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TOXICOLOGICAL ASSESSMENT OF RIOT CONTROL SPRAY DEVICES AND FILLINGS

by

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EDGEWOOD ARSENAL

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CS in polyethylene glycol (PEG 200)
CS in propylene glycol
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In the search for effective but nonhazardous riot control devices, both commercial items which contained chloroacetophenone (CN) and locally prepared formulations which contained o-chlorobenzylidene malononitrile (CS) have been studied. Their effects on the eyes, skin, and trachea of animals and on human skin have been assessed and the different formulations compared.

The commercial items were the MK IV Chemical Mace and the Federal Streamer

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20. ABSTRACT (Contd)

No. 280; the locally prepared formulations were CS in trioctylphosphate (TOF), CS in polyethylene glycol (PEG 200), and CS in propylene glycol.

It was found that the Federal Streamer No. 280 and the MK IV Chemical Mace had similar effects on the eyes and skin of rabbits and monkeys, and on the trachea and lungs of dogs. They produced opacity of the cornea, severe tracheitis, and pseudomembrane formation. CS/TOF did not have these effects. CS/PEG 200 had minimal ocular effects. CS/propylene glycol, tested only by tracheal intubation, had no effects.

Both the Federal Streamer No. 280 formulation and CS/TOF produced marked cutaneous reactions when applied to cloth patches taped to the clipped backs of rabbits. All three formulations produced necrosis when applied to the bare skin of rabbits. In monkeys, Mace and the Federal Streamer No. 280 produced necrosis, but 1% CS/TOF had no effect.

On human skin, both bare and covered with a patch, Mace and the Federal Streamer No. 280 produced erythema. Slight stinging occurred when 0.01 ml of 1% CS/TOF was applied under patches; stinging and mild immediate erythema occurred when concentrations of up to 1.0% CS1/TOF was applied to uncovered patches at different temperatures. Based on the overall results, CS/TOF is definitely safer than the two commercial items.

PREFACE

The work described in this report was authorized under Project 1W662619AD22, Medical Effects of Riot Control Agents. This work was started in October 1967 and completed in July 1969. The experimental data are contained in notebooks MN 2130, 2195, 2277, and 2290.

The volunteers in these tests are enlisted US Army personnel. These tests are governed by the principles, policies, and rules for medical volunteers as established in AR 70-25 and the Declaration of Helsinki.

In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals" as promulgated by the Committee on Revision of the Guide for Laboratory Animals Facilities and Care of the Institute of Laboratory Animal Resources, National Research Council.

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I. BACKGROUND.

In the search for effective but nonhazardous riot control devices, both commercial items [which contained chloroacetophenone (CN)] and locally prepared formulations [which contained o-chlorobenzylidene malononitrile (CS)] have been studied. Their effects on the eyes, skin, and trachea of animals and on human skin have been assessed and the different formulations compared.

The commercial items were the MK IV Chemical Mace and the Federal Streamer No. 280; the locally prepared formulations were CS in trioctylphosphate (TOF), CS in polyethylene glycol (PEG 200), and CS in propylene glycol.

II. DESCRIPTION OF COMMERCIAL RIOT CONTROL SPRAY DEVICES.

A. MK IV Chemical Mace.

The MK IV Chemical Mace is a riot control device made by the General Ordnance Equipment Corporation, Pittsburgh, Pennsylvania. It is a plastic, cylindrical aerosol can, 1-1/2 inches in diameter, 6 inches long, that contains about 30 ml of liquid material. Chemical analysis* revealed that this material contains 0.92% CN, 88.1% Freon 113, 4.6% kerosene hydrocarbons, and 6.4% 1,1,1-trichloroethane. The pressurizing gas is carbon dioxide. When sprayed, the material collected in a chilled flask contained 0.93% CN, 88.7% Freon 113, 5.2% kerosene fraction, and 5% 1,1,1-trichloroethane.

B. Federal Laboratories Items.

1. Federal Streamer No. 280.

The Federal Streamer No. 280 is a liquid-squirting riot control device made by the Federal Laboratories, Inc., Saltsburg, Pennsylvania. Chemical analysis* in 1968 revealed 0.96% CN, 93.7% Freon 113, 5.2% 1,1,1-trichloroethane, and 0.15% paradioxane. When sprayed into a chilled flask, the material collected contained 0.85% CN, 92.5% Freon 113, 6.3% 1,1,1-trichloroethane, and 0.25% paradioxane.

2. Federal Laboratories Peacemaker.

No toxicological information is available on the Peacemaker. It is mentioned here only to differentiate it from the Federal Streamer No. 280. The Peacemaker was analyzed* in 1968 and found to contain 1.5% CN, 73.1% propylene glycol, 24.4% isopropyl alcohol, and 1% Blancophore AW. When sprayed into a chilled flask, the material collected was 1.9% CN, 77.6% propylene glycol, 19.7% isopropyl alcohol, and 0.8% Blancophore AW. The pressurizing gas is nitrous oxide.

III. TOXICITY OF SEPARATE INGREDIENTS OF COMMERCIAL ITEMS.

A. Chloroacetophenone.

Chloroacetophenone is a white crystalline solid with a boiling point of 244° to 245°C and a vapor pressure of 0.0054 mm Hg at 20°C. It is poorly soluble in water but soluble in organic solvents.

*Analytical Chemistry Branch, Chemical Research Division, Chemical Laboratory.

The toxic and irritant properties of CN have been investigated in man and animals since 1918. A detailed description of those studies has been written by McNamara *et al.*[1]

For study of its inhalation toxicity as well as its eye irritant properties, CN has been dispersed in various ways; e.g., as a dry dust, as an aerosol from the molten solid, as a spray, dissolved in acetone or other organic solvents, and as a disseminate from several types of munitions (grenades). Monkeys, dogs, swine, goats, rabbits, guinea pigs, rats, and mice have been exposed to airborne concentrations of CN. Among the numerous toxic signs observed in exposed animals were nasal discharge, erythema, lacrimation, conjunctivitis, dyspnea, salivation, corneal damage, and death. These signs were present in all species. Direct application of CN to the eye of the rabbit produced conjunctivitis, blepharitis, and transient-to-permanent corneal opacity. Direct application of CN to the skin of rabbits produced mild-to-severe erythema and necrosis.[1]

Pathologic findings in animals that died following exposure to aerosols of CN were: congestion and edema of the lungs, emphysema, membranous tracheitis, and bronchopneumonia.[1]

The acute inhalation toxicity of CN to various species of animals has been studied. The data show that CN dispersed from the No. 112 Spedeheat burning grenade is less toxic than when dispersed as the pure agent from molten material, dry dust, or solvent spray. A composite summary of the times to death of all the animals in all these experiments showed that 75% of the deaths occurred in the first 3 days following exposure.[1]

Based on a study of subacute effects in monkeys, dogs, and guinea pigs that were exposed on 10 consecutive days to CN dispersed from the No. 112 Spedeheat grenade, there is little evidence of cumulative toxicity of CN.[1]

Physiological studies of the following parameters were made on anesthetized dogs inhaling CN in acetone at Ct's ranging from 12,500 to 57,600 mg min/cu m: arterial blood pressure, electrocardiogram, arterial oxygen, respiratory rate and depth, and heart rate. The most noteworthy finding was a decrease in blood oxygen content despite an increase in respiratory rate and amplitude in those animals that eventually died.[1]

In August 1966, all of the toxicity data on CN from 1918 to 1965 on all animals by all laboratory-type dispersions (excluding munitions) were combined and a value of 7,000 mg min/cu m was derived as the human estimate for the inhaled LCt50 of CN.[1,2] Also in August 1966, the toxicity data for CN dispersed from the Spedeheat grenade for tests involving rats, guinea pigs, rabbits, dogs, monkeys, swine, and goats were combined, and a value of 14,000 mg min/cu m was obtained as a human estimate for the inhaled LCt50 of CN.[1,2]

In man, CN acts on the mucous membranes to produce irritation, burning, and pain in the eyes, nose, throat, and respiratory tract. The action on the eyes causes lacrimation, blepharospasm, and conjunctivitis. Effects in the air passages and lungs cause coughing, sneezing, and a feeling of suffocation. These effects are noted immediately and persist from 5 to 20 minutes after withdrawal from the contaminated atmosphere.[1]

Tests in September 1965, when the compound was dispersed in cold acetone spray and spectrophotometric analysis was used, yielded an ICt50 for man of about 40 mg/cu m for exposures of 1 minute or less. The ICt50 for men exposed to CN dispersed from the commercial grenade was 20 mg/cu m for 1 minute or less.[1]

Five deaths have occurred in men following exposure to CN in inclosed spaces as a result of police actions.[3] The cause of death has been attributed to damage to the respiratory system because of secondary bronchopneumonia from inflammation of air passages[4] or acute pulmonary edema.[3]

B. 1,1,1-Trichloroethane (Methyl Chloroform).

Methyl chloroform, a colorless liquid with a specific gravity of 1.3249 (26°/4°C) and a boiling point of 74.1°C, is used as a solvent. Chlorinated solvents sometimes require the addition of an inhibitor to prevent corrosion

of metals. Methyl chloroform sometimes contains 2% to 3% dioxane, 0.1% to 0.3% butanol, and small amounts of ethylene dichloride, water, etc.[5]

There were no detectable injuries in rats after acute vapor exposure for 18 minutes to 18,000 ppm (1 ppm = 5.46 mg/cu m) and for 5 hours to 8,000 ppm. Maximum doses survived were 6 minutes at 30,000 ppm, 1-1/4 hours at 15,000 ppm, and 7 hours at 8,000 ppm.[6] Animals were also exposed repeatedly for 7 hours per day, 5 days per week for 1 to 3 months.[6] The growth of guinea pigs was slightly retarded at 650 ppm. At 3,000 ppm, rabbits and monkeys showed no response during a 2-month period. The growth of rabbits was slightly retarded at 5,000 ppm. Although this same concentration caused a mild narcotic effect in rats within 1 hour, there were no injuries or deaths in 31 animals exposed during a 41-day period. Concentrations of 10,000 ppm produced weakness and staggering in rats in 10 minutes and semiconsciousness in 3 hours. Some deaths occurred; survivors recovered overnight.

The oral LD50's for male rats, female rats, female mice, female rabbits, and male guinea pigs, respectively, are 12.3, 10.3, 11.24, 5.66, and 9.47 gm/kg.[7] Patty[5] states that 3.9 gm/kg and 15.8 gm/kg applied under a cuff for 24 hours did not kill any animals; skin irritation was mild.

