrosive Decontamination Solution

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TECHNICAL REVIEW AND APPROVAL

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The animals used in this study were handled in accordance with the principles stated in the *Guide for the Care and Use of Laboratory Animals* prepared by the Institute of Laboratory Animal Resources, National Research Council, National Academy Press, 1996, and the Animal Welfare Act of 1966, as amended.

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

Terry A. Childress

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U.S. Navy requested evaluation of a new noncorrosive chemical warfare decontamination solution (NDS) designed for removal of toxic chemicals from equipment. This investigation contained three experiments: acute oral limit test, acute dermal limit test, and acute inhalation limit test. Oral gavage with 5 g NDS/kg resulted in 100% mortality of male and female F-344 rats. Clinical signs included whole body tremors and chromodacryorrhea. Treatment at lower oral concentrations of NDS resulted in the determination of an LD_{50} at 0.78 g/kg. All male and female NZW rabbits died after dermal treatment with 2 g NDS/kg. Signs of toxicity prior to death included whole body tremors and excessive salivation. Dermal treatment at lower doses of NDS resulted in the determination of a dermal LD_{50} of 0.36 g/kg. Inhalation exposure of male and female rats to near the limit test concentration (4.4 mg/L) also resulted in 100% mortality. The 4-h LC_{50} for NDS aerosol was determined to be 1.36 mg/L. The 100% fatality associated with the higher levels of exposure for all routes of exposure, coupled with a lack of significant gross or histologic lesions, suggests that deaths were not necessarily due to corrosive action. Additional studies would be required to explain the cause(s) of mortality following administration of NDS.

14. SUBJECT TERMS
Acute toxicity, limit test, LD_{50}, LC_{50}, oral gavage, dermal, inhalation, Fischer 344 rats, New Zealand white rabbits, noncorrosive decontamination solution

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PREFACE

This is one of a series of technical reports describing results of the experimental laboratory programs conducted at the Toxicology Division under the ManTech Geo-Centers Joint Venture Contract. This document serves as a final report on the acute toxicity evaluation of a new noncorrosive decontamination solution. The research described in this report began in September 1996 and was completed in February 1997 under Department of Defense Contract No. F41624-96-C-9010. Lt Col Terry A. Childress served as the Contracting Officer's Representative for the U.S. Air Force, AL/OET. Darol E. Dodd, Ph.D., served as Program Manager for ManTech/Geo-Centers Joint Venture. Lt Patrick Callaghan served as Project Director for the U.S. Navy, Naval Medical Research Institute, Toxicology Detachment.

The animals used in this study were handled in accordance with the principles stated in the *Guide for the Care and Use of Laboratory Animals*, Institute of Laboratory Animal Resources, National Research Council, National Academy Press, 1996, and the Animal Welfare Act of 1966, as amended.

ABBREVIATIONS

°C	Degrees centigrade
cm	Centimeter
F-344	Fischer 344 (rat)
g	Gram(s)
h	Hour(s)
kg	Kilogram
L	Liter
LC_{50}	Median lethal concentration
LD_{50}	Median lethal dose
mg	Milligram
min	Minute(s)
mL	Milliliter
mm	Milliliter
NDS	New noncorrosive decontamination solution
NZW	New Zealand white (rabbits)
psi	Pounds per square inch
SD	Standard deviation
sec	Seconds
µL	Microliter

SECTION I

INTRODUCTION

The U.S. Navy requested evaluation of a new chemical warfare decontamination solution designed for removal of toxic chemicals from equipment. The current decontamination material, DS2, is very effective, but it is also very corrosive and toxic. A research objective at the Naval Warfare Center, Dhalgren, VA, is to develop a decontamination solution that is non-corrosive, less toxic, and environmentally friendly. No toxicity data are available for this new decontamination material. The purpose of this study was to determine the acute toxicity of this new decontamination material following oral, dermal, or inhalation exposure. The new noncorrosive decontamination solution (NDS) was developed by the Naval Warfare Center in Dhalgren, VA. Uses of this material include all the chemical agent decontamination uses of DS2, as well as the decontamination of aircraft.

Exposure of personnel to this solution should be minimal while in use, but general toxicity data are still needed for cases where personnel are exposed to the solution as a result of leakage or other accidental release when they are not wearing any personal protection equipment.

