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HEALTH, SAFETY AND ENVIRONMENTAL AFFAIRS

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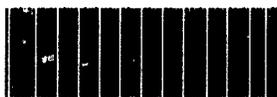
October 31, 1991

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88928000105

Attn: Section 8(e) Coordinator (CAP Agreement)

Re: CAP Agreement Identification No. 8ECAP-0110

Dear Sir or Madam:

Union Carbide Corporation ("Union Carbide") herewith submits the following report pursuant to the terms of the TSCA §8(e) Compliance Audit Program and Union Carbide's CAP Agreement dated August 14, 1991 (8ECAP-0110). This report describes an assessment of toxicity and pulmonary effects in the rat with various UCON® Lubricant samples (CASRN 9036-95-3, others).

"UCON® Lubricant Samples: Assessment of Toxicity and Pulmonary Effects in the Rat Following Single Endotracheal Injection", Bushy Run Research Center, Project Report 52-53, August 14, 1989.

A complete summary of this report is attached.

Previous TSCA Section 8(e) or "FYI" Submission(s) related to this substance are:

8EHQ-1086-0635

Previous PMN submissions related to this substance are: (none)

UCONLAB

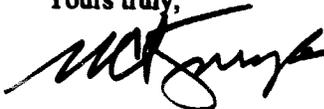
39 OLD RIDGEBURY ROAD, DANBURY, CT 06817-0001

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This information is submitted in light of EPA's current guidance. Union Carbide does not necessarily agree that this information reasonably supports the conclusion that the subject chemical presents a substantial risk of injury to health or the environment.

In the attached report the term "BUSINESS CONFIDENTIAL" is entered on the first page. This precautionary statement was for internal use at the time of issuance of the report. Confidentiality is hereby waived for purposes of the needs of the Agency in assessing health and safety information. The Agency is advised, however, that the publication rights to the contained information are the property of Union Carbide.

Yours truly,



William C. Kuryla, Ph.D.
Assistant Director
Product Safety
(203/794-5230)

WCK/cr

Attachment (3 copies of cover letter, summary, and report)

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SUMMARY

52-53

UCON® Lubricant Samples

Assessment of Toxicity and Pulmonary Effects in the Rat Following Single Endotracheal Injection

Sponsor: Specialty Chemicals Division
Union Carbide Corporation

* * * * *

SUMMARY

Seven UCON® Lubricant samples, TERGITOL® 24-L-60N (positive control) and saline (negative vehicle control) were tested for toxicity and pulmonary injury in the rat, using an endotracheal injection technique. Approximately 0.5 ml of each material, or its dilution, was injected through the trachea into the lungs of lightly-anesthetized rats.

Initial tests were conducted to establish lethal and nonlethal dosages. One to 3 males received various endotracheal doses of test material. The highest nonlethal doses were then used for the definitive study in which groups of 15 males received single endotracheal doses. Three animals/sex were then sacrificed at one, 2, 3 and 7 days (unless an insufficient number of animals survived to permit the serial sacrifices). Remaining survivors were sacrificed at 14 days. All rats were necropsied at death or sacrifice and the lungs were weighed and subjected to microscopic evaluation.

Based on mortality alone (initial tests), the most toxic samples tested were UCON® Lubricants LB-65, 50-HB-260, 50-HB-2000 and 50-HB-5100 as well as TERGITOL® 24-L-60N (positive control). Deaths resulted from doses of 0.01 ml/kg to 0.05 ml/kg. Somewhat less toxic was UCON® Lubricant 50-HB-660 with death at 0.2 ml/kg. Lethality data indicated that the least toxic materials were LB-1145 (no deaths from 2.0 ml/kg) and LB-3000 (death from 2.0 ml/kg but not from 1.0 ml/kg). Both of these fluids have relatively high molecular weight (> 2000) and low solubility in water. Previous tests have shown that rats survive endotracheal doses of 2.0 ml/kg of saline.

Results of the definitive study including gross signs, lung weights, incidence of lung lesions (gross and microscopic) and to some degree, body weights, indicated that the most toxic materials were UCON® Lubricant 50-HB-2000 and 50-HB-5100. Less severe effects were produced by the LB-1145, 50-HB-660 and the positive control (TERGITOL® 24-L-60N). The least toxic materials were UCON® Lubricants LB-65, LB-3000 and 50-HB-260. The negative control saline, did not produce remarkable toxic responses in the rat.