There was no response in humans to 1000 ppm in exposures lasting up to 70 minutes. Drunkenness and incoordination occurred at 2000 ppm. Two fatalities have occurred from exposures in a tank (30 minutes in one case, time unknown in other) where the concentration may have approached saturation.[5] The threshold limits for humans to methyl chloroform established by the American Conference of Governmental Industrial Hygienists is 500 ppm (2700 mg/cu m).[5]

C. Dioxane (p-Dioxane 1,4-Dioxane).

Dioxane is a colorless liquid with a specific gravity of 1.035 (20°/20°C) and a boiling point of 101.3°C (760 mm Hg).[8]

Intravenous injection of dioxane in guinea pigs, rabbits, and cats produced acute hydropic degeneration of the convoluted tubules of the kidney. Deaths were due to uremia caused by intrarenal obstruction.[9] Deaths due to lung edema and respiratory failure occurred in guinea pigs that inhaled 1,000 to 30,000 ppm for 3 hours[10] and in rats, mice, guinea pigs, and rabbits that inhaled 4,000 to 11,000 ppm for 8 hours.[11] Animals also exhibited congestion of the brain, and liver and kidney damage was noted. In rats, mice, guinea pigs, and rabbits that were exposed for 1-1/2 hours per day to 1,000, 2,000, 5,000, and 10,000 ppm, death from lung injury was high at the lower levels. Those animals that survived repeated exposure at all doses developed marked liver and kidney damage.[12] The single oral LD50 doses for mice, rats, and guinea pigs, respectively, were 5.66, 5.17, and 3.90 gm/kg. Hemorrhagic areas were seen in the stomach and the kidneys were enlarged. Microscopic changes were noted in the liver and kidneys.[13] Rabbits and guinea pigs fed 10 doses of 0.1 ml/kg showed changes in the liver and 5, 16, and 20 doses of 0.5 ml/kg killed some animals.[11] Dioxane is not an irritant to the skin.[8] Liver and kidney damage has been noted in guinea pigs and rabbits following repeated cutaneous applications.[12] The compound has also been reported as having hepatocarcinogenic activity in rats.[14]

Five humans died following inhalation of dioxane in a textile factory.[8] The effects were irritation of the upper respiratory tract and eyes, coughing, drowsiness, vertigo, headache, stomach pains, nausea, vomiting, uremia, coma, and death. The lungs and brain were congested and edematous, and there was marked damage to the liver and kidneys. The recommended industrial hygienic standard is 100 ppm. A concentration of 1000 ppm may be relatively safe for a single exposure not exceeding 1/2 hour.[8]

D. Freon 113.

Freon 113 is a colorless gas or liquid with a boiling point of 45.8°C[15,16] and a density of 1.5702. Freon 113 has mild irritant properties, causes narcosis, and can sensitize the heart muscle to epinephrine. The latter effect presents the most acute hazard to man.[17] Inhalation of 20% in air (200,000 ppm) may cause confusion, tremors, pulmonary irritation, and, in rare cases, coma. Its effects are usually transient and there are no sequelae.[16,18,19]

No official value has been established for the maximum allowable concentration, but Sax[16] and Elkins[18] suggest 1000 ppm (7,650 mg/cu m). This value will undoubtedly be lowered to reflect the sensitizing properties of the material. At high temperatures or in open flame it decomposes and may liberate toxic materials such as hydrogen fluoride, hydrogen chloride, and possibly phosgene.[16]

E. Kerosene.

Kerosene is a petroleum hydrocarbon mixture of olefinic, naphthenic, and aromatic hydrocarbons that boils between 200° and 300°C. The principal constituents are aliphatics containing 5 to 16 carbon atoms. The density is about 0.80. Although relatively nontoxic, kerosene may cause local irritation,[20,21] drowsiness, collapse, twitching of muscles, and coma.[21] It damages the heart, liver, and kidneys.[21]

The intravenous, intraperitoneal, intragastric, and intratracheal toxicity in animals has been determined by Richardson and Pratt-Thomas.[22] Intratracheal doses of 0.25 and 1.0 mg/kg killed rabbits and dogs, respectively. A fatal dose to rabbits by stomach tube was 35 ml/kg. It has been found that hydrocarbon mixtures of low viscosity (kerosene) were readily aspirated and considered highly toxic by this route; deaths often occurring in less than 24 hours.[23] Mineral oil and motor oils of similar viscosity did not cause severe pulmonary edema and hemorrhage characteristic of kerosene and similar low viscosity hydrocarbon mixtures. Toxicity of kerosene by aspiration was markedly reduced by blending with an equal volume of lubricant oil.

The accidental ingestion of petroleum distillates is considered to be an important cause of poisoning in children in the United States.[24] The principal pathological finding in clinical kerosene intoxication is a chemical pneumonitis which may be complicated by bacterial pneumonia.[25-27] Death results in 4% to 10% of the cases reported.[28] Although animal experimentalists and clinicians disagree about the cause of the pneumonitis following congestion, a great deal of evidence points to direct entry and spread into the lungs (aspiration) rather than absorption through the gastrointestinal tract. For kerosene, the LD50 ratio for oral/intracheal routes is 140/1.[23-29]

IV. TOXICITY OF MIXTURES CONTAINED IN COMMERCIAL ITEMS.

A. MK IV Chemical Mace.

The effects of materials contained in the MK IV Chemical Mace were studied for the manufacturer in 1966 by a commercial testing laboratory[30,31] and also by the Toxicology Department, Research Laboratories, Edgewood Arsenal in 1968.**,[32]

1. Effects on Animals.

The commercial testing laboratory[30] reported that the eyes of monkeys exposed for 1, 2, and 5 seconds to aerosols ejected from the MK IV Chemical Mace at a distance of 6 feet produced no detectable conjunctival irritation or corneal damage. A single exposure of rabbit eyes to 0.1 ml of MK IV formula caused a slight conjunctival erythema 24 and 48 hours after exposure which disappeared by 72 hours.[31] The material was not considered to be an eye irritant under the Federal Hazardous Substances Labeling Act.

*Grobecker, A. J. Freon/Ozone Problems. Department of Transportation Climatic Impact Assessment Program. January 31, 1975. Unpublished data.

**Now known as Toxicology Division, Biomedical Laboratory.

In the tests conducted at Edgewood Arsenal,[32] the spray produced conjunctivitis, blepharitis, swollen eyelids, depilation around the eyelids, and patches of erythematous skin in rabbits in 1 to 7 days. They recovered within 14 days and there was no corneal damage. The application of the liquid to the eyes of rabbits and monkeys caused conjunctivitis, blepharitis, and corneal opacity; the last effect still evident at 30 days in some rabbits. The liquid applied to the skin of rabbits and monkeys caused erythema, dermatitis, and necrosis in some animals of each species within 1 week. In the rabbit, scar formations and cutaneous lesions persisted for 30 days. The skin of the monkeys appeared normal in 30 days. When liquid was injected into the trachea of dogs, tracheitis and bronchitis were noted within the first week and at 30 days.

2. Effects on Humans.

In further tests performed at Edgewood Arsenal,[32] the liquid was applied to the arms of US Army volunteers and produced immediate burning and itching which subsided in 20 to 30 minutes. Some erythema persisted up to 48 hours. Twenty-four-hour patch tests produced erythema which was discernible up to 7 days.

3. Conclusion.

As a result of our tests and a news release[38] by The Surgeon General, US Public Health Service, warning that Chemical Mace may be harmful, tests of another riot control device (the Federal Streamer No. 280) were conducted at Edgewood Arsenal.

B. Federal Streamer No. 280.

1. Ocular and Cutaneous Tests.

The contents of several Federal Streamer No. 280 units were removed and applied directly to the skin or eyes in the first tests. The material was drawn into syringes and applied as discrete droplets to the right eyes and the clipped backs of rabbits and monkeys. Additional animals that were prepared in the same way received an isotonic saline solution in equivalent doses and served as controls. For the spray tests, several Federal Streamer No. 280 units were actuated for 1 or 5 seconds and the spray was collected in tared flasks and weighed before the animal tests. Based on calibration, the 1-second firing yielded about 1.0 ml of formulation and the 5-second firings about 10.0 ml.

Both eyes of each animal were examined and any animals with eye defects or irritation were not used. Before and during the tests, the animals were individually caged in raised pens free from animal bedding and animal droppings. One day after administration all dosed eyes were flushed with isotonic saline and cleansed with surgical gauze. Clinical observations of the dosed and undosed eyes were then recorded. Following this, one drop of fluorescein sodium ophthalmic solution (USP) was instilled into each eye, and the eyes flushed with isotonic saline. Corneal involvement was then assessed. Two days following exposure, after clinical observations, all dosed eyes were flushed with isotonic saline and treated with one drop of modified 15% sodium sulfacetamide ophthalmic solution. On subsequent days of observation, only those eyes which warranted treatment were flushed, cleansed, and treated. The evaluation of eye irritancy was done in accordance with a modified Draize technique (table A-1).*

The animals were prepared for cutaneous testing by clipping their skins free of hair on the trunk. Any animals with skin abnormalities (abrasions, discoloration, etc.) were eliminated from testing. After dosing, no subsequent treating was done other than reclipping hair in some instances to observe masked skin reactions. The grading system used to evaluate skin irritation is shown in table A-2.

*Tables A-1 through A-17 are in the appendix.

a. Direct Application of Liquid to Rabbits.

The formulation was applied to both the eyes and skin of 36 healthy rabbits; six rabbits served as controls. The animals were observed for 30 days for gross ocular and cutaneous effects. At 30 days, 12 of the dosed and six of the control rabbits were sacrificed and necropsied. The experimental design data are shown in table 1.

Table 1. Ocular and Cutaneous Doses of Federal Streamer No. 280 Applied Directly to Rabbits

No. of rabbits dosed	Ocular dose	Cutaneous dose	No. of rabbits necropsied
	ml	ml	
6	0.2	1.0	4
2*	0.2	1.0	2
6	0.1	0.50	
6	0.05	0.25	
6	0.025	0.10	4
2*	0.025	0.10	2
6	0.010	0.05	
6	0.005	0.025	4
2*	0.005	0.025	2

*Isotonic saline controls.

Three additional groups of four rabbits each received ocular doses of 0.2, 0.025, and 0.005 ml and cutaneous doses of 1.0, 0.1, and 0.025 ml, respectively. Two control rabbits per group received equivalent ocular and cutaneous doses of isotonic saline. All of these rabbits were sacrificed and necropsied 3 days later. This supplemental test was to reveal any early pathological changes in the eye or skin. Data are presented in table 2 and table A-3.

Table 2. Ocular and Cutaneous Lesions Found in Rabbits Necropsied 3 Days After Exposure to Federal Streamer No. 280

Dose		Effects	
Ocular	Cutaneous	Ocular	Cutaneous
ml			
0.005	0.025	Some reddening of conjunctiva	Mild erythema
0.025	0.1	Mild to moderate conjunctivitis; some chemosis	Minimal to moderate erythema
0.2	1.0	Moderate to severe conjunctivitis; some chemosis and corneal opacity	Moderate erythema pinpoint to 3 mm

In the 30-day tests, gross clinical observations indicated that the lowest dose (0.005 ml) instilled in the eye affected only one of six rabbits, causing transient mild chemosis that disappeared by the third day. A dose of 0.010 ml caused chemosis and redness that disappeared in 6 days in five out of six rabbits. A dose of 0.025 ml produced chemosis and redness in five animals; one rabbit died for reasons not related to the tests. One animal showed scattered corneal opacity which disappeared in 6 days. This group recovered in 5 to 13 days. Doses of 0.05, 0.10, and 0.20 ml produced marked chemosis, redness, and corneal opacity. The corneal opacity disappeared in 9 to 12 days. Most of the animals displayed mild chemosis and redness that was still present 15 to 21 days after these doses. No iritis was noted in any of the animals at any dose level. The saline controls showed no effects. Details are shown in table A-4.

Gross clinical observations of the skin indicated that all cutaneous dose levels (0.025 to 1.0 ml) produced increasing erythema, dehydration, and necrosis. The erythema and necrosis were still evident at 14 days. Erythema persisted in some animals throughout the 30-day observation period. The saline controls showed no effects. Details are shown in table A-5.

Pathological findings on animals necropsied 30 days after exposure confirm gross clinical observations for both eye and skin studies.

b. Direct Applications of Liquid to Monkeys.

Three groups of eight monkeys each received ocular doses of 0.1, 0.025, and 0.005 ml and cutaneous doses of 1.0, 0.1, and 0.025 ml, respectively; and three groups of four monkeys each received equivalent ocular and cutaneous doses of isotonic saline. Four dosed and two control animals from each dose level were sacrificed and necropsied 3 days later (table 3). The remaining monkeys were observed 30 days for gross ocular and cutaneous effects. At 30 days they were sacrificed and necropsied.

