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PDBARON:mtw
September 29, 1967

002674

Trade Name: Vikane Fumigant

Chemical Name: Sulfuryl Fluoride

Structural Formula: $F-\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}-F$

Empirical Formula: SO_2F_2

Melting Point: 136°C at 760 mm Hg. (approximately 213°F.)

Boiling Point: 55°C at 760 mm Hg. (approximately 67°F.)

Solubility at 25°C: Practically insoluble in water, only very slightly soluble in organic solvents, vegetable oils and Stoddard Solvent.

Stability: Stable to heat normally encountered in structural and other fumigation. Non-flammable in all atmospheric concentrations.

Reactivity: Sulfuryl fluroide is highly unreactive as evidenced by its low solubility, marked stability to heat and the fact that to date, no odor contamination or corrosive effects have been detected following numerous fumigation tests. The material is reactive with strong bases.

Heat of vaporization: 4513 Cal/mole. at -55.2°C.

Expansion coefficient: One pound of gas occupies 3.85 cu. ft. at 25°C. and 760 mm hg. One pound of gas per 1000 cubic feet of unoccupied space equals approximately 3850 ppm at ordinary room temperature (25°C. and 760 mm Hg.)

Infrared analysis of the samples used in this study indicated better than 99% purity. The balance was found to be largely SO_2 and air.

Usage Pattern: ∿ 5 ppm concentration in fumigated rooms. PCO's handling the product were instructed to wear specific acid gas cannisters.

Non food or food crop use.

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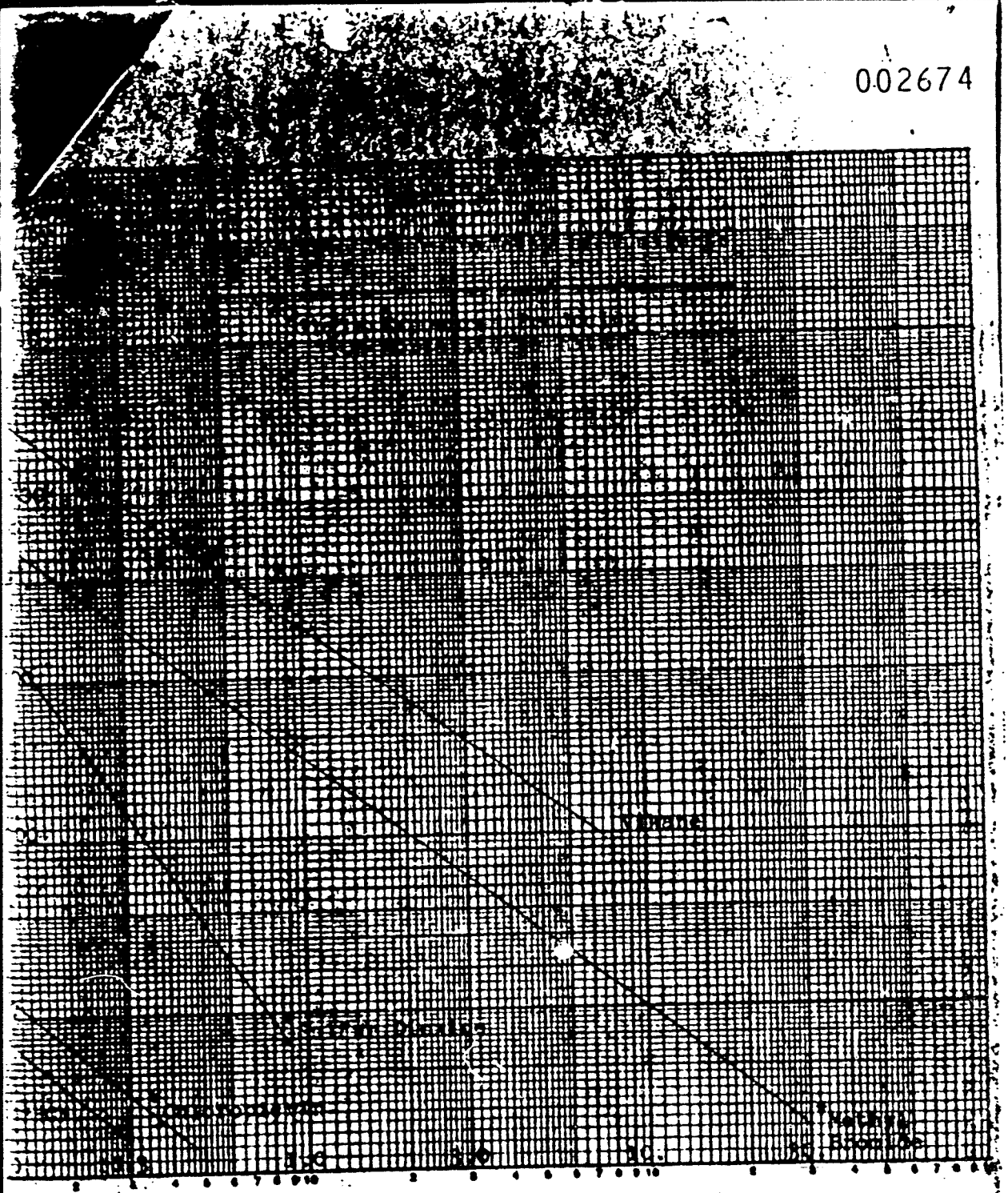
Acute Rat Oral	:	LD_{50} = ∿ 100 mg/kg
Acute Guinea Pig Oral	:	LD_{50} = ∿ 100 mg/kg
Subacute Rat Feeding (66 days)	:	No effect level: Vikane fumigated diets of 2 lbs/1000 cu feet Higher levels (10, 100, 200 lbs/1000 cu feet) produced growth retardation, fluorosis of the teeth, increased body weight ratios.
Acute Rat Inhalation	:	Convulsions, salivation, loss of bladder control noted at dosages used. LC_{50} = 4200 ppm at 1 hour exposure LC_{50} = 7000 ppm at 1/2 hour exposure
Subacute Inhalation (6 mo. & 1yr):		Animals dosed at 20 ppm for 6 mos. had no adverse pathology. Those dosed at 20, 50, and 150 ppm for 1 year were noted to have pneumonia and changes in lungs consistent with early neoplasm. Liver and kidney pathology was noted at the higher dosage level.