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Project Report 52-53
BRRC Number 88-15-11005
15 Pages
August 14, 1985

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Sponsor: Specialty Chemicals Division
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Based on mortality alone (initial tests), the most toxic samples tested were UCON® Lubricants LB-65, 50-HB-260, 50-HB-2000 and 50-HB-5100 as well as TERGITOL® 24-L-60N (positive control). Deaths resulted from doses of 0.01 ml/kg to 0.05 ml/kg. Somewhat less toxic was UCON® Lubricant 50-HB-660 with death at 0.2 ml/kg. Lethality data indicated that the least toxic materials were LB-1145 (no deaths from 2.0 ml/kg) and LB-3000 (death from 2.0 ml/kg but not from 1.0 ml/kg). Both of these fluids have relatively high molecular weight (> 2000) and low solubility in water. Previous tests have shown that rats survive endotracheal doses of 2.0 ml/kg of saline.

Results of the definitive study including gross signs, lung weights, incidence of lung lesions (gross and microscopic) and to some degree, body weights, indicated that the most toxic materials were UCON® Lubricant 50-HB-2000 and 50-HB-5100. Less severe effects were produced by the LB-1145, 50-HB-660 and the positive control (TERGITOL® 24-L-60N). The least toxic materials were UCON® Lubricants LB-65, LB-3000 and 50-HB-260. The negative control saline, did not produce remarkable toxic responses in the rat.

Bushy Run Research Center
A Joint Mellon Institute—Union Carbide Corporation Operation

Results from this study indicate that, although one or two samples were not significantly injurious to rat lungs and did not cause death even at relatively high doses, several of the UCONO Lubricant samples are as toxic or more toxic than TERGITOL® 24-L-60N to lung tissue. Moreover, many produce death, following endotracheal injection, at relatively low dosages. Therefore, aspiration of certain of these materials, especially those of the SO-EB series (which have high water solubility) and those with low molecular weight, should be avoided.

INTRODUCTION/OBJECTIVES

In previous studies conducted at BRRC, a large number of UCONO Lubricants have been evaluated for acute toxic effects. Although most were not remarkably toxic by the oral or dermal routes, some appeared to be relatively toxic by inhalation. To evaluate the effects of direct contact on the lungs, and to assess the potential hazards associated with aspiration of several UCONOs, rats were subjected to single endotracheal injection of a series of test or control substances. The animals were then examined for signs of systemic toxicity (including lethality) as well as gross and microscopic lung pathology.

SAMPLES

Seven UCONO Lubricants were received from P. L. Matlock, Union Carbide Corporation, Tarrytown, NY. Commercially available sterile saline (0.9% sodium chloride) was obtained from RICCA Chemicals. This solution was used, as necessary, to dilute the test or positive control materials. It also served as the negative control material. TERGITOL® 24-L-60N was received from Union Carbide Corporation, South Charleston, WV. This positive control material, and/or similar materials, has been previously shown to produce pulmonary lesions following cutaneous and endotracheal administration.

Detailed sample information is presented in Table 1. No chemical content analyses on these materials or their dilutions were performed by BRRC. Dilutions of the liquids were made on a volume/volume basis. Dilutions were prepared once a week for readily soluble liquids or each day for less soluble materials. Dilutions were mixed on a magnetic stirrer for several minutes before dosing and during dosing. Insoluble liquids were mixed with saline and homogenized (to form an emulsion) immediately before each dose.

ANIMALS/HUSBANDRY

Male and female Sprague-Dawley albino rats, weighing between 250 and 300 grams (approximately 8 to 10 weeks of age), were used. The rats were obtained from Harlan Sprague-Dawley, Inc. (Indianapolis, IN). Upon receipt, they were housed in Room 109 where they were subsequently dosed and observed until death or sacrifice. All rats were assigned unique animal numbers and identified by toe-clipping.

On arrival at the laboratory, the rats were examined by a qualified technician before being accepted into the animal holding area. During an acclimation period of one week, the rats were weighed twice and observed at regular intervals with respect to appearance, behavior, appetite and waste elimination.

The rats were housed in cages, one to 5 per cage, with wire floors under which animal cage board was placed. They were maintained on Agway RPH3000 and on water provided by an automatic water system. The feed was available ad libitum before dosing and again following dosing. Water was supplied by the Municipal Authority of Westmoreland County (Greensburg, PA) and was available at all times except during the actual dosing period.