Table 3. Ocular and Cutaneous Lesions Found in Monkeys Necropsied 3 Days After Exposure to Federal Streamer No. 280

Dose		Effects	
Ocular	Cutaneous	Ocular*	Cutaneous*
ml			
0.005	0.025	Mild blepharitis	No significant lesions
0.025	0.1	Mild to moderate conjunctivitis and blepharitis	No significant lesions
0.1	1.0	Moderate to severe conjunctivitis and blepharitis Corneal ulcer (1)	Slight thickening (2)

*Numbers in parentheses indicate portion of four monkeys at each dose showing sign. Absence of a number indicates all four showed the sign.

Gross observations of the eyes indicated that at the lowest dose (0.005 ml), the only sign noted was a reddening of the eyelid which persisted for 1 day. A dose of 0.025 ml produced mild chemosis and corneal opacity. These signs disappeared in 6 days. A dose of 0.1 ml produced marked chemosis, redness, and corneal opacity. Corneal opacity disappeared in 11 days, and the chemosis and redness persisted for 10 to 15 days. All saline controls appeared normal throughout the observation period. See table A-6 for detailed observations.

Gross observations of the skin indicated that a cutaneous dose of 0.025 ml produced no effect throughout the observation period. A dose of 0.10 ml produced transient erythema in two of eight monkeys; no signs were apparent after the fifth day. A dose of 1.0 ml produced marked erythema in five of eight monkeys in 3 days. Edema was noted in two of eight monkeys in 3 days also. Necrosis was evident in one monkey on the sixth day and in another by the eighth day. This necrosis persisted up to the thirteenth day in one animal. None of the controls showed any cutaneous effects. Pathological examination of all monkeys necropsied at 30 days showed no lesions. Table A-7 presents detailed data.

c. Spray Tests in Rabbits.

Rabbits were restrained and their left eyes sprayed according to the design shown in table 4.

Table 4. Design of Spray Tests

No. of rabbits	Total time sprayed	Distance of rabbits from dissemination point	Observation period
	sec	ft	days
5	1	1	30
5	1	3	30
5	1	6	30
5	5	1	30
5	5	3	30
5	5	6	30
4*	1	3	3
4*	5	3	3
2**	1	3	3
2**	5	3	3

*Sacrificed and necropsied at 3 days.

**Isotonic saline controls; also sacrified and necropsied at 3 days.

All of the rabbits sprayed with the formulation (except those sprayed for 1 second at 6 feet) displayed severe chemosis and redness of eyes (tables A-8 and A-9). In the group observed for 30 days, corneal opacity occurred in several rabbits at each test condition except for those sprayed 1 second at 6 feet. The signs were still present in most rabbits at 3 weeks and persisted throughout the 30-day observation period in four rabbits.

Histological examination of the group sacrificed at 3 days showed that the 1-second spray caused moderate conjunctivitis and blepharitis. These effects were severe in the group sprayed for 5 seconds.

There was scar tissue formation in areas 1 to 3 inches around the sprayed eye in the majority of the rabbits, with no hair growth evident at 30 days. A few rabbits appeared to have eye muscle damage. No ocular or cutaneous reactions were seen in the saline controls.

d. Patch Tests in Rabbits.

Sateen patches, 3-inch-square, were taped to the clipped backs of rabbits and the formulation was applied to the surface. Doses of 0.1 and 1.0 ml were given to two groups of eight rabbits each; the patches were

removed at 24 hours and the animals were observed for 30 days. Two control groups of four rabbits each received 0.1 and 1.0 ml of isotonic saline. Four rabbits from each formulation group and two rabbits from each saline group were necropsied at 3 days.

Both doses of the formulation produced mild to moderate erythema within 24 hours in all animals. Moderate necrosis was seen in two of eight rabbits receiving 1.0 ml and in one of the eight rabbits receiving 0.1 ml at 48 hours. Of the four rabbits (1.0-ml dose) submitted for necropsy at this time, three showed moderate to severe erythema without formation of necrotic tissue, and one showed moderate erythema with patches of necrotic tissue covering more than 50% of the dosage site. The skin of the other four rabbits in the 1.0-ml dose group was necrotic at 5 days, ranging in extent from 50% to 100% of the total area of spread of the solution on the cloth. Severe erythema was also seen in all four of these rabbits. The areas of necrosis were pronounced throughout the 30-day observation period. Mild to moderate erythema was seen at 72 hours in four rabbits that received the 0.1-ml dose; necrotic tissue was seen in 3 to 10 days and persisted in three rabbits throughout the 30-day observation period. Of the four rabbits at this dose that were sacrificed at 72 hours, none had any necrosis but all had moderate erythema. The controls showed no effects within 24 hours or during the 30-day observation period. Details of the gross observations are shown in table A-10.

e. Effects on Human Skin.

Eight male volunteers received a dose of either 0.01 ml or 0.025 ml of the Federal Streamer No. 280 formulation applied to the bare skin of the volar surface of the forearm or to sateen patches taped to the volar surface of the forearm (table A-11). They were asked not to wash the area or to remove the patches for 24 hours. The test areas were examined through the first 4 hours after application and at 24 hours. Daytime temperatures during the test period averaged 59°F and relative humidity was greater than 90%.

The Federal Streamer No. 280 formulation applied to the bare skin or sateen patches caused only slight erythema.

2. Tracheal Tests in Dogs.

The Federal Streamer No. 280 formulation was put into the trachea of 48 beagle hounds under 2 years of age by either intubation after the animals were given a short-acting anesthesia, or by injection directly into the trachea through a puncture in the neck after the animals were tranquilized with chlorpromazine hydrochloride. Each animal was given a physical examination including red and white blood cell counts, packed cell volume, blood urea nitrogen level, and rectal temperature; and their quarantine history and general state of health were noted.

Three groups of eight dogs each received the formulation by tracheal intubation in doses of 0.50, 0.25, and 0.10 ml per animal, respectively, and three groups of four received saline in the same doses. In another group of eight dogs, 0.50 ml per animal was injected intratracheally and four controls received saline in the same dose. All animals tested were examined critically at either 72 or 96 hours after dosing and dose effects were recorded. Four dogs from each group dosed with agent, and two from each saline group were sacrificed and necropsied at 72 or 96 hours after dosing; the rest of the dogs were sacrificed and necropsied at 30 days. The protocol for these tracheal tests is included with that for other formulations in table A-12.

None of the dogs that received the formulation by intubation died or were severely listless or prostrate. Results of an examination at 72 hours of dogs receiving all doses of both agent and saline are shown in tables A-13 through A-15. The blood values at all dose levels of the agent did not vary significantly from control values. The values varied even less within a dose group. The same impression is given by temperature data (table A-13). Signs seen were dehydration, cough on tracheal pressure, and auscultable congestion in the lungs (table A-15). The general appearance of all of the dosed animals at 72 hours was good; grossly, it was difficult to observe any difference between exposed and control animals. Histological findings are shown in table A-16.

In the eight dogs that received the formulation by injection, coughing was an immediate common sign. Three of the dogs coughed up bloody foam soon after being put back in the cage. Two dogs had edema in the ventral

neck region 24 hours after dosing. The mean blood values before and 96 hours after dosing are shown in table A-14; there were no significant changes. Signs observed were the same as those exhibited by the intubated dogs (table A-15). There was no difference in dehydration among dosed and control animals. Five of the eight dosed animals exhibited tracheal coughs; the controls did not. No lung congestion was detectable in either the dosed or the control group.

When the dogs that were given 0.5 ml of the formulation by injection were compared with the dogs that received the the same amount by intubation, a higher incidence of cough on tracheal pressure and a lower incidence of auscultable congestion was seen in the dogs given intratracheal injections.

3. Oral Spray Tests in Dogs.

Physical examination, method of observation, and necropsy schedule were the same as for the tracheal and intratracheal tests. The Federal Streamer No. 280 was sprayed into the mouths of eight dogs to determine the effect of the solution on oral mucosal membranes and to see if the material would enter the trachea when administered in this way. The dogs were comfortably restrained in a sitting position with their heads held level, their mouths held open, and their tongues depressed. The Federal Streamer No. 280 device was held an inch or two in front of the opened mouth, and a 1-second spray was directed into the throat. Based on calibration, the estimated dose delivered to each dog was 1 ml. Four dogs were sprayed with isotonic saline in an identical manner. The test protocol is shown in table A-12.

The dogs reacted immediately to the agent. They displayed profuse salivation and chewing action, became frightened, and huddled together. No coughing was noted. There were no significant changes in blood values (table A-14), temperatures were not recorded. The exposed and control dogs had the same signs; none of the signs seen in the tracheal or intratracheal tests were noted.

V. TOXICITY OF CS FORMULATIONS.

A. CS in Trioctylphosphate (TOF).

CS is believed to be a more potent and safer irritant than CN.[34-37] It appears to be less damaging to the eyes and skin.[35] The incapacitating dose for riot control for 50% of a population (ICt50) is a Ct (concentration X time) of 0.1 to 10 mg min/cu m.[35] Toxicological testing has shown trioctylphosphate (TOF) to have some toxicity when used in large doses or when applied repeatedly to the same skin area.[38,39] It was felt that these untoward effects would not occur if TOF were used as a riot control spray material.

Tests of CS/TOF solutions in animals and man were performed. The details of this work have been reported separately;[37,40,41] however, the conclusions are summarized briefly here.

1. Ocular Effects of CS/TOF and TOF Alone.

The highest dose (0.1 ml) of 1% CS/TOF and TOF alone instilled in the eyes of monkeys had no effect. The highest dose (0.2 ml) put in the eyes of rabbits produced very mild effects which regressed within 2 weeks.[37]

Severe chemosis and redness, which persisted for 1 week, were produced when 10 ml of a 1% CS/TOF solution or TOF alone was sprayed into the eyes of rabbits from a distance of 1, 3, and 6 feet. No corneal lesions were seen.[37]

Various concentrations of up to 1.0% CS/TOF were given to 18 volunteers in either a single drop or in a brief spray in one eye.[40] They could not open their eyes for 20 to 85 seconds, and only after 70 to 450 seconds were they able to read 20/20 letters. The incapacitation appeared similar for all concentrations tested. Trioctylphosphate alone had no obvious effects. It was concluded that small quantities of up to 1.0% CS/TOF in contact with the human eye are extremely irritating and cause transient conjunctivitis but no corneal damage in man. Trioctylphosphate alone had no obvious effect.[40]

2. Cutaneous Effects of CS/TOF and TOF Alone.

The lowest dose (0.025 ml) of 1% CS/TOF and TOF alone applied in drops to the skin of rabbits caused immediate erythema that progressed to necrosis in 8 to 10 days. Higher doses caused the same reaction with the area affected being more extensive due to the greater spread of the liquid over the skin. In most instances the skin had healed by the end of 2 weeks. The highest dose (1 ml) of the CS/TOF mixture or TOF alone had no effect on the skin of monkeys.[37]

Patch tests with 0.1 and 1.0 ml of 1% CS/TOF caused necrosis of rabbit skin that healed in 9 days. The same doses of TOF produced no reaction.[37]

When 0.01 ml of 1% CS/TOF was applied to the bare skin of the volar forearm or on a sateen patch that was taped to the skin of the forearm of four volunteers, one of the two subjects patch-tested experienced a slight stinging sensation for the first 30 minutes. When the dose was increased to 0.025 ml on both bare and covered skin, no reactions were seen (table A-11).