A toxicology program for evaluating the safety of a chemical warfare decontaminant (Hayes et al., 1984) states that a toxicity profile of a candidate decontamination agent should include systemic toxicity studies by the oral and dermal route in both male and female animals. These studies would provide information on the intrinsic toxicity of the compound after a single exposure. This information would be useful for formulating safety measures, determining symptomatology, and to determine proper labeling for the compound. Hayes reported that the compound should be evaluated in at least two species, with rats and rabbits as the preferred species. Besides mortality, the toxicological endpoints measured should include toxic signs (with onset and recovery), body weight changes, necropsy observations, and histopathologic examination. Sufficient numbers of animals should be used to establish a close range of the dose that produces approximately 50% mortality in a group of animals. The acute toxicity evaluation of NDS was performed utilizing three routes of exposure: oral, dermal, and inhalation. Inhalation exposure was included since NDS will be used to decontaminate aircraft and other equipment through use of spraying NDS on the equipment, and therefore, exposure to aerosol of this material may occur.

This investigation contained three experiments: acute oral limit test, acute dermal limit test, and acute inhalation limit test. EPA's test guidelines (U.S. EPA, 1992) encourage the use of methods that minimize the requirement for animals, such as the "limit" test in which a single group of animals receives a large dose of the test agent. If no lethality is demonstrated during these limit tests, no further testing for acute toxicity is pursued. The limit test is 5.0 g/kg for acute oral toxicity, 2.0 g/kg for acute dermal toxicity, and 5 mg/L for acute inhalation toxicity.

SECTION II

MATERIALS AND METHODS

Test Material

The NDS matrix, as received from the U.S. Navy, was composed of the following:

25% Benzyltrimethylammonium chloride (CAS 56-93-9)

5% Benzyltriethylammonium chloride (CAS 56-37-1)

55% 2-Amino-2-Methyl-1-Propanol (CAS 124-68-5)

~1% Sodium Perborate Tetrahydrate (CAS 10486-00-7)

12% Water (CAS 7732-18-5)

~1% Sodium Percarbonate (CAS 15630-89-4)

~1% Sodium Persulfate (CAS 7775-27-1)

The NDS is still under development, but the above formulation is not expected to change substantially. NDS was determined to have a density of 0.9978 g/mL, and to have a pH of 10-10.5.

Test Animals

Male and female Fischer-344 (CDF®[F-344]/CrlBR) rats weighing between 100 and 125 and 75 and 100 g, respectively, were purchased from Charles River Breeding Laboratories. Male and female New Zealand white (NZW) rabbits weighing between 2 and 3 kg were purchased from Myrtle's Rabbitry. All animals were subjected to a two-week quarantine period. Rats were group housed (two per cage) in clear plastic cages with wood chip bedding (SANI-CHIPS®, P.J. Murphy Forest Products, Montville, NJ). The rabbits were housed in wire-bottom, stainless-steel cages. Water and feed (Purina Rabbit Chow #5320, and Purina Formulab #5008 for rats) were available *ad libitum*, except during the inhalation exposure period and for 12 h prior to oral dosing. Animal room temperatures were maintained at 21 to 25 °C and the light/dark cycle was set at 12-h intervals.

Experimental Approach

Oral Toxicity

Groups of five male or five female F-344 rats were fasted 12 h prior to the administration of the oral dose. Each rat was weighed prior to oral gavage dosing. 5.0, 1.0, or 0.5 g/kg of neat NDS were each administered to one group of male rats, and 5.0, 0.63, or 0.5 g/kg of neat NDS were each administered to one group of female rats. Surviving animals were weighed at 1, 2, 7, 10, and 14 days postexposure and signs of toxicity recorded. On the 14th day postexposure, rats were euthanatized via CO_2 inhalation and gross pathology was performed. Tissues displaying gross lesions at necropsy were taken for histopathologic examination.

Dermal Toxicity

Twenty-four hours prior to dosing, the back and sides of five male or five female NZW rabbits were clipped. The undiluted dose of 2.0, 0.4, or 0.2 g NDS/kg (males) and 2.0, 0.252, or 0.2 g NDS/kg (females) was applied to the back of the rabbits and spread evenly to both sides. The dose was kept in place by applying an eight-ply gauze patch over the liquid. A clear plastic wrap was then applied over the entire midsection and was held in place with Vetrap® and elastoplast tape. The dose was kept in contact with the rabbit skin for 24 h. The tape, plastic wrap, and gauze were then removed and the residual test material was wiped from the animal. Surviving animals were weighed 1, 2, 7, 10, and 14 days posttreatment. Signs of toxicity and mortality were monitored and gross necropsy was performed for each animal upon death or euthanasia (intravenous injection of Euthol® euthanasia solution). Tissues were taken for histopathologic examination from animals with gross lesions at necropsy.