*Estimated from data in literature

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Comments

Data on Vikane Fumigant (Sulfenyl Fluoride) has been reveiwed.

This gas has a Class II toxicity, acute rat inhalation LD_{50} = 4200 ppm, less lethal than other known fumigants such as Chloropicrin and sulfur dioxide.

The product has no odor, but a warning agent such as Chloropicrin is suggested for use in clearing a structure prior to labelling. The Chloropicrin is not in the formulation.

The chronic six months inhalation data suggests that the no effect level is 20 ppm for Guinea Pigs and slight increase in fluroide content of some was noted in rats and mice. No determination for serum calcium or bone marrow sections were made. The autopsy reports were noted included in the studies presented.

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Vikane Fumigant

Acute Rat Oral

Four each male and female rats were fed 0 to 400 mg/kg Vikane. Feeding was carried out by administering aliquots of a 1% corn oil solution prepared by bubbling the gas through chilled oil. The gas is slightly soluble in vegetable oil.

Results

LD_{50} = approximately 100 mg/kg, at 40 and 50 mg/kg no unusual behavior was noted. The report states that very slight pathology was possibly present in the liver and lung. At 80 and 100 mg/kg diarrhea and dehydration was noted. This could possibly have been because of large volumes of corn oil fed to rats. The liver and lungs were slightly congested. Appreciable gastritis and cloudy swelling in the kidneys was noted. At dosage levels of 160 and 200 mg/kg all animals died in a few hours. Mechanism of death was not determined.

Acute Guinea Pig Oral

Four female guinea pigs were treated at each dosage level according to the protocol stated in the Acute Rat Oral Study.

Results

LD_{50} = approximately 100 mg/kg. The same observations noted for the rats was present in the Guinea Pigs.

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Subacute Rat Feeding (66 Days)

Samples of laboratory feed were fumigated with Vikane for 24 hours at 80°C with 200, 100, 10 and 2 pounds respectively of Vikane per 1000 cubic feet. The diets were then analyzed for fluoride. Using a control diet with an average of 36 ppm in fluoride the net dietary levels of fluoride were for the 19, 53, 350, and 704 ppm.

Ten each male and female animals were maintained on the Vikane fumigated diets for 66 days. Two additional rats of each sex were set up at each dietary level for autopsy after 30 days. During the course of the experiment the animals were weighed twice weekly for the first 28 days, and once a week thereafter. They were observed frequently for gross changes in appearance or behavior. The teeth of all rats were checked for any visual evidence of fluorosis. Records of mortality and food consumption were recorded for these animals. Urinary samples were obtained from all male rats for fluoride analysis.