In other tests,[41] CS1/TOF was applied on uncovered patches to the foreheads of five volunteers, each being exposed to all concentrations [0.1, 0.2, 0.3, 0.5, 0.75, and 1.0% CS1/TOF (w/v)] at the same time. Initial testing was performed at room temperature (75° to 80°F); additional tests were performed in a chamber at 105° and 80°F. The men were kept in the chamber for about 30 minutes before the tests began, and then CS1 [0.01, 0.05, 0.1, 0.25, 0.5, and 1.0% in TOF (w/v)] was applied. CS1 in TOF caused stinging of the skin in all concentrations tested (0.1% to 1.0%) at the low temperature and in all concentrations tested (0.01% to 1.0%) at the high temperature. Immediate erythema occurred variably at both temperatures, with both exposure times, and at all concentrations. Irritant dermatitis did not occur. Trioctylphosphate (1% to 100% in propylene glycol) caused mild and variable sensations in few subjects and mild immediate erythema in one subject.[41]

3. Effects of CS/TOF and TOF Alone on the Upper and Lower Respiratory Tract.

When 1% CS/TOF was introduced into the trachea of dogs by either intubation or injection, only mild clinical signs were noted. These signs were not dose-related; in fact, they were most frequent at the lowest dose.[37]

The results indicate that injection of 0.5 ml of CS/TOF or TOF alone into the trachea of the dog does not cause enough damage to be discernible by clinical observation. This dose did not result in secondary infection severe enough to cause fever, pronounced dehydration, spontaneous coughing, generalized auscultatory sounds, or elevation in white blood cell count. In general, the severity and duration of signs were not in a category that would warrant veterinary treatment under the conditions of normal animal care. This is especially significant in view of the method of exposure, i.e., direct injection into the trachea.[37]

4. Systemic Effects of CS/TOF and TOF Alone.

The only effects seen in the dogs, rabbits, and monkeys used in the eye, skin, and lung studies were mild respiratory signs in the dogs exposed by instilling the materials directly into the trachea.[37]

No irreversible damage is expected with 1% CS/TOF solutions in the dose ranges tested.

B. CS in Polyethylene Glycol (PEG 200).

Polyethylene glycol (PEG 200) is of low toxicity intravenously,[42] intramuscularly,[42] intraperitoneally,[43] percutaneously,[44,45] and orally.[44-47] It is not damaging to the eyes[44] or skin[48] and does not cause sensitization when applied intracutaneously to guinea pigs.[49] Since CS is adequately soluble in this relatively nontoxic solvent, tests on eyes and skin were initiated.

Solutions of CS (1.0% and 0.1%) in PEG 200 were instilled in the right eyes of groups of four rabbits each at dose levels of 0.05 ml and 0.5 ml. Two control rabbits each received equivalent dose levels of PEG 200 alone (table A-17). All doses of CS in PEG 200 produced severe chemosis that disappeared in 1 day. A dose level of 0.5 ml of CS (1.0%) in PEG 200 also produced redness and scattered corneal opacity which appeared in 3 days and disappeared within 10 days. Polyethylene glycol given alone at either dose level produced no ocular effects. Six of the rabbits received a cutaneous dose of 1 ml of CS (1% in PEG 200); no significant reactions occurred in the 14-day observation period.

C. CS in Propylene Glycol.

Eight dogs were given CS/propylene glycol (0.5 ml) by tracheal intubation; two dogs were given equivalent doses of propylene glycol alone. Half of the dosed animals and the two control animals were necropsied at 3 days, and the other four dosed animals were necropsied at 30 days. No signs were seen at this dose (tables A-13 and A-15). There was no evidence of pathological lesions in any of the dogs.

VI. STABILITY OF CS SOLUTIONS.

The stability of CS/TOF and CS/PEG 200 solutions, stored under various conditions for 15 days, was determined by ultraviolet analysis. The two solutions were monitored daily, and changes in ultraviolet absorbance peaks at 300 and 228 mμ were recorded. The concentrations of unreacted CS found in the solutions were compared to the control peak height (300 mμ), and the percent of this value was recorded every 24 hours.

A. CS/TOF Solutions.

The CS/TOF solutions containing 1.0% agent were relatively stable for various time periods at either 25° or 12°C with fluorescent light, but they were degraded when the temperature was raised to 90°C. Concentrations of 0.1% or 0.06% were degraded at 25° and 12°C in room light in direct proportion to solution strength. Samples containing 1.0% CS stored in darkness were less stable than those stored at the same temperature (25°C) under fluorescent light.[37]

B. CS/PEG 200 Solutions.

The CS/PEG 200 solutions were less stable than the CS/TOF solutions when stored at 25° or 12°C in lighted areas. The CS/PEG 200 solutions were more stable at the higher concentrations than at the lower, and stability was increased at both concentrations when the storage temperature was lowered from 25° to 12°C.

VII. SUMMARY AND DISCUSSION.

The data generated in the present study on the Federal Streamer No. 280 and CS/TOF mixture and previous studies on Mace support certain differences between the three formulations. Although the differences in each aspect of these studies may not appear significant, the overall results suggest a definite safety factor in favor of CS. Additionally, the results of the previous study on Mace would place it in the category of being at least as damaging as Federal Streamer No. 280.

Based on the pathology data in the present study and on the work on human eye effects,[40] the following statements may be made:

1. The ocular lesions produced in rabbits by Federal Streamer No. 280 were more severe than those produced by CS/TOF.

2. Severe ocular lesions were produced in monkeys by Federal Streamer No. 280 while no ocular or cutaneous changes resulted from CS/TOF.

3. The spray test showed clearly that more severe eye damage is produced by Federal Streamer No. 280 than by CS/TOF.

4. CS/TOF in concentrations up to 1.0% administered in either a single drop or in a brief spray to the human eye was extremely irritating and caused transient conjunctivitis but no corneal damage.

5. Federal Streamer No. 280 produced much more severe tracheal damage in dogs than did CS/TOF; however, the pulmonary effects were similar.

6. TOF alone, at the high dose level, is capable of inducing pulmonary damage.

These statements are supported by the following summarized comparisons of the formulations, bearing in mind that Mace is at least as damaging as the Federal Streamer No. 280.

A. Effects of Federal Streamer No. 280 Formulation, CS/PEG 200, CS/TOF Solutions, and TOF Alone Instilled into the Eyes of Rabbits and Monkeys.

The ocular responses produced in rabbits and monkeys indicate that 1% CS/TOF was the least irritating, causing only mild effects to the rabbit eye at a dose of 0.1 ml and no effects to the monkey eye at this dose.

Trioctylphosphate alone produced no responses in the monkey but was slightly more irritating to the rabbit.

The CS/PEG 200 solutions containing 1% agent caused moderate to severe effects in the rabbit eye, but it should be pointed out that corneal involvement disappeared after 10 days without scarring. Monkeys were not tested.

The Federal Streamer 280 formulation was the most irritating substance to both the rabbit and monkey eye. A no-effect dose could not be determined for either species although micro-techniques were used to deliver the dosages. Doses of 0.025 ml caused moderate to severe chemosis and redness in the rabbit eye, the severe effects including corneal involvement. In the monkey, a dose of 0.025 ml caused moderate eye effects, and a dose of 0.10 ml caused severe chemosis, redness, and corneal opacity. See table 5 for detailed data.

Table 5. Ocular Effects After Instillation of Four Liquids Into Eyes of Rabbits and Monkeys

Solution	Highest dose causing no effect		Lowest dose causing mild chemosis and/or redness		Lowest dose causing moderate chemosis and/or redness		Dose causing severe chemosis, redness with corneal involvement	
	Rabbit	Monkey	Rabbit	Monkey	Rabbit	Monkey	Rabbit	Monkey
	ml		ml		ml		ml	
Federal Streamer 280	[a]	[a]	0.005	0.005	0.025	0.025	0.025	0.10
CS/TOF 1%	[a]	[a]	0.10	0.005	[b]	[b]	[b]	[b]
CS/PEG 200 0.1%	[a]	Not tested	0.05	Not tested	0.05	Not tested	[c]	Not tested
CS/PEG 200 1.0%	[a]	Not tested	0.05	Not tested	0.05	Not tested	0.50	Not tested
TOF (control)	0.05	0.10	0.10	[b]	0.20	[b]	–	[b]

[a] All doses effective.

[b] No response at highest dose.

[c] Only severe chemosis.

NOTE: 0.005 ml = Lowest dose used, rabbits and monkeys.
0.50 ml = Highest dose used, CS/PEG 200 solutions only.
0.20 ml = Highest dose used for all formulations on rabbits, except CS/PEG 200.
0.1 ml = Highest dose used on monkeys.

B. Effects of Federal Streamer No. 280 Formulation, CS/PEG 200, CS/TOF Solutions, and TOF Alone Applied Directly to the Skin of Rabbits and Monkeys (Table 6).

Although the skin irritant properties of TOF and 1% CS/TOF solutions were similar, the two species responded differently. Doses of 0.025 ml per rabbit produced erythema that became more severe over a 7-day period; necrotic tissue formed in from 8 to 10 days. Higher doses produced similar reactions on rabbit skin, with the area of involvement being proportional to the spread of the liquid over the skin. Recovery occurred in a significant number of rabbits at all dose levels with either solution after 14 days.

No effects were produced in monkeys given the highest dose, 1 ml, of either TOF or 1% CS/TOF solutions.

Monkeys were not tested cutaneously with CS/PEG 200, and the highest dose administered to rabbits (1.0 ml per animal) produced no effects.

The Federal Streamer No. 280 formulation produced mild to severe skin reactions on rabbit skin at all dose levels. The lowest dose (0.025 ml per animal) caused mild to severe effects that were similar to those produced by the same dose of 1% CS/TOF solutions in the rabbit. A comparable dose-response relationship was seen between the two solutions. Monkeys, however, were affected by the Federal Streamer No. 280 formulation but not by CS/TOF solutions. Doses of 0.1 ml per monkey caused moderate to severe erythema and 1.0 ml per monkey caused necrosis. These responses show the Federal Streamer No. 280 formulation to be more hazardous to skin than CS/TOF solutions.

Table 6. Cutaneous Effects of Four Liquids Applied Directly to the Bare Skin of Rabbits and Monkeys

Solution	Highest dose causing no effects		Lowest dose causing mild effects		Lowest dose causing moderate effects		Lowest dose causing severe effects	
	Rabbit	Monkey	Rabbit	Monkey	Rabbit	Monkey	Rabbit	Monkey
	ml		ml		ml		ml	
Federal Streamer 280	*	0.025	0.025	0.10	0.025	1.0	0.025	1.0
CS/TOF 1%	*	1.0	0.025	**	0.025	**	0.025	**
CS/PEG 200 0.1%	1.0	Not tested	**	Not tested	**	Not tested	**	Not tested
CS/PEG 200 1.0%	1.0	Not tested	**	Not tested	**	Not tested	**	Not tested
TOF	*	1.0	0.025	**	0.025	**	0.025	**

*All doses effective.

**No response at highest dose.

NOTE: 0.025 ml = Lowest dose used, rabbits and monkeys.
1.0 ml = Highest dose used, rabbits and monkeys.
Mild effects – mild to moderate erythema.
Moderate effects – moderate to severe erythema.
Severe effects – necrotic tissue formation.

C. Effects of Federal Streamer No. 280 Formulation, CS/TOF, CS/Propylene Glycol, and TOF Solutions Administered Intratracheally to Dogs.

In dogs dosed intratracheally, by either intubation or ingestion techniques, with Federal Streamer No. 280 contents or with CS/TOF solutions, only mild signs attributable to the compounds were noted. The only consistent signs exhibited were slight to moderate dehydration, moderate upper respiratory irritation, and slight congestion. These signs were not dose-related in dogs tested with graded doses of either of the solutions. In most cases, the signs were more frequent in dogs receiving the lowest dose than the highest.