EXPERIMENTAL PROCEDURES

Rats were lightly anesthetized by inhalation of methoxyflurane immediately prior to dosing. An oral speculum was then inserted into the rat's mouth. The speculum was a curved, tongue-shaped strip of smooth metal with a perpendicular wire bridge. It was attached to the lighted end of a commercial transilluminator (with battery holder). The wire bridge was positioned behind the rat's upper incisor teeth, holding the mouth open.

The rat was suspended from the speculum in such a manner that its pharynx and epiglottis were visible (with the light) and a 3 3/4-inch, 16-gauge Teflon needle was inserted into the trachea via the mouth. The needle was inserted to a point just above the bifurcation of the trachea. The characteristic "bumping" of the tracheal rings verified the correct pathway of the needle (opposed to the smooth feel of the esophagus).

Approximately 0.5 ml of undiluted test material or of a continuously stirred mixture in saline was drawn into a syringe and slowly injected through the Teflon needle into the lung. The needle was quickly withdrawn, the speculum removed and the rat placed on its ventral surface until recovery from the anesthesia. If death occurred immediately and appeared to be associated with anesthesia, the rat was eliminated from the study and was replaced.

EXPERIMENTAL DESIGN

An initial study was performed to determine relative toxicity of each material (based primarily on mortality) and to aid in establishing a suitable dosing concentration for the definitive study. One to 3 male animals were included in each preliminary test group. A constant volume of 2.0 ml of liquid per kg of body weight (0.4 to 0.6 ml per rat) was administered. For materials of suspected low pulmonary toxicity, rats were dosed with undiluted sample. If both animals survived this "limit test" for a 7-day period, no further preliminary dosing was performed. If a material produced mortality at this dose level (or if relatively high pulmonary toxicity was anticipated), smaller dosages were administered to obtain a nonlethal level.

A second (definitive) study was conducted in order to characterize the nature of lung injury produced by these materials. Groups of 15 male rats received single endotracheal doses of each sample. The animals received the highest nonlethal dosage of each material as determined in the initial tests. As much as possible, doses that produced signs of toxicity short of death were selected. The test material was diluted in saline, as necessary, to give a total dose volume of 2.0 ml per kg of body weight. TARCITOL® 24-L-60W was administered to 15 males in a similar fashion. Another group of 15 animals received 2.0 ml/kg of saline. Because of the large number of samples tested, the study groups were equally divided to permit dosing over a 3 week period. There was a total of 135 rats for the 7 test groups, positive control group and negative control group.

OBSERVATIONS

Dosed rats were observed frequently for signs of toxic effect on the first day of the test and twice a day thereafter until death or sacrifice (except on weekends or holidays, when they were examined for death alone). Weights were recorded shortly before dosing, weekly thereafter and at sacrifice (or at death). In order to evaluate early progression of pulmonary lesions, 3 rats were sacrificed at one, 2, 3, 7 and 14 days after dosing (except for instances of insufficient numbers of survivors). All rats were necropsied by qualified BRRC Pathology Department personnel after death or sacrifice.

PATHOLOGY

Lungs of all animals were removed, weighed and inflated with fixative (formalin vapor). All lungs were histologically processed and sections were examined microscopically. Any significant lesions not related directly to the respiratory system were also evaluated macroscopically at the discretion of the pathologist. Details of the pathology procedures are presented in the attached pathology report (Appendix 1).

RESULTS

Mortality data from the initial endotracheal injections are given in Table 2. Animal weights and signs of toxicity for the second study are summarized in Table 3. Pathologic findings are presented in Appendix 1.

The results presented below are separated by degree of acute endotracheal toxicity. To aid in comparison of the results from the various test materials, a brief description of the chemistry is given for each, followed by results from the initial and second (definitive) studies. Body weight patterns are based on small numbers of animals, making comparisons difficult, but any "apparent" weight effects (based on mean weights) are discussed.

A. UCONE Lubricants Exhibiting Relatively High Toxicity

LB-65

UCONE Lubricant LB-65 (Cas No. 9003-13-8) is a polyalkylene glycol with a molecular weight of 360. Its structural formula is $C_4H_9(OCH_2 CH(CH_3))_5 OH$. This slightly viscous liquid is no more than slightly soluble in water.

In the initial study, dosages of 0.01 ml/kg or higher were lethal to male rats. Concentrations of 0.5% or higher were administered at these lethal levels. Death occurred within 30 seconds after dosing. Rats survived endotracheal doses of 0.005 ml/kg (0.25% in saline) or less.