Inhalation Toxicity

Initial estimates of the inhalation toxicity of NDS were obtained by exposing five male and five female rats to a target concentration of 5 mg/L of the test material aerosol for 4 h using nose-only Cannon chambers (Cannon et al., 1983). The test substance was 100% lethal at this concentration. Consequently, two additional 4-h inhalation exposures were conducted at lower concentrations of test material aerosol. Records were maintained for body weights (days 0, 1, 2, 7, 10, and 14). At sacrifice, gross pathology was performed on any tissues displaying gross lesions and these tissues were taken for histopathologic evaluation. Animals which died during exposure had lungs removed for histopathology.

The Cannon-52 nose-only chambers (Lab Products, Inc., Maywood, NJ) were used as the exposure apparatus due to the limited amount of test material available for this study. The inhalation exposure of this material was to be as a respirable aerosol. The material as received did not aerosolize well, but when mixed with water to a 50% solution, a Collison type nebulizer readily produced an aerosol in the respirable range at the required concentration of 5 mg/L at an acceptable volume flow. A Sage syringe pump, driving a 20-mL syringe supplied the input mixture at 55 to 60 µL/min, while the air pressure at 45 psi using a single jet nebulizer provided a flow of 5 L/min. The water portion of the aerosol evaporated leaving an aerosol with a mass median aerodynamic diameter of one micron, and a measured mass concentration of 4.4 mg/L. The generator output was combined with additional air to arrive at the required exposure concentrations.

The NDS concentration analyses were performed using 25-mm, Extra Thick Glass Fiber Filters (Gelman Sciences, Ann Arbor, MI). A one L/min sample was drawn for five min every 15 min during exposure from a port delivery tube in the Cannon-52 system. The particle size analysis was done separately from the exposure since this method required a 20 L/min flow. A seven stage Lovelace type cascade impactor was used for the determination of particle size. The generator was operated as normal, except a "T" connection was introduced just ahead of the impactor entrance port to allow additional air for the necessary volume flow. A Cahn C-31 Microbalance (Cahn Instruments, Cerritos, CA) was used for the determination of the mass on each stage, as well as for the filter sample.

Statistical Analysis

Mean body weights of the animals were compared using the Multivariate Analysis of Covariance for Repeated Measures Test (Barcikowski, 1983). A probability of 0.05 or less inferred a significant change from controls. LD_{50} and LC_{50} calculations were performed using the Method of Finney, 1971.

SECTION III

RESULTS

Oral Toxicity

All rats orally gavaged with 5 g NDS/kg body weight died within minutes of dosing (Table 1). Immediate signs of toxicity were observed within 30 sec of oral dosing. Clinical signs prior to death were salivation, whole body tremors, and chromodacryorrhea (excessive excretion of porphyrin) from the eyes and nose. The chromodacryorrhea suggests further that the compound induced stress and/or discomfort in the animals. Gross examination at necropsy revealed one male had a perforated thoracic esophagus (dosing trauma). No other lesions were noted for this animal. All other animals had congestion and mild intraluminal hemorrhage in the stomach and proximal duodenum. Histologically, mild to minimal superficial congestion and hemorrhage in the glandular stomach mucosa and duodenal villi was noted in most animals. Eyes from several of these animals were examined histologically, and fluorescent light-induced retinal degeneration (loss of inner and outer nuclear zones) was noted. This finding was considered incidental, and not related to treatment.

All male rats orally gavaged with 1.0 g NDS/kg died within 10 min of dosing. Clinical signs observed prior to death were identical to those observed for the 5 g/kg animals. Gross lesions and histopathologic findings were also the same as those observed in the 5.0 g/kg animals.

Of the five female rats dosed with 0.63 g NDS/kg, one survived the treatment. Three of the 5 animals died within 30 min of dosing, and one died 2 h post dosing. Clinical observations noted immediately posttreatment for all five animals were chromodacryorrhea and rapid breathing. The surviving animal gained weight during the 14-day observation period (Table 2). Grossly, the four animals which died posttreatment had hemorrhage in the stomach and proximal duodenum. Histologic findings noted were mild to minimal congestion in the glandular stomach and proximal duodenal mucosa. At necropsy, the animal surviving 14-days posttreatment had no gross lesions, and histologic examination of the stomach and duodenum revealed normal tissues. Eyes were examined for all animals treated with 0.63 g/kg, and light-induced retinal degeneration (not treatment related) was the only finding.