The generally good health of the animals 3 days after dosing indicates that instillation of 0.5 ml of either solution into the trachea did not cause enough tissue damage to be revealed by critical veterinary examination. This dose did not precipitate secondary infection severe enough to cause fever, pronounced dehydration, spontaneous coughing, generalized congestion, or changes in white blood cell counts. In general, the severity and duration of signs were not in the category that would warrant veterinary treatment under the conditions of normal animal care.

No changes from normal were seen in dogs 72 hours after receiving intratracheal doses of TOF, propylene glycol, or CS/propylene glycol solutions by intubation.

Dogs whose throats were sprayed with the Federal Streamer No. 280 formulation while their tongues were depressed salivated profusely for a few minutes after dosing and continued to chew and lick until most of the dose had been swallowed or expelled by salivary flow. Coughing and choking were not generally seen.

Critical examinations of these dogs revealed no changes from normal after 96 hours. Particular care was exercised in examining the tissue lining of the oral cavity but no signs of irritation in this area or in the throat were detected. Nor was the upper respiratory tract irritated or congested.

D. Effects of Spraying Federal Streamer No. 280 Formulation and CS/TOF Solutions on the Eyes and Skin of Rabbits.

The Federal Streamer No. 280 formulation, CS/TOF solution, and TOF alone sprayed for 5 seconds at rabbits from the Streamer and an equivalent 10-ml spray of CS/TOF or TOF alone directed at rabbits from 1-, 3-, and 6-feet produced severe chemosis and redness which persisted throughout the first week of observation. Scattered corneal opacity was seen in most of the rabbits sprayed for time intervals of 5 seconds or 1 second with the Federal Streamer No. 280. No corneal involvement was noted in any of the rabbits sprayed with CS/TOF or TOF only. In the first 7 days, skin erythema was noted after CS/TOF, TOF alone, and the Federal Streamer No. 280. The erythema abated at this time with CS/TOF and TOF alone; however, the spray disseminated from the Federal Streamer No. 280 produced scar tissue and underlying muscular damage which persisted throughout the 30-day observation period in some rabbits.

Respiratory distress (wheezing) was noted in four of the rabbits sprayed with the Federal Streamer No. 280 formulation, but this sign abated on the second day and the rabbits appeared normal.

The Chemical Mace (MK IV) previously tested under the same conditions produced moderate ocular effects of shorter duration with no corneal involvement.[32]

E. Effects of Federal Streamer No. 280 Formulation and CS/TOF Solutions Applied to Cloth Over Rabbit Skin.

Erythema was noted in all animals at both dose levels (0.1 and 1.0 ml) of the Federal Streamer No. 280 formulation when the sateen patches were removed at 24 hours. Increasing erythema and necrotic tissue formation at both dose levels occurred during the second day and was still prevalent on the tenth day.

The CS/TOF solutions at both dose levels (0.1 and 1.0 ml) produced erythema which was noted after removal of the patches at 24 hours. Increasing erythema and necrotic tissue formation occurred at both dose levels

during the fourth day. The erythema persisted for 10 days but the necrosis had disappeared in all rabbits by the ninth day.

No skin reaction was seen during the 10-day observation period in the control rabbits receiving TOF alone.

F. Effects of Federal Streamer No. 280 Formulation and CS/TOF Solutions in Man.

Only CS/TOF was tested in the human eye; no corneal damage resulted from the small quantities tested.

In man, the Federal Streamer 280 formulation (0.01 or 0.025 ml) caused only slight erythema; concentrations of up to 1% CS in TOF produced erythema but did not cause irritant dermatitis.

G. Systemic Effects of Federal Streamer No. 280 Formulation, CS/TOF, and CS/PEG 200 Solutions.

No systemic effects were seen in rabbits, dogs, or monkeys tested with the Federal Streamer No. 280, CS/TOF, TOF, CS/PEG 200, or PEG 200 solutions except for mild, gross signs of respiratory involvement seen in dogs tested intratracheally with Federal Streamer No. 280 and CS/TOF solutions.

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APPENDIX

TABLES

Table A-1. Grading System Used to Evaluate Eye Irritation [a]

Cornea	
No ulceration or opacity	0
Scattered or diffuse areas of opacity (other than slight dulling of normal luster), details of iris clearly visible	[1] [b]
Easily discernible translucent areas, details of iris slightly obscured	2
Nacreous areas, no details of iris visible, size of pupil barely discernible	3
Complete corneal opacity, iris not discernible	4
Iris	
Normal	0
Markedly deepened folds, congestion, swelling, moderate circumcorneal injection (any of these or combination of any thereof), iris still reacting to light (sluggish reaction is positive)	[1] [b]
No reaction to light, hemorrhage, gross destruction (any or all of these)	2
Conjunctivae	
Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris).	
Vessels normal	0
Some vessels definitely injected	1
Diffuse, crimson red, individual vessels not easily discernible	[2] [b]
Diffuse beefy red	3
Chemosis	
No swelling	0
Any swelling above normal (includes nictitating membrane)	1
Obvious swelling with partial eversion of lids	[2] [b]
Swelling with lids about half closed	3
Swelling with lids more than half closed	4

[a] A modified Draize technique described in the "Illustrated Guide for Grading Eye Irritation by Hazardous Substances" published by the Food and Drug Administration.

[b] Bracketed figures indicate lowest grades considered positive under Section 191.12 of the Federal Hazardous Substances Labeling Act.

Table A-2. Grading System Used to Evaluate Skin Irritation

Erythema	
No erythema	0
Mild erythema	1
Moderate erythema	2
Severe erythema	3
Erythema with edema	4
Necrosis	
No necrotic tissue	0
Less than 50% necrotic tissue	1
50%-100% necrotic tissue	2
100% necrotic tissue with well defined eschar formation	3
Dehydration and/or Desquamation	
No dehydration or desquamation	0
Mild dehydration or desquamation	1
Moderate dehydration or desquamation	2
Severe dehydration or desquamation	3

Table A-3. The Ocular and Cutaneous Effects of Federal Streamer No. 280 (0.9% CN) Applied to the Eyes and Skin of Rabbits[a]

Dose	Rabbit No.	Ocular effects									Cutaneous effects									
		Days after dose									Days after dose									
		1[b]			2			3				1[b]			2			3		
		CH	R	C	CH	R	C	CH	R	C		E	N	D	E	N	D	E	N	D
ml											ml									
0.2	101	2	0	0	1	0	0	2	0	0	1.0	1	0	0	4	0	0	2	1	0
0.2	102	2	0	0	2	2	2	3	0	2	1.0	1	0	0	0	0	0	2	1	0
0.2	103	2	2	0	2	2	2	2	0	3	1.0	2	0	0	1	0	0	1	1	0
0.2	104	2	2	0	2	2	1	2	0	2	1.0	0	0	0	2	0	0	3	0	0
0.2[c]	113	0	0	0	0	0	0	0	0	0	1.0[c]	0	0	0	0	0	0	0	0	0
0.2[c]	114	0	0	0	0	0	0	0	0	0	1.0[c]	0	0	0	0	0	0	0	0	0
0.025	105	0	1	0	0	1	0	0	0	0	0.1	0	0	0	0	0	0	2	0	0
0.025	106	1	1	0	0	1	0	2	0	0	0.1	3	0	0	3	0	0	2	2	0
0.025	107	1	0	0	0	1	0	1	0	0	0.1	0	0	0	0	0	0	0	0	0
0.025	108	0	0	0	0	1	0	0	1	0	0.1	0	0	0	1	0	0	0	0	0
0.025[c]	115	0	0	0	0	0	0	0	0	0	0.1[c]	0	0	0	0	0	0	0	0	0
0.025[c]	116	0	0	0	0	0	0	0	0	0	0.1[c]	0	0	0	0	0	0	0	0	0
0.005	109	0	1	0	0	0	0	0	0	0	0.025	1	0	0	4	0	0	2	0	0
0.005	110	0	1	0	0	1	0	0	0	0	0.025	0	0	0	0	0	0	2	0	0
0.005	111	0	0	0	0	0	0	0	0	0	0.025	0	0	0	0	0	0	2	0	0
0.005	112	0	1	0	0	0	0	<1	0	0	0.025	0	0	0	2	0	0	3	0	0
0.005[c]	117	0	0	0	0	0	0	0	0	0	0.025[c]	0	0	0	0	0	0	0	0	0
0.005[c]	118	0	0	0	0	0	0	0	0	0	0.025[c]	0	0	0	0	0	0	0	0	0

[a]These rabbits were sacrificed and submitted for necropsy 3 days after exposure.
[b]Observation days post dosage.
[c]Isotonic saline controls.

NOTES: See tables A-1 and A-2 for grading systems.

CH – Chemosis
R – Redness
C – Cornea
E – Erythema
N – Necrosis
D – Dehydration and/or desquamation

Table A-4. The Ocular Effects of Federal Streamer No. 280 (0.9% CN) Contents Instilled in the Right Eyes of Rabbits