Control animals and those on 19 and 53 net ppm were given terminal hematologic studies. At autopsy the lungs, heart, liver, kidney, spleen, and testes were removed and weighed. Sections of these as well as the pancreas and adrenals were made for histologic studies. Samples of blood, urine, kidney, lung, liver and bones were collected and analyzed for fluoride from all the rats killed at 30 days.

Results

Gross Appearance and Behavior

Male and female rats fed diets fumigated with 200 pounds of Vikane per 1000 cubic feet (Net fluoride content 704 ppm) showed a severe retardation of growth. Darkening and banding of the teeth which would indicate fluorosis were observed in both sexes. Animals on the net 350 ppm fluoride in the diet were found to have gross retardation and darkening and banding of the teeth. Male rats fed the diet fumigated with 10 pounds of Vikane per 1000 cubic feet (53 net ppm) exhibited a slightly statistically significant decrease in the final average body weight. Early indications of fluorosis were noted in the teeth of both males and females. The teeth had much pigmentation and appeared whiter than the controls. Animals on the two pounds Vikane per 1000 cubic feet (net 19 ppm) showed no evidence of adverse effects, namely gross appearance and behavior.

Food Consumption

Animals on the highest dosage level (200 pounds per 1000 cubic feet) had severe retardation of growth. Food consumption data were not included in the report.

Hematology and Urine Analysis

An increase of urine fluorides in proportions to the amount of Vikane fed into the diet was noted in all animals. Results of the analyses of the blood kidney, lung and liver for fluorides could not be called consistently with dosage levels.

Gross and Histo Pathology

Animals on the two pounds of Vikane per 1000 cubic feet had no gross and microscopic changes which could be attributable to drug toxicity. The average final body weight and organ weights of these animals was also unremarkable. In animals fed 200 pounds Vikane per 1000 cubic feet dietary level there was an increase in the average weight of the liver and testes of male rats. Microscopically there were some glomerular involvement of the kidneys. Animals on 100 pounds Vikane per 1000 cubic foot dietary level were noted to have no changes on microscopic examination. In these animals the average weight of the testes was increased on the grams per 100 grams body weight basis. Animals on the ten pounds of Vikane per 1000 cubic feet had a slight increase in the average weight of the liver (grams per 100 grams body weight).

No effect level two pounds of Vikane per 1000 cubic feet (net 19 ppm fluoride).

Acute Rat Inhalation

Eight to twenty each male and female rats were exposed to 1000 to 15,000 ppm Vikane for a period of 0.1 to 6 hours. Results of LD_{50} are concluded in the accompanying chart. When inhaled in lethal amounts, Vikane caused tremors and repeated convulsions. The convulsions in rats are similar to those caused by strychnine and are characterized by opisthotonus and toppling over backward. This was accompanied by excessive salivation, loss of bladder control and occasionally by bloody tears (chromodaryorrhea).

Generally the convulsions were followed by death although a few rats survived the convulsions and recovered. Animals exposed for periods of two and three hours at 1000 ppm concentration had the least effect, possibly slight tremors after exposure and only slight weight loss.

Subacute Inhalation (6 Months and 1 Year) (Rats, Guinea Pigs, Rabbits and Monkeys)
The studies were conducted in three successive phases.

Phase I

A preliminary study in which all groups of animals were exposed to 400 and 200 ppm.

Phase II

Twenty rats, ten guinea pigs, three rabbits, of each sex and two female monkeys received daily exposures of either 200 or 100 ppm Vikane seven hours daily five days per week for a period of six months. Matched control animals for all species were provided except for monkeys. Animals were examined frequently for changes in gross appearance and behavior. Mortality and body weights were recorded. Half the rats and guinea pigs were sacrificed at the end of the exposure period for examination. The remaining animals were held for one month and then sacrificed. Samples of blood from representative groups of animals were collected for hematological examination as well as determination of growth by content. The lungs and teeth of some animals were also analyzed for fluoride content.

Phase III

48 male and 48 female rats, 22 male and 22 female guinea pigs and 80 female mice were exposed to 20, 50, and 150 ppm Vikane in the air. Another group was used as controls. The animals exposed at each concentration and the controls were split into five groups. Animals in Group I were exposed for six months and were sacrificed immediately after exposure. Animals in Group II were exposed for six months and sacrificed three months after exposure. Animals in Group three were exposed for six months and sacrificed six months after exposure. Those of Group IV were exposed for 12 months and sacrificed immediately after exposure. Animals in Group V were exposed for 12 months and sacrificed six months after exposure. In addition three other groups of 15 female rats each were exposed for three months and sacrificed at 0, 3 and 15 months after exposure respectively. This was done for evaluation of the nature of lung pathology.

ing the course of the experiment the chamber containing 150 ppm was ified so that groups of rats could be introduced for four hours, two hours hour, and one half hour daily exposures. Four groups of five female rats were exposed in this manner for four months and a similar group was main- ed as unexposed controls.