Animals orally gavaged with 0.5 g NDS/kg body weight also displayed chromodacryorrhea and labored breathing immediately postdosing. Animals were prostrate in their cages for the first few hours

following dosing. All rats survived the 14-day observation period. All males gained weight over the 14-day observation period (Table 3). Four of 5 female rats also gained weight during this postdosing period (Table 2). No gross lesions were noted at necropsy, and no tissues were taken from these animals.

TABLE 1. ACUTE ORAL TOXICITY OF NDS

Dose Level (g/kg)	Sex	Mortality Ratio	Approximate Time to Death
5.0	Male	5/5	5 min
1.0	Male	5/5	10 min
0.5	Male	0/5	-----
5.0	Female	5/5	5 min
0.63	Female	4/5	0.5 - 2.0 h
0.5	Female	0/5	-----
	LD_{50} Sexes Combined =		0.777 (0.776, 0.778)[a] g/kg
	LD_{50} Males =		0.790 (0.786, 0.794)[a] g/kg
	LD_{50} Females =		0.777 (0.776, 0.778)[a] g/kg

[a]95% confidence interval.

TABLE 2. BODY WEIGHTS[a] OF FEMALE F-344 RATS AFTER GAVAGE WITH A NEW NONCORROSIVE DECONTAMINATION SOLUTION

	Study Day					
	0	**1**	**2**	**7**	**10**	**14**
5.0 g /kg						
Animal #						
46	134.5[b]	-----	-----	-----	-----	-----
47	142.0[b]	-----	-----	-----	-----	-----
48	130.0[b]	-----	-----	-----	-----	-----
49	136.6[b]	-----	-----	-----	-----	-----
50	129.5[b]	-----	-----	-----	-----	-----
0.63 g/kg						
Animal #						
66	154.6[c]	-----	-----	-----	-----	-----
67	148.4[c]	-----	-----	-----	-----	-----
68	145.8	142.3	150.7	153.6	157.5	162.0
69	131.9[d]	-----	-----	-----	-----	-----
70	148.4[c]	-----	-----	-----	-----	-----
0.5 g/kg						
Animal #						
61	139.1	130.7	140.6	153.5	154.5	136.6
62	128.5	111.0	114.4	133.9	138.8	144.1
63	139.6	135.8	142.5	148.3	149.7	155.5
64	140.2	141.1	145.3	152.9	153.0	154.9
65	122.9	129.0	132.7	137.2	137.8	136.9
Mean	134.1	129.5	135.1	145.2	146.8	145.6
SD	7.9	11.4	12.5	9.1	7.9	9.3

[a]Animal body weight in grams.
[b]Animal died within 5 min of dosing.
[c]Animal died within 30 min of dosing.
[d]Animal died within 2 h of dosing.

TABLE 3. BODY WEIGHTS[a] OF MALE F-344 RATS AFTER GAVAGE WITH A NEW NONCORROSIVE DECONTAMINATION SOLUTION

	Study Day					
	0	**1**	**2**	**7**	**10**	**14**
5.0 g/kg						
Animal #						
41	208.1[b]	-----	-----	-----	-----	-----
42	214.0[b]	-----	-----	-----	-----	-----
43	218.7[b]	-----	-----	-----	-----	-----
44	217.0[b]	-----	-----	-----	-----	-----
45	207.1[b]	-----	-----	-----	-----	-----
1.0 g/kg						
Animal #						
51	292.8[c]	-----	-----	-----	-----	-----
52	275.9[c]	-----	-----	-----	-----	-----
53	268.9[c]	-----	-----	-----	-----	-----
54	253.1[c]	-----	-----	-----	-----	-----
55	269.8[c]	-----	-----	-----	-----	-----
0.5 g/kg						
Animal #						
56	196.5	185.1	186.5	207.5	214.9	227.0
57	210.2	219.3	221.9	241.6	242.6	253.2
58	206.0	217.6	214.2	233.2	238.3	250.7
59	206.6	216.8	218.2	238.0	246.0	254.5
60	216.6	216.9	222.5	239.4	242.0	252.3
Mean	207.2	211.1	212.7	231.9	236.8	247.5
SD	7.31	14.6	15.0	14.0	12.5	11.6

[a]Animal body weight in grams.
[b]Animals died within 5 min of dosing.
[c]Animals died within 10 min of dosing.