Dose	Rabbit No.	Ocular effects: Days after dose 1			2			3			4			5			6			7			8			9			10			11			12			13			14			Recovery day
		CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	
ml																																												
0.20	1	2	1	0	2	1	0	2	1	0	2	1	0	2	1	1	3	1	0	2	1	0	2	1	0	2	1	0	1	1	0	1	1	0	1	1	0	1	1	0	<1	1	0	21
0.20	2	2	0	1	2	2	1	2	1	1	2	0	1	2	0	1	3	0	1	3	0	1	3	1	0	3	1	0	3	1	0	2	1	0	4	0	0	3	0	0	4	1	0	21
0.20	3	2	1	1	2	2	1	2	1	1	2	1	1	3	1	1	3	0	1	3	2	2	3	2	1	3	2	1	3	2	1	2	2	0	2	2	0	2	2	0	2	1	0	21
0.20	4	2	1	0	2	2	1	2	1	1	2	1	1	3	1	1	2	1	1	2	1	1	2	1	0	2	2	0	1	0	0	1	0	0	2	1	0	2	1	0	1	1	0	18
0.20	5	2	2	0	2	2	1	1	1	1	1	1	1	3	2	1	2	2	1	3	2	2	3	2	1	2	2	1	2	2	1	2	2	1	2	2	0	2	2	0	1	2	0	19
0.20	6	2	1	0	2	2	1	1	1	1	1	0	1	3	1	1	3	0	1	3	2	1	3	<2	1	2	2	1	2	2	<1	1	1	0	1	1	0	1	1	0	1	<1	0	19
0.10	7	2	1	1	2	2	2	1	1	1	2	2	1	4	2	1	3	2	1	3	2	1	3	2	1	2	2	1	2	2	0	2	2	0	2	2	0	2	2	0	<1	1	0	19
0.10	8	1	<1	0	1	1	<1	1	1	1	1	1	1	2	1	1	2	1	0	2	1	0	2	1	0	2	1	0	1	1	0	<1	<1	0	<1	<1	0	1	0	0	<1	1	0	19
0.10	9	2	2	0	2	1	<2	2	1	1	2	1	1	3	2	1	2	2	1	3	2	2	2	1	1	2	1	1	2	1	1	<1	1	0	<1	0	0	<1	0	0	<1	<1	0	17
0.10	10	2	2	0	2	2	1	2	1	1	1	1	1	2	2	1	3	1	1	2	2	1	2	2	1	2	2	1	1	1	<1	2	2	<1	2	2	0	2	2	0	1	2	0	19
0.10	11	<2	1	0	2	2	1	2	2	1	2	2	1	3	2	1	3	0	1	2	2	1	2	2	1	2	2	1	2	2	0	1	1	0	2	1	0	2	1	0	1	1	0	19
0.10	12	1	0	0	1	1	0	1	1	0	1	1	0	2	<1	<1	2	1	1	2	2	1	2	2	1	2	1	1	<1	<1	0	1	1	0	2	1	0	2	1	0	1	<1	0	19
0.05	13	<1	0	0	<1	0	0	0	<1	0	0	1	0	2	1	1	1	1	0	1	1	0	1	1	0	1	1	0	1	1	0	1	1	0	2	1	0	2	1	0	<1	1	0	17
0.05	14	2	1	0	2	1	0	<1	<1	0	1	0	0	3	1	0	2	1	0	1	1	0	1	1	0	1	1	0	1	1	1	1	2	0	1	1	0	1	1	0	<1	1	0	17
0.05	15	0	0	0	<1	0	0	<1	<1	0	0	1	0	1	0	0	1	1	0	1	1	0	1	1	0	1	1	0	0	<1	0	0	<1	0	0	0	0	0	0	0	<1	<1	0	15
0.05	16	2	1	1	2	1	<2	2	1	1	1	1	1	2	0	1	2	0	1	1	2	1	2	2	1	1	1	0	2	<1	0	<1	<1	0	1	1	0	1	1	0	<1	<1	0	17
0.05	17	1	<1	0	<1	<1	0	2	1	0	0	1	0	1	1	0	1	1	0	1	1	0	0	1	0	0	<1	0	0	<1	0	0	<1	0	0	0	0	0	0	0	0	<1	0	15
0.05	18	2	2	1	2	2	1	1	1	0	1	1	0	2	1	0	2	2	0	2	2	0	<1	<1	0	<1	<1	0	<1	<1	0	<1	<1	0	<1	<1	0	<1	<1	0	0	<1	0	15
0.025	19	2	1	0	2	1	<1	<1	1	<1	1	0	<1	2	1	1	1	0	0	1	2	0	<1	<1	0	<1	<1	0	0	<1	0	0	<1	0	<1	<1	0	<1	<1	0	0	0	0	13
0.025	20	<1	0	0	0	1	0	0	1	0	0	1	0	1	0	0	1	1	0	1	1	0	<1	<1	0	<1	<1	0	0	<1	0	0	<1	0	0	0	0	0	0	0	0	0	0	12
0.025	21	Dead*																																									
0.025	22	0	0	0	<1	<1	0	0	<1	0	0	1	0	<1	0	0	<1	0	0	<1	0	0	<1	1	0	<1	0	0	0	<1	0	0	<1	0	0	0	0	0	0	0	0	0	0	12
0.025	23	<2	0	0	<1	0	0	0	<1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5
0.025	24	<2	1	0	<1	1	0	0	<1	0	0	1	0	1	0	0	<1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	7
0.010	25	0	0	0	<1	<1	0	<1	<1	0	0	<1	0	<1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
0.010	26	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.010	27	<1	0	0	<1	<1	0	0	<1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4
0.010	28	<2	1	0	<1	<1	0	<1	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
0.010	29	1	0	0	<1	0	0	0	1	0	0	<1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
0.010	30	1	<1	0	0	1	0	0	1	0	0	<1	0	<1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
0.005	31	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.005	32	0	0	0	<1	<1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
0.005	33	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.005	34	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.005	35	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.005	36	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–

*Death not agent-induced.

NOTE: CH = Chemosis
R = Redness
C = Cornea

Table A-5. The Cutaneous Effects of Federal Streamer No. 280 (0.9% CN) Contents Applied to the Clipped Skin of Rabbits

Dose	Rabbit No.	Days after dose																																								Recovery day
		1			2			3			4			5			6			7			8			9			10			11			12			13			14			
		E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	
ml																																										
1.0	1	0	0	0	3	0	0	2	0	0	2	0	0	2	0	0	3	1	1	3	2	0	4	2	0	4	2	0	2	2	0	1	2	0	0	3	0	0	3	0	1	2	0	**
1.0	2	1	0	0	2	0	0	2	0	0	2	0	0	2	0	0	2	2	0	3	0	0	3	0	0	3	0	0	2	0	0	1	0	0	1	0	0	1	0	0	3	2	0	23
1.0	3	1	0	0	1	0	0	1	0	0	1	2	0	2	2	0	3	2	0	3	1	0	2	2	0	3	2	0	3	0	0	3	0	0	0	2	0	0	2	0	0	2	0	27
1.0	4	2	0	0	3	0	0	1	0	0	3	1	0	3	1	0	3	3	0	3	1	0	4	2	0	3	3	0	2	2	0	3	2	0	3	3	0	3	3	0	3	2	0	**
1.0	5	2	0	0	3	0	0	2	0	0	3	1	0	2	1	0	2	2	0	2	2	0	2	2	0	4	2	0	4	2	0	1	2	0	0	3	0	0	3	0	2	2	0	**
1.0	6	3	2	0	3	2	0	3	2	0	3	2	0	2	2	0	2	2	0	3	2	0	3	2	0	4	2	0	2	2	0	3	2	0	0	3	0	0	3	0	0	2	0	**
0.5	7	2	0	0	1	0	0	2	0	0	1	0	0	3	0	0	2	0	2	2	0	2	1	2	2	2	2	2	0	0	2	2	0	2	2	0	2	2	0	2	0	2	0	20
0.5	8	2	0	0	2	0	0	2	0	0	1	0	0	2	0	0	2	0	0	2	0	0	2	0	0	2	0	0	2	0	2	2	2	0	1	2	0	1	2	0	0	2	0	23
0.5	9	1	0	0	2	1	0	2	0	0	2	0	0	2	0	0	2	0	0	2	0	0	4	0	0	4	2	1	2	2	0	2	2	0	2	2	0	2	2	0	0	2	0	27
0.5	10	0	0	0	2	1	0	2	0	0	2	0	0	1	0	0	2	0	0	2	0	0	2	0	0	4	0	2	2	2	0	1	0	0	1	2	0	1	2	0	1	2	0	27
0.5	11	0	0	0	3	0	0	1	0	0	2	0	0	2	0	0	2	0	0	1	0	0	1	0	0	4	0	0	2	1	0	1	0	0	0	1	0	0	1	0	0	1	0	24
0.5	12	0	0	0	2	0	0	2	0	0	2	0	0	1	0	0	2	0	0	2	0	0	1	0	0	2	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	25
0.25	13	1	0	0	2	0	0	1	0	0	2	0	0	2	0	0	2	0	0	1	0	0	2	1	2	2	1	2	4	2	0	1	2	0	0	2	0	0	2	0	2	2	0	**
0.25	14	1	0	0	3	0	0	3	0	0	2	0	0	2	0	0	2	0	0	1	0	0	1	1	0	1	1	0	4	0	0	0	1	0	0	1	0	0	1	0	1	2	0	**
0.25	15	0	0	0	2	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	1	0	1	1	0	1	0	0	0	0	0	0	1	0	0	0	0	1	2	0	25
0.25	16	1	0	0	2	0	0	1	0	0	1	0	0	1	0	0	2	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	1	0	0	1	0	0	2	0	16
0.25	17	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	2	0	0	2	0	0	2	0	1	2	0	1	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	11
0.25	18	1	0	0	1	0	0	3	0	0	3	0	0	2	0	0	2	0	0	2	0	0	1	0	1	1	0	1	1	0	0	0	1	0	0	1	0	0	1	0	0	2	0	20
0.10	19	1	0	0	1	0	0	3	0	0	3	0	0	2	0	0	2	0	0	3	0	0	2	0	0	2	0	0	1	2	0	1	2	0	0	2	0	0	2	0	0	2	0	17
0.10	20	0	0	0	1	0	0	1	0	0	2	0	0	2	0	0	2	0	0	2	0	0	1	1	0	1	1	0	0	2	0	1	2	0	0	2	0	0	2	0	0	2	0	19
0.10	21	Dead*																																									-
0.10	22	0	0	0	2	0	0	2	0	0	2	0	0	2	0	0	2	0	0	2	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	11
0.10	23	0	0	0	1	0	0	2	0	0	2	0	0	2	0	0	2	0	0	2	0	0	1	0	0	1	1	0	1	0	2	0	1	0	0	1	0	0	1	0	1	2	0	19
0.10	24	1	0	0	1	0	0	1	0	0	3	0	0	2	0	0	3	0	0	2	0	0	1	1	0	1	1	0	1	0	0	0	1	0	0	1	0	0	1	0	2	2	0	19
0.05	25	1	0	0	2	0	0	2	0	0	3	0	0	2	0	0	3	0	0	2	0	0	4	0	0	1	1	0	0	2	0	1	0	0	1	0	0	1	0	0	0	2	0	19
0.05	26	2	0	0	1	0	0	1	0	0	3	0	0	2	0	0	3	0	0	3	0	0	2	0	0	2	0	0	2	2	0	1	2	0	0	2	0	0	2	0	0	2	0	19
0.05	27	2	0	0	1	0	0	1	0	0	2	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	17
0.05	28	1	0	0	1	0	0	2	0	0	4	0	0	2	0	0	3	0	0	2	0	0	4	0	0	1	0	1	1	0	0	1	0	0	0	1	0	0	1	0	0	2	0	19
0.05	29	0	0	0	1	0	0	2	0	0	4	0	0	3	0	0	4	0	0	2	0	0	4	0	0	2	2	1	1	2	0	0	2	0	0	2	0	0	2	0	0	2	0	16
0.05	30	0	0	0	1	0	0	1	0	0	4	0	0	4	0	0	4	0	0	1	0	0	4	0	0	4	0	0	4	2	0	0	2	0	0	2	0	0	2	0	0	2	0	19
0.025	31	0	0	0	1	0	0	1	0	0	1	0	0	1	0	0	2	0	0	2	0	0	1	0	0	1	0	0	1	0	0	0	0	0	Dead*									-
0.025	32	1	0	0	1	0	0	2	0	0	2	0	0	3	0	0	2	0	0	3	0	0	1	0	0	1	0	0	1	0	0	0	1	0	0	1	0	0	1	0	0	2	0	16
0.025	33	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	1	0	0	1	0	0	0	0	0	0	0	16
0.025	34	1	0	0	2	0	0	1	0	0	4	0	0	2	0	0	4	0	0	4	0	0	4	0	0	4	0	0	2	0	0	0	1	0	0	1	0	0	1	0	0	2	0	19
0.025	35	1	0	0	2	0	0	1	0	0	1	0	0	2	0	0	2	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	11
0.025	36	0	0	0	1	0	0	2	0	0	2	0	0	3	0	0	3	0	0	3	0	0	2	0	0	2	0	0	1	1	0	1	1	0	0	1	0	0	1	0	0	2	0	19

*Death not agent-induced.