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Results

A. Preliminary Studies (400 ppm Short Term)

3/5 male rats exposed to 400 ppm died or were sacrificed in moribund state after 10, 11, and 14 exposures. Death was generally accompanied by convulsions and inanition. The two surviving rats were sacrificed after 15 exposures. Pulmonary hemorrhages and cloudy swelling of the kidneys were seen at autopsy. 3/5 female rats died after five or six exposures. The two survivors were sacrificed after the sixth exposure after losing a large amount of weight. A second group of female rats was exposed similarily. This group appeared slightly more resistent than the first, however, bloody noses were evident after the third exposure and deaths occurred after ten exposures. One of the two guinea pigs died after five exposures and the others were sacrificed after 13 exposures. General congestion was particularly in the lungs and kidneys. Fatty and necrotic livers were also evident in the animals that died. Rabbits exposed to 400 ppm showed rather diverse symptoms when sacrificed after 13 and 17 exposures. Wet noses, loss of control and tremors of the hind quarters, lungs, liver and kidney pathology and loss in weight were seen in the two rabbits so exposed.

Phase I

200 ppm--One Month

Five male and five female rats, one female rabbit and two male guinea pigs received 22 seven hour exposures in 35 days to a concentration calculated to be 200 ppm. When sacrificed all animals were gaining weight and ap-

peared normal, however, the livers of most animals except for the two guinea pigs were congested.

Phase II

200 ppm-Six Months (7 hours per day)

Male Rats (Six Months at 200 ppm)

The animals appeared sick after one and one-half months of exposure. Mortality was increased and growth was below normal. There was a definite increase in fluoride in the urine after one and one-half months of exposure. Final organ weights were comparable to those of controls except for considerable increase in lung weight. Microscopic evidence of pneumonia was found, this was characterized by metaplasia and hyperplasia of the bronchial epithelium and granuloma disformation. X-rays of the entire bodies of the three rats were essentially normal in appearance but indicated that the bone structures may have been more dense than those of the controls. Fluoride levels in bone, blood, lungs and teeth were also increased. Those allowed to recover one month before autopsy had normal lung weights but the micropathological changes were still present. Fluoride content of the bones and teeth was lowered but still higher than the controls.

Female Rats (Six Months at 200 ppm)

Growth was decreased and mortality increased. Hematologic values appeared to be within normal limits after three months exposure. The lungs and kidney weights were higher than that of the controls and microscopically, evidence of lung pathology similar to that of the male rats was seen. Those allowed to recover for one month after six months exposure had normal kidney weights and apparently better lung to body weight ratios but were still appreciably higher than the controls. The histological changes were still present in the lungs.

Male Guinea Pigs (Six Months at 200 ppm)

These animals appeared normal but growth was depressed and mortality was slightly higher than the controls. To body weight and testes to body weight ratios was higher than that of the controls. Increased testicular weight does not appear in the other groups however. Histologically there was no evidence of lung or liver pathology, however pneumonia was apparent in the groups sacrificed one month after exposures were ceased.

Female Guinea Pigs (Six Months at 200 ppm)

These animals appeared normal and although growth and mortality were both adversely effected the average weights of the lungs and heart were increased over that of the controls. Histologically there was evidence of slight lung pathology similar to that seen in the male rats. Additionally there was some slight fatty degeneration of the liver. The concentration of fluoride in the bone at autopsy was roughly three times that of the controls. Those animals allowed to recover for one month after exposure

still had histologic evidence of lung injury. The average weight of the heart was normal and lung weights were approaching normal.

Male and Female Rabbits (Six Months at 200 ppm)

All of the three male rabbits died before the end of the experiment. All female rabbits survived the 126 exposures and were normal in appearance and growth. Pathology was negative.

Female Monkeys (Six Months at 200 ppm)

The two female monkeys were found to be thin, listless and unkempt. Both animals lost a small amount of weight during the experiment. X-rays of the monkeys showed no significant difference in the bones from those of the controls. Pathology was negative when compared with controls.

Phase III

100 ppm--Six Months Exposure

Male Rats

Male rats exposed to 100 ppm were normal in appearance, growth, and mortality. Fluoride content of the urine was appreciably higher than that of the controls when analyzed after five months exposure, as were the fluoride levels of the teeth and bone. Final organ to body weight ratios were normal. Histologic changes seen in the lungs were similar to those described for male rats exposed to 200 ppm. Pneumonia was also present in rats allowed to recover for one month, however lung to body weight ratios had returned to normal.