Dermal Toxicity

Five male and five female rabbits per test material were treated with 2 g NDS/kg body weight. Male rabbits died within one to two hours of treatment, and females died within two hours posttreatment (Table 4). Signs of toxicity observed were whole body tremors within 20 min of dosing, and profuse salivation. Females developed diarrhea prior to death. At necropsy, gross observations in one male and three females included scattered, irregular-shaped 1- to 2-cm diameter foci of red epidermal discoloration at the site of test material application. No other significant gross lesions were noted. Histologically, the affected sites exhibited mild acute epidermal necrosis, consistent with chemical irritation.

Male rabbits treated with 0.4 g NDS/kg displayed no signs of toxicity immediately posttreatment; however, three of the five males were found dead the next morning. Another animal died later that afternoon. The only surviving animal gained 0.1 kg by study day 4 and maintained that weight over the 14-day observation period (Table 5). At necropsy, the four animals that died had small foci of dark reddish to black epidermal discoloration at the site of test material application; however, most of the treated skin appeared normal. No additional gross lesions were observed. Histologically, dermal lesions at the application site ranged from minimal epidermal necrosis to mild epidermal degeneration, characterized by pyknosis of keratinocyte nuclei and mild cytoplasmic vacuolation. The surviving animal had no gross lesions at necropsy, and no tissues were taken for histological examination.

Female rabbits dermally treated with 0.252 g NDS/kg displayed no clinical signs of toxicity. Most animals gained weight during the posttreatment period (Table 6). At necropsy, two animals had small (0.5-cm × 2-cm) linear crusty, scabbed foci on the dorsal midline epidermis. No additional gross lesions were noted. Histologically, the dermal foci exhibited marked granulomatous inflammation of the dermis and epidermis, often centered around follicular structures. Loss of follicles and adnexa, dermal fibrosis, and pronounced epidermal hyperplasia, and scattered foci of epidermal ulceration were also present. The remaining three animals had subtle gross lesions consisting of small foci of shallow epidermal depression along the dorsal midline. Histologic examination of the tissues from these animals revealed mild epidermal hyperplasia in one animal. The other two animals had essentially normal tissues.

Rabbits treated with 0.2 g NDS/kg body weight survived, and gained weight over the 14-day observation period (Tables 5 and 6). No signs of toxicity were observed. At necropsy, one male and one female animal had solitary scabbed foci on the dorsal epidermis. No additional gross lesions were noted. Histologically, lesions were characterized by marked epidermal hyperplasia, and granulomatous

dermatitis centered around hair follicles, with follicular destruction, and dermal fibrosis. Two of the remaining eight animals had minute epidermal scabs. All of these animals had essentially normal tissues when examined histologically.

TABLE 4. ACUTE DERMAL TOXICITY OF NDS

Dose Level (g/kg)	Sex	Mortality Ratio	Approximate Time to Death
2.0	Male	5/5	1-2 h
0.4	Male	4/5	24 h
0.2	Male	0/5	-----
2.0	Female	5/5	2 h
0.252	Female	0/5	-----
0.2	Female	0/5	-----
	LD_{50} Sexes Combined =		0.363 (0.362, 0.364)[a] g/kg
	LD_{50} Males =		0.282 (0.277, 0.287)[a] g/kg
	LD_{50} Females =		0.755 (0.754, 0.755)[a] g/kg

[a]95% confidence interval.