**Erythema still present on 30th observation day.

NOTE: E = Erythema
N = Necrosis
D = Dehydration and/or desquamation

Table A-6. The Ocular Effects of the Contents of Federal Streamer No. 280 (0.9% CN) Instilled in the Right Eyes of Monkeys

Dose	Monkey No.	Ocular effects																																						Recovery day
		Days after dose																																							
		1			2			3			4			5			6			7			8			9			10			11			12			13			14			
		CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	
ml																																									
0.10	25*	3	0	0	3	0	2	2	0	1																														
0.10	26*	3	0	0	3	0	1	1	0	1																														
0.10	27*	4	0	0	4	0	1	3	0	2																														
0.10	28*	≤2	0	0	1	0	2	1	0	1																														
0.10	29	2	0	0	2	0	2	4	0	2	3	0	1	3	2	1	3	1	1	3	1	1	2	0	1	2	0	≤1	2	0	≤1	1	0	0	1	0	0	1	0	0	1	0	0	16
0.10	30	2	0	0	3	0	2	2	0	2	3	0	2	3	2	2	2	2	1	2	2	1	2	1	1	2	1	≤1	2	1	≤1	1	0	0	1	0	0	1	0	0	1	0	0	16
0.10	31	2	0	0	1	0	2	1	0	1	3	0	2	2	2	2	2	2	1	2	2	1	2	1	1	2	0	1	2	0	1	1	0	0	1	0	0	1	0	0	1	0	0	16
0.10	32	2	0	0	1	0	2	≤1	0	1	2	0	1	2	0	1	2	1	1	2	1	1	1	0	≤1	≤1	0	≤1	≤1	0	≤1	0	0	0	0	0	0	0	0	0	1	0	0	11
0.025	33*	1	0	0	1	0	0	≤1	0	0																														
0.025	34*	2	0	0	2	0	1	2	0	1																														
0.025	35*	≤1	0	0	1	0	1	1	0	1																														
0.025	36*	≤1	0	0	1	0	0	1	0	0																														
0.025	37	1	0	0	1	0	1	1	0	1	1	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
0.025	38	1	0	0	≤1	0	0	1	0	1	1	0	2	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
0.025	39	1	0	0	≤1	0	0	1	0	1	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
0.025	40	≤1	0	0	≤1	0	0	1	0	1	1	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
0.005	41*	0	0	0	0	0	0	0	0	0																														
0.005	42*	0	≤1	0	0	0	0	0	0	0																														
0.005	43*	0	0	0	0	0	0	0	0	0																														
0.005	44*	0	0	0	0	0	0	0	0	0																														
0.005	45	0	≤1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
0.005	46	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.005	47	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.005	48	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.10	49*	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.10	50*	0	0	0	0	0	0	0	0	0	0	0	0																													
0.10	51	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.10	52	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.025	57*	0	0	0	0	0	0	0	0	0	0	0																														
0.025	58*	0	0	0	0	0	0	0	0	0	0	0																														
0.025	59	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.025	60	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.005	65*	0	0	0	0	0	0	0	0	0																														
0.005	66*	0	0	0	0	0	0	0	0	0																														
0.005	67	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–
0.005	68	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	–

Saline controls

* These animals were submitted for necropsy at 3 days.

NOTE: CH = Chemosis
R = Redness
C = Cornea

Table A-7. The Cutaneous Effects of the Contents of Federal Streamer No. 280 (0.9% CN) Applied to the Clipped Skin of Monkeys

Dose	Rabbit No.	Days after dose																																									
		1			2			3			4			5			6			7			8			9			10			11			12			13			14		
		E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	F	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D
ml																																											
1.0	25*	0	0	0	0	0	0	1	0	0																																	
1.0	26*	0	0	0	0	0	0	4	0	0																																	
1.0	27*	0	0	0	0	0	0	2	0	0																																	
1.0	28*	0	0	0	0	0	0	1	0	0																																	
1.0	29	0	0	0	0	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1.0	30	1	0	0	0	0	0	4	0	0	1	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1.0	31	0	0	0	0	0	0	2	0	0	2	0	0	2	0	0	4	0	0	4	0	0	1	1	0	1	1	0	1	1	0	1	1	0	0	1	0	0	1	0	0		0
1.0	32	0	0	0	0	0	0	2	0	0	2	0	0	2	0	0	2	1	0	2	1	0	0	2	0	0	2	0	0	2	0	1	0	0	0	0	0	0	0	0	0	0	0
0.10	33*	0	0	0	0	0	0	0	0	0																																	
0.10	34*	0	0	0	0	0	0	0	0	0																																	
0.10	35*	0	0	0	0	0	0	0	0	0																																	
0.10	36*	0	0	0	0	0	0	1	0	0																																	
0.10	37	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.10	38	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.10	39	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.10	40	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.025	41*	0	0	0	0	0	0	0	0	0																																	
0.025	42*	0	0	0	0	0	0	0	0	0																																	
0.025	43*	0	0	0	0	0	0	0	0	0																																	
0.025	44*	0	0	0	0	0	0	0	0	0																																	
0.025	45	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.025	46	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.025	47	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.025	48	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1.0	49*	0	0	0	0	0	0	0	0	0																																	
1.0	50*	0	0	0	0	0	0	0	0	0																																	
1.0	51	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1.0	52	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.10	57*	0	0	0	0	0	0	0	0	0																																	
0.10	58*	0	0	0	0	0	0	0	0	0																																	
0.10	59	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.10	60	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.025	65*	0	0	0	0	0	0	0	0	0																																	
0.025	66*	0	0	0	0	0	0	0	0	0																																	
0.025	67	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.025	68	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Saline controls

*These animals were submitted for necropsy at 3 days.

NOTE: E = Erythema
N = Necrosis
D = Dehydration and/or desquamation

Table A-8. The Ocular Effects in Rabbits of the Federal Streamer No. 280 Foundation Sprayed at the Left Eye for Various Times and Distances

Distance	Spray time	Rabbit No.	Days after dose																													Recovery day
			1			2			3			4			5			6			7			8			9			10			
			CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	
ft	sec																																
1	1[a]	155	3	2	1	4	2	1	3	2	1	3	2	1	3	1	1	3	1	1	3	2	0	3	1	0	3	1	0	2	1	0	20
1	1	156	4	2	0	3	2	1	3	2	1	4	2	1	4	2	1	4	1	0	3	2	0	4	1	0	3	1	0	2	1	0	22
1	1	157	2	2	0	2	2	0	2	1	1	2	1	1	2	1	1	2	1	1	2	2	0	1	2	0	2	1	0	2	1	0	20
1	1	158	1	2	0	2	2	0	2	1	1	2	1	1	0	1	0	2	1	0	2	1	0	1	2	0	2	1	0	1	0	0	12
1	1	159	2	2	1	2	2	1	2	1	1	2	1	<1	1	1	<1	2	1	1	2	1	0	3	2	0	4	2	0	3	2	1	26
1	5[b]	160	4	2	1	4	2	1	4	2	1	3	2	<1	2	1	<1	3	1	1	4	2	1	4	2	0	4	2	0	4	2	0	d
1	5	161	4	2	1	4	2	1	4	2	1	3	1	1	3	1	<1	3	2	1	4	2	0	4	2	0	4	2	0	4	2	0	d
1	5	162	3	2	1	4	2	1	3	2	1	3	2	1	3	1	<1	3	2	1	4	2	0	4	2	0	4	2	1	4	2	0	28
1	5	163	4	2	1	4	2	1	3	2	1	3	2	1	3	2	1	3	2	0	3	2	0	3	2	0	3	2	0	4	2	0	25
1	5	164	4	2	1	4	2	1	4	2	1	4	2	1	4	2	1	4	2	1	4	2	0	4	2	0	4	2	0	3	2	0	25
3	1	165	2	2	0	2	1	0	3	1	1	3	1	1	2	1	1	Dead[c]															
3	1	166	1	2	0	1	1	0	2	2	0	2	2	0	2	2	0	2	2	1	3	2	1	2	2	1	2	2	1	2	2	0	20
3	1	167	2	2	0	2	1	0	2	1	0	2	2	1	2	2	<1	2	2	<1	3	2	<1	2	1	0	2	2	0	2	1	0	20
3	1	168	3	2	0	2	2	0	2	1	0	2	1	1	2	1	1	2	2	0	3	2	0	2	1	0	2	2	0	1	1	0	19
3	1	169	1	2	0	<1	2	0	2	1	1	1	1	0	2	1	0	2	1	1	1	1	1	2	1	1	2	1	1	1	1	0	14
3	5	170	4	1	1	4	2	0	4	2	0	4	2	0	3	2	0	4	2	0	4	2	0	4	2	0	4	2	0	4	2	0	27
3	5	171	4	1	1	3	2	1	3	2	1	2	2	1	2	<2	1	3	1	1	3	2	1	3	2	1	3	2	1	3	2	0	d
3	5	172	4	1	1	4	2	1	4	2	1	4	2	1	4	2	1	4	2	1	4	2	1	4	2	1	4	2	1	4	1	1	25
3	5	173	4	1	1	3	1	1	3	1	1	3	2	1	3	2	0	3	2	1	3	2	1	4	2	1	3	2	1	4	2	1	d
3	5	174	Dead[c]																														
6	1	175	2	2	0	2	1	0	2	2	0	2	1	0	2	1	0	2	1	0	2	1	0	1	0	0	1	0	0	<1	0	0	18
6	1	176	0	0	0	<1	<1	0	<1	1	0	<1	1	0	1	1	0	1	1	0	1	1	0	0	1	0	0	0	0	0	0	0	9
6	1	177	0	1	0	1	1	0	1	0	0	1	0	0	<1	1	0	<1	<1	0	<1	<1	0	0	0	0	0	0	0	0	0	0	8
6	1	178	0	1	0	1	1	0	1	<1	0	1	0	0	<1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6
6	1	179	<1	0	0	<1	2	0	1	1	0	1	1	0	1	1	0	<1	<1	0	<1	<1	0	0	0	0	0	0	0	0	0	0	8
6	5	180	4	2	1	4	2	1	4	2	1	4	2	1	4	2	1	4	2	0	4	2	0	4	2	0	4	2	<1	4	2	<1	27
6	5	181	4	2	1	4	2	0	2	1	0	2	1	0	2	1	0	3	2	0	4	2	0	4	1	0	4	2	0	4	1	0	27
6	5	182	3	1	0	3	2	0	3	2	0	4	2	0	4	2	1	4	2	1	4	2	1	4	2	1	4	2	1	4	2	<1	27
6	5	183	4	2	1	4	2	1	3	2	1	2	2	1	2	2	1	3	2	1	3	2	1	3	2	1	2	2	0	2	2	0	20
6	5	184	4	2	1	3	2	1	3	1	1	2	1	1	3	1	1	3	2	1	4	2	1	4	2	1	3	2	1	3	2	0	20

[a] A 1-second spray = 1 ml.

[b] A 5-second spray = 10 ml.

[c] Death not agent-induced.

[d] Effects still apparent at 30 days.

NOTE: CH = Chemosis
R = Redness
C = Cornea

Table A-9. The Ocular Effects in Rabbits of the Federal Streamer No. 280 Formulation Sprayed at the Left Eye for 1 or 5 Seconds at a Distance of 3 Feet

Conditions		Rabbit No.	Ocular effects								
			Days after dose								
			1[a]			2			3[b]		
Spray time	Distance		CH	R	C	CH	R	C	CH	R	C
sec	ft										
1	3	261	3	2	0	2	2	0	2	2	0
1	3	262	4	2	0	4	2	0	3	2	0
1	3	263	4	2	0	4	2	0	4	2	0
1	3	264	4	2	0	3	2	0	2	2	0
1	3	255[c]	0	0	0	0	0	0	0	0	0
1	3	256[c]	0	0	0	0	0	0	0	0	0
5	3	257	4	2	<1	4	2	1	3	2	1
5	3	258	4	2	1	4	2	1	4	2	1
5	3	259	4	2	2	4	2	1	3	2	0
5	3	260	4	2	1	4	2	1	3	2	0
5	3	277[c]	0	0	0	0	0	0	0	0	0
5	3	278[c]	0	0	0	0	0	0	0	0	0

[a]Observation days post dosage.

[b]All animals sacrificed and submitted for necropsy in 3 days.

[c]Isotonic saline control.