Female Rats

These animals were normal in appearance, growth and mortality. Organ to body weight ratios were normal except for the lungs. Histologic examination of the lungs revealed pneumonia which was present in rats allowed to recover for one month, but the lung to body weight ratio had returned to normal in the rats sacrificed at this time.

Male Guinea Pigs (Six Months at 100 ppm)

These animals were normal in appearance, growth and mortality. Organ to body weight ratios were normal. Histologic examinations showed no effect in animals killed immediately after exposure ceased, however the guinea pigs sacrificed one month after exposure had what was considered evidence of pneumonia.

Female Guinea Pigs

These animals were normal in appearance, however growth was slightly depressed and there was a very questionable increase in mortality. At autopsy there was an increase in fluoride content of the bone. Organ to body weight ratios were apparently normal but evidence of pneumonia was seen in animals sacrificed immediately after exposure. Slight damange to the liver was also seen. Female guinea pigs allowed to recover one month still had evidence of pneumonia but the liver damage had disappeared.

Male and Female Rabbits

All male and female rabbits survived this experiment and were normal in appearance and growth. New pathology due to the compound was seen in the female rabbits. Male rabbits, however, gave evidence of pneumonitis as well as slight kidney damage.

Female Monkeys

The two monkeys exposed at a 100 ppm were normal in appearance and activity. There was no evidence of gross or micropathological changes.

Exposure to 20 ppm

Male Rats

These animals were normal in appearance and average body weights were essentially equal to that of the controls. Mortality was equal to that of the control group. The organ to body weight ratios were normal and no significant pathological findings could be seen. The urine contained about twice the level of fluoride found in the controls and the bone was also considerably higher in fluoride than the controls. The teeth were not analyzed for fluoride but were normal in appearance. Those animals exposed for six months and allowed to recover for three months were normal in appearance and weight. Organ to body weight ratios were normal with no significant histopathology noted. Those animals exposed for six months and allowed to recover for six months were apparently normal in all respects although the fluoride level in the teeth was considerably above that of the controls. Male rats exposed to 20 ppm for double that 1 year period of time had essentially the same findings.

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Animals exposed for three months and allowed to recover for three months were also normal as were the female rats allowed to recover for 15 months after a three month exposure. Those animals exposed double that time were normal in appearance, weight and mortality. Organ to body weight ratios were normal. Growth and micropathology were also not significant and there was no gross evidence of fluorosis of the incisors. The fluoride content of the urine was about twice that of the controls. The bones also contained slightly more fluoride than normal. Those animals exposed for six months and allowed to recover for three months and six months were normal as judged by appearance, weight, mortality, organ to body weight ratios and histopathological examination of the organs. Animals exposed for one year and allowed to recover for six months were normal in all respects.

Guinea Pigs

Male animals exposed for one year and allowed to recover for six months were normal in all respects when compared to controls. Those animals exposed 125 times and 180 days were normal in appearance, weight, and mortality. The organ to body weight ratios were normal. No histopathologic changes were noted. Results of the female animals were similar

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Female Mice

Animals exposed to 20 ppm 125 times in 187 days were normal in body weight. Mortality was slightly higher than that of the control group. Organ to body weight ratios were normal as were growth and microscopic-pathology. There was no evidence of fluorosis of the incisors. Female mice exposed for six months and allowed to recover for three months showed slight evidence of pneumonia and a slightly elevated heart to body weight ratio. Animals exposed for six months and allowed to recover for six months were normal in body weight but had high lung to body weight ratios. Pneumonia as well as kidney damage was noted. The teeth were apparently lighter in color than that of the controls, indicating some effect of the fluoride. Female mice exposed to 20 ppm, 255 times were noted to have apparently normal weight but the mortality was increased. Several of these animals had lost hair. This was not seen in the animals exposed to higher concentrations, however, and was probably not due to the exposure. There was a considerable increase in the ratio of lung and kidney to body weight ratios and pneumonia was seen in the lungs examined microscopically. Teeth were lighter in color and similar to those in the animals killed after six months exposure. Animals exposed to 20 ppm for one year and allowed to recover for six months showed no abnormal pathology when compared with the controls.

The highest exposure level without evidence of changes in the lung after six months of exposure was 20 ppm. A years exposure to 20 ppm however, resulted in characteristic changes in all groups except the female rats. Animals exposed to 50 and 150 ppm for a year and allowed to recover six months were also normal and compared with the controls.