TABLE 5. BODY WEIGHTS[a] OF MALE NZW RABBITS AFTER DERMAL TREATMENT WITH A NEW NONCORROSIVE DECONTAMINATION SOLUTION

	Study Day					
	0	**1**	**2**	**7**	**10**	**14**
2.0 g/kg						
Animal #						
01	3.1[b]	-----	-----	-----	-----	-----
02	2.8[b]	-----	-----	-----	-----	-----
03	2.8[b]	-----	-----	-----	-----	-----
04	2.7[b]	-----	-----	-----	-----	-----
05	2.8[b]	-----	-----	-----	-----	-----
0.4 g/kg						
Animal #						
15	3.5[c]	-----	-----	-----	-----	-----
16	3.4[c]	-----	-----	-----	-----	-----
17	3.7[c]	-----	-----	-----	-----	-----
18	3.3	3.3	3.4[d]	3.4	3.4	3.4
19	3.3	2.7[e]	-----	-----	-----	-----
0.2 g/kg						
Animal #						
10	2.6	2.7	2.7	2.9	2.9[f]	2.9
11	2.8	2.8	2.9	3.1	3.3[f]	3.2
12	2.7	2.7	2.7	3.0	3.1[f]	3.0
13	2.6	2.5	2.6	2.7	2.7[f]	2.7
14	2.6	2.6	2.6	2.8	2.9[f]	2.9
Mean	2.7	2.7	2.7	2.9	3.0	2.9
SD	0.1	0.1	0.1	0.2	0.2	0.2

[a]Animal body weights in kg.
[b]Animal died within 2 h of dosing.
[c]Animal found dead less than 24 h after dosing.
[d]Animal body weight recorded on Study Day 4.
[e]Animal died afternoon Day 1.
[f]Animal body weight recorded on Study Day 11.

TABLE 6. BODY WEIGHTS[a] OF FEMALE NZW RABBITS AFTER DERMAL TREATMENT WITH A NEW NONCORROSIVE DECONTAMINATION SOLUTION

	Study Day					
	0	**1**	**2**	**7**	**10**	**14**
2.0 g/kg						
Animal #						
01	2.6[b]	-----	-----	-----	-----	-----
02	2.6[b]	-----	-----	-----	-----	-----
03	2.8[b]	-----	-----	-----	-----	-----
04	2.5 [b]	-----	-----	-----	-----	-----
05	2.6[b]	-----	-----	-----	-----	-----
0.252 g/kg						
Animal #						
25	3.7	3.6	3.6	3.9	3.9	3.9
26	3.6	3.5	3.5	3.9	3.7	3.6
27	3.3	3.3	3.5	3.4	3.5	3.4
28	3.3	3.2	3.2	3.3	3.3	3.3
29	3.3	3.2	3.3	3.4	3.4	3.3
Mean	3.4	3.4	3.4	3.6	3.6	3.5
SD	0.2	0.2	0.2	0.3	0.2	0.3
0.2 g/kg						
Animal #						
20	2.8	2.8	2.8	2.9	3.0	2.9
21	2.7	2.7	2.7	2.8	2.9	2.9
22	2.7	2.7	2.7	2.9	2.9	2.9
23	2.8	2.9	2.9	3.1	3.1	3.1
24	2.8	2.8	2.9	3.0	3.1	3.2
Mean	2.8	2.8	2.8	2.9	3.0	3.0
SD	0.1	0.1	0.1	0.1	0.1	0.1

[a]Animal body weight in kg.
[b]Animal died within 2 h of dosing.

Inhalation Toxicity

Aerosol exposure of male and female rats to a target concentration of 5 mg NDS/L resulted in 100% mortality. All animals were dead before the 4-h exposure was completed. No clinical signs of toxicity were observed during the exposure. No gross lesions were noted at necropsy, and histologic examination of lungs revealed normal tissues.

Male and female rats were exposed to a target concentration of 1.0 mg NDS/L. All animals exhibited chromodacryorrhea during exposure, which resolved postexposure. All 10 animals survived the 4-h exposure. No clinical signs of toxicity were noted during the 14-day postexposure observation period. No gross lesions were noted at necropsy for these animals.

Male and female rats were exposed to a target concentration of 0.5 mg NDS/L. Two animals exhibited chromodacryorrhea during exposure. All animals survived the 4-h exposure. One animal exhibited transient right hindlimb paresis one day postexposure. All animals recovered uneventfully and survived the 14-day postexposure observation period. No gross lesions were noted at sacrifice.

TABLE 7. ACUTE INHALATION TOXICITY OF NDS

Target Conc. (mg/L)	Analyzed Conc. (mg/L)	Sex	Mortality Ratio	Time to Death
5.0	4.4	Male	5/5	1 dead at 0.33 h 1 dead at 0.5 h 3 dead at 1 h
		Female	5/5	1 dead at 0.33 h 1 dead at 1 h 1 dead at 1.83 h 1 dead at 2.33 h 1 dead at 2.5 h
1.0	0.86	Male	0/5	-----
		Female	0/5	-----
0.5	0.41	Male	0/5	-----
		Female	0/5	-----
		LC_{50} Sexes Combined =		1.36 (1.359, 1.360)[a] mg/L

[a]95% confidence interval.