NOTE: CH = Chemosis

R = Redness

C = Cornea

Table A-10. The Cutaneous Effects of the Contents of the Federal Streamer No. 280 (0.9% CN) Applied in 24-Hour Patch Tests to the Skin of Rabbits

Dose	Rabbit No.	Days after dose																												Recovery day
		1			2			3			4			5			6			7			8			9			10			
		E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	E	N	D	
ml																																
1.0	185	1	0	0	2	1	0	1	1	0	1	1	0	3	1	0	0	2	0	0	2	0	0	2	0	0	2	0	0	2	0	c
1.0	186	1	0	0	2	0	0	2	0	0	2	0	0	3	2	0	1	1	0	1	1	0	1	1	0	1	1	0	1	1	0	22
1.0	187	1	0	0	1	2	0	1	1	0	2	1	0	3	1	0	2	2	0	2	2	0	2	2	0	1	1	0	1	1	0	c
1.0	188	1	0	0	2	1	0	1	1	0	2	2	0	3	1	0	2	2	0	2	2	0	2	2	0	1	1	0	1	1	0	c
1.0	205[a]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
1.0	206[a]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
1.0	227	1	0	0	1	0	0	3	0	0[b]																						
1.0	228	1	0	0	1	0	0	2	2	0[b]																						
1.0	229	2	0	0	1	0	0	2	0	0[b]																						
1.0	230	1	0	0	2	0	0	2	0	0[b]																						
1.0	231[a]	0	0	0	0	0	0	0	0	0[b]																						
1.0	232[a]	0	0	0	0	0	0	0	0	0[b]																						
0.1	189	2	0	0	2	2	0	1	1	0	2	2	0	2	2	0	3	1	0	1	1	0	1	1	0	1	1	0	1	1	0	23
0.1	190	1	0	0	1	0	0	1	0	0	2	2	0	2	1	0	3	1	0	1	1	0	1	1	0	1	1	0	1	1	0	c
0.1	191	1	0	0	1	0	0	2	0	0	2	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	0	0	1	0	c
0.1	192	1	0	0	1	0	0	1	0	0	2	0	0	2	0	0	2	0	0	1	0	0	1	0	0	0	0	0	0	1	0	c
0.1	207[a]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
0.1	208[a]	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
0.1	233	1	0	0	1	0	0	2	0	0[b]																						
0.1	234	1	0	0	1	0	0	2	0	0[b]																						
0.1	235	1	0	0	1	0	0	2	0	0[b]																						
0.1	236	1	0	0	1	0	0	2	0	0[b]																						
0.1	237[a]	0	0	0	0	0	0	0	0	0[b]																						
0.1	238[a]	0	0	0	0	0	0	0	0	0[b]																						

[a] Isotonic saline control.

[b] Rabbits sacrificed and submitted for necropsy 3 days postexposure.

[c] Scar tissue apparent at 30 days; no hair growth.

NOTE: E = Erythema
N = Necrosis
D = Dehydration and/or desquamation

Table A-11. Effects of Federal Streamer No. 280 and CS/TOF Solutions on Human Skin

Subject	Formulation	Dose	Test area	Response
		ml		
OV	Federal Streamer	0.01	Bare	Slight erythema at 30 minutes. No erythema at 6 hours.
G1	Federal Streamer	0.01	Bare	Slight erythema at 30 minutes. No erythema at 2 hours.
W1	Federal Streamer	0.025	Bare	No signs or symptoms
SE	Federal Streamer	0.025	Bare	No signs or symptoms
BR	Federal Streamer	0.01	Sateen	No signs or symptoms
VE	Federal Streamer	0.01	Sateen	No signs or symptoms
WA	Federal Streamer	0.025	Sateen	No signs or symptoms
FR	Federal Streamer	0.025	Sateen	No signs or symptoms
PE	CS (1% in TOF)	0.01	Bare	None
WH	CS (1% in TOF)	0.01	Bare	None
BU	CS (1% in TOF)	0.025	Bare	None
EL	CS (1% in TOF)	0.025	Bare	None
TR	CS (1% in TOF)	0.01	Sateen	Slight stinging sensation for first 30 minutes
HA	CS (1% in TOF)	0.01	Sateen	None
STUM	CS (1% in TOF)	0.025	Sateen	None
STUT	CS (1% in TOF)	0.025	Sateen	None

Table A-12. Canine Testing Protocol for Federal Streamer No. 280, CS/TOF, CS/Propylene Glycol, TOF, and Propylene Glycol Solutions

Test solution	Method and route of administration	Dose	No. of animals		No. of animals necropsied					
					Experimental day			Control day		
			Experimental	Control[a]	3	7	30	3	7	30
		ml								
Federal Streamer No. 280	Trachael intubation	0.50	8	4	4		4	2		2
		0.25	8	4	4		4	2		2
		0.10	8	4	4		4	2		2
CS/TOF 1% solution	Trachael intubation	0.50	8	4	4		4	2		2
		0.25	8	4	4		4	2		2
		0.10	8	4	4		4	2		2
Federal Streamer No. 280	Intratrachael injection	0.50	8	4		4	4		2	2
CS/TOF 1% solution	Intratrachael injection	0.50	8	4		4	4		2	2
CS/Propylene glycol	Trachael intubation	0.50	8	2[b]	4		4	2		
TOF	Trachael intubation	0.50	8		4[c]		4			
Federal Streamer No. 280	Device sprayed into mouth	1-second spray (1 ml)	8	4		4	4		2	2

[a] Saline controls – same volumes as for test solution.

[b] Propylene glycol controls – same volume as for test solution.

[c] TOF controls.

Table A-13. Comparison of Rectal Temperatures of Dogs Dosed with Federal Streamer No. 280 or CS/TOF Solutions

Dose	Test solution	Rectal temperature	
		Preexposure	72 Hours postexposure
ml		°F	
0.5	Federal Streamer	102.2	102.8
0.5	CS in TOF	102.3	102.5
0.25	Federal Streamer	101.4	102.7
0.25	CS in TOF	102.0	102.6
0.1	Federal Streamer	101.6	102.7
0.1	CS in TOF	102.2	102.7
0.5	TOF	Not taken	101.6
0.5	CS/Propylene glycol	Not taken	102.3
0.5	Propylene glycol	Not taken	101.7
	Grouped control mean	102.3	102.5

NOTE: Temperatures were not recorded at the 96-hour examination of animals exposed by injection and by spraying in the mouth as the climate was hot and humid, and all temperatures were running between 103° and 105°F.

Table A-14. Average Blood Chemistry Values in Dogs Dosed by Tracheal Intubation, Intratracheal Injection, or Oral Spray with Federal Streamer No. 280 or CS/TOF Solutions

Test solution	Method	Dose	Number tested	Sample	RBC	WBC	PCV	BUN
		ml			$\times 10^6$	$\times 10^3$	%	S-F units
Federal Streamer No. 280	Tracheal intubation	0.50	8	Preexposure	7.7	15.6	48.9	14.1
				72-Hr postexposure	7.4	15.8	47.3	13.6
		0.25	8	Preexposure	7.3	16.0	46.3	16.4
				72-Hr postexposure	6.9	15.0	46.3	15.8
		0.10	8	Preexposure	6.9	10.4	50.4	15.6
				72-Hr postexposure	7.4	13.4	47.3	13.5
		Grouped control	12	Preexposure	7.8	13.9	48.0	15.7
				72-Hr postexposure	6.8	13.0	47.5	16.2
CS/TOF 1% solution	Tracheal intubation	0.50	8	Preexposure	7.1	13.5	50.3	16.4
				72-Hr postexposure	8.0	16.5	51.3	16.8
		0.25	8	Preexposure	6.7	9.8	47.4	17.4
				72-Hr postexposure	7.5	14.0	48.0	15.5
		0.10	8	Preexposure	7.6	15.9	51.8	16.3
				72-Hr postexposure	8.0	14.6	51.2	16.0
		Grouped control	12	Preexposure	7.4	13.9	48.8	16.9
				72-Hr postexposure	7.4	12.4	47.5	17.1
Federal Streamer No. 280	Intratrachael injection	0.50	8	Preexposure	6.9	14.0	40.0	16.0
				96-Hr postexposure	7.1	15.4	47.0	16.0
CS/TOF 1% solution	Intratrachael injection	0.50	8	Preexposure	6.8	16.4	46.0	18.0
				96-Hr postexposure	7.3	15.5	48.0	15.0
Federal Streamer No. 280	Oral spray	1-Second spray (1 ml)	8	Preexposure	6.8	15.9	41.0	20.0
				96-Hr postexposure	6.5	14.6	45.0	20.0
		Grouped control	12	Preexposure	7.0	13.8	47.0	16.0
				96-Hr postexposure	7.1	12.8	46.0	14.0

Table A-15 Summary of Signs Seen in Dogs Dosed by Tracheal Intubation or by Intratracheal Injection with Federal Streamer No. 280 or CS/TOL Solutions

Test solution	Method	Time of examination	Dosage group	Signs		
				Dehydrated*	Cough on tracheal pressure	Auscultable congestion
Federal Streamer No. 280	Tracheal intubation	72 Hr after dosing	Agent ml			
			0.5	1/12	0/12	2/12
			0.25	3/0	2/8	3/8
			0.10	2/8	2/8	2/8
			Saline controls ml			
			0.5	0/4	1/4	0/4
			0.25	0/4	0/4	0/4
			0.10	0/4	0/4	0/4
CS 10% PEG solution	Tracheal intubation	72 Hr after dosing	Agent ml			
			0.5	0/8	1/8	1/8
			0.25	0/8	4/8	4/8
			0.10	0/8	3/8	1/8
			Saline controls ml			
			0.5	0/4	1/4	0/4
			0.25	0/4	0/4	1/4
			0.10	0/4	0/4	0/4
Federal Streamer No. 280	Intratracheal injection	96 Hr after dosing	Agent ml			
			0.5	2/8	5/8	0/8
			Saline controls ml			
			0.5	2/4	0/4	0/4
CS 10% PEG solution	Intratracheal injection	96 Hr after dosing	Agent ml			
			0.5	0/8	1/8	1/8
			Saline controls ml			
			0.5	1/4	0/4	0/4
Federal Streamer No. 280	Spray in mouth	96 Hr after dosing	Agent			
			1-Second spray (1 ml)	0/8	0/8	0/8
10% CS in propylene glycol	Intratracheal intubation	72 Hr after dosing	Agent ml			
			0.5	0/8	0/8	0/8
10% alone	Intratracheal intubation	72 Hr after dosing	Agent ml			
			0.5	0/8	0/8	0/8
Propylene glycol alone	Intratracheal intubation	72 Hr after dosing	Agent ml			
			0.5	0/2	0/2	0/2

*Dehydration assayed by elasticity of skin and subcutaneous tissues

Table A-16. Lesions Found in Dogs Necropsied 3 Days After Intratracheal Exposure (Intubation) to Federal Streamer No. 280

Dose	Trachea	Lungs
ml		
0.1	No significant lesions	No significant lesions
0.25	Hyperemia, ecchymosis (2/4) Focal tracheitis (1/4)	Congestion (3/4)
0.5	Severe tracheitis (3/4) [fibrinoid membrane (2/3)]	Pneumonia (2/4) Congestions (2/4)

*Numbers in parentheses are fractions showing signs.

Table A-17. The Ocular Effects of CS (0.1% and 1.0% in PEG 200) in Rabbits

Solution strength	Dose	1*			3			4			6			10			21		
		CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C	CH	R	C
% of CS	ml																		
0.1	0.05	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1	0.05	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1	0.50	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.1	0.50	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1.0	0.05	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1.0	0.05	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1.0	0.50	4	0	0	0	2	1	0	0	1	0	0	1	0	0	0	0	0	0
1.0	0.50	4	0	0	0	2	2	1	0	1	0	0	1	0	0	0	0	0	0
Controls	0.05	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Polyethylene	0.05	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
glycol	0.50	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(200)	0.50	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

*Observation days post dosage.

NOTES: See tables A-1 and A-2 for grading systems.

CH = Chemosis

R = Redness

C = Cornea

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Director of Toxicology National Research Council 2101 Constitution Ave, NW Washington, DC 20418	1
Director Central Intelligence Agency Attn: ORD/DD/S&T Washington, DC 20505	1

END