TABLE 8. BODY WEIGHTS[a] OF SURVIVING MALE AND FEMALE F-344 RATS AFTER 4-h, NOSE-ONLY AEROSOL INHALATION EXPOSURE TO A NEW NONCORROSIVE DECONTAMINATION SOLUTION

	Study Day					
	0	**1**	**2**	**7**	**10**	**14**
0.86 mg/L						
Male Animal #						
15	196.5	195.3	202.0	222.9	228.5	238.3
16	209.3	202.0	204.1	222.3	226.8	234.1
17	214.1	211.3	217.1	237.9	240.7	248.5
18	209.5	203.9	215.0	234.7	239.1	244.1
19	218.5	209.7	220.5	237.0	249.4	249.7
Mean	209.6	204.4	211.7	231.0	236.9	242.9
SD	8.2	6.4	8.2	7.7	9.3	6.7
Female Animal #						
35	131.8	127.1	129.5	138.5	140.1	142.6
36	141.0	133.8	139.0	150.5	149.9	149.5
37	136.8	132.1	137.3	148.9	145.2	152.7
38	130.8	127.8	131.1	142.9	141.3	144.5
39	126.5	124.5	127.9	137.5	138.8	141.5
Mean	133.4	129.1	133.0	143.7	143.1	146.2
SD	5.6	3 .8	4.9	5.9	4.5	4.8
0.41 mg/L						
Male Animal #						
10	208.6	205.2	211.5	233.1	243.3	253.1
11	202.9	195.2	202.1	228.5	232.5	241.3
12	198.5	194.7	196.2	222.3	229.4	240.8
13	194.6	188.7	192.6	217.4	227.0	234.9
14	189.0	187.0	189.6	212.2	225.5	231.7
Mean	198.7	194.2	198.4	222.7	231.5	240.4
SD	7.5	7.2	8.7	8.4	7.1	8.2
Female Animal #						
30	121.9	121.0	122.4	134.0	137.9	141.2
31	127.8	128.5	130.1	140.4	145.2	149.0
32	128.1	128.9	126.0	136.7	144.8	148.2
33	130.4	129.4	129.2	143.4	145.7	147.5
34	131.5	131.8	133.5	146.2	146.2	149.5
Mean	127.9	127.9	128.2	140.1	144.0	147.1
SD	3.7	4.1	4.2	4.9	3.4	3.4

[a]Animal body weight in grams.

SECTION IV

DISCUSSION

Oral gavage of NDS resulted in 100% mortality of male and female F-344 rats at the limit test dose of 5 g/kg. Clinical signs included whole body tremors and chromodacryorrhea. Subsequent oral treatment at lower concentrations of NDS resulted in the determination of an LD_{50} of 0.78 g/kg (sexes combined). Therefore NDS would have a toxic class rating of 4 (slightly toxic) via the oral route of exposure (Deichman and Gerarde, 1969). The mild congestion in the upper gastrointestinal tract observed in animals of all dose levels, except the lowest (0.5 g/kg), may be associated with irritation due to the pH of the material (10-10.5).

All male and female NZW rabbits dermally treated with 2 g NDS/kg died within two hours of treatment. Signs of toxicity included whole body tremors and excessive salivation. Although there were scattered dermoepidermal lesions indicating mild to minimal corrosive action, it should be noted that the majority of the exposed epidermal surface appeared normal. Dermal treatment with lower doses of NDS resulted in the determination of a dermal LD_{50} of 0.36 g/kg (sexes combined). NDS would be considered moderately toxic by the dermal route of administration, with a toxic class rating of 3 (Deichman and Gerarde, 1969).

Inhalation exposure of male and female rats to near the limit test concentration (4.4 mg/L) also resulted in 100% mortality. All animals were dead within 2.5 h of exposure initiation. In the subsequent exposures at lower concentrations of NDS, chromodacryorrhea was noted. The LC_{50} for NDS aerosol was determined to be 1.36 mg/L (sexes combined).

The 100% fatality associated with the higher levels of exposure for all routes of exposure, coupled with a lack of significant gross or histologic lesions, suggests that deaths were not necessarily due to corrosive action. Additional studies would be required, incorporating hematology, clinical chemistry parameters, blood gas analysis, and histopathology to explain the cause(s) of mortality following administration of NDS.

SECTION V

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