In the second study, 15 male rats received 0.005 ml/kg of LB-65, administered in a 0.25% dilution in saline. There were no deaths or other signs of toxicity observed. A slight mean body weight decrease was evident on the day after dose administration. At 2 days, the animals began to exhibit a consistent pattern of weight gains. Lung weights, expressed as both absolute and as percentage of body weight, were generally similar to those of saline treated control animals. There were essentially no significant gross lung lesions at necropsy. Upon microscopic examination of lung tissue, most lesions were comparable to those of negative controls with the possible exception of increased medial hyperplasia of the arteries.

50-HB-260

UCONE Lubricant 50-HB-260 (CAS No. 9038-95-3) is a polyalkylene glycol with an approximate molecular weight of 940. The structural formula is $C_4H_9(OCH_2 CH_2)_n(OCH_2 CH(CH_3))_m OH$. This material is a slightly viscous liquid and is completely soluble in water.

In initial testing, deaths resulted from endotracheal dosages of 0.05 ml/kg or higher. Dilution concentrations for these lethal levels were 2.5% and above. Times to death were all within 30 seconds after treatment. There were no deaths from dosages of 0.02 ml/kg or less, using dilutions of 1.0% or lower.

In the second study, 15 male rats were dosed with 0.02 ml/kg of 50-HB-260 using a 1.0% dilution. No deaths were noted and none of the animals exhibited any other signs of toxic effect. Body weights appeared to be depressed for the first day after dosing, but consistent increases in mean body weight were evident thereafter. Examination of absolute and relative lung weights revealed little apparent differences from saline control values. Necropsy did not reveal any remarkable gross lesions. The only microscopic finding in the lung that varied substantially from control lung lesions was the high instance medial hyperplasia of the arteries.

50-HB-2000

UCONE Lubricant 50-HB-2000 (CAS No. 9038-95-3) is a polyalkylene glycol which has an approximate molecular weight of 2600. Structurally, it has the general formula $C_4H_9(OCH_2 CH_2)_n(OCH_2 CH(CH_3))_m OH$. It exhibits complete water solubility and is a viscous liquid.

All endotracheal dosages in the first study, ranging from 0.05 to 0.2 ml/kg (concentrations of 2.5 to 10%), were lethal to male rats. Unexpectedly, there were delayed deaths at the lowest dosage and a non-lethal level was not determined. Several deaths (at higher dosages) occurred at 7 to 30 minutes. Other deaths were noted after 3 days.

The dosage in the second study, 0.02 ml/kg (1.0% dilution), produced death in 5 of 15 animals before their scheduled sacrifice. These deaths occurred at 3 to 5 days. Among the survivors, there appeared to be minimal weight depression for the first one to 2 days after dosing. From 3 days on, however, weights were more severely affected. Signs of toxicity included sluggishness, anacriation, breathing difficulties and discharge around the nose and eyes. Lung weights (absolute and relative) were substantially higher than those of controls, especially at 3 through 14 days. Necropsy revealed abnormal tracheal contents, emphysema (in one), lung discoloration, lung consolidation and liver discoloration. These lesions were not as evident in saline controls.

Microscopically, there were numerous lung lesions that were more prevalent in test animals than in the negative controls. These included congestion, edema, alveolar histiocytosis, hemorrhage (relatively common in controls), emphysema, perivascular infiltrates, interstitial pneumonitis and medial hyperplasia of the arteries (also observed in several controls).

50-EB-5100

UCONE Lubricant 50-EB-5100 (CAS No. 9038-95-3) is a polyalkylene glycol with the structural formula $C_4 H_9 (OCH_2 CH_2)_n (OCH_2 CH (CH_3))_m OH$. It has an approximate molecular weight of 4000. This material is a high viscosity liquid which is completely soluble in water.

Initial testing of 0.05 ml/kg and higher resulted in deaths among male rats. The dosing dilutions were of 2.5% concentrations and above. Because of unexpected delayed deaths, a non-lethal dosage was not established. Times to death ranged from one day to 5 days.

In the second study, 15 male rats were treated with 0.02 ml/kg of 50-EB-5100, using a 1.0% concentration. Although survival was anticipated from this level, based on initial test results, 7 rats died before their scheduled sacrifice dates. These deaths occurred at 3 to 5 days after endotracheal dose administration. There were only sufficient numbers of survivors for single sacrifices at 3 and 7 days. None remained at 14 days. Substantial weight loss was noted throughout the observation period. Also noted were sluggishness, labored breathing, piloerection and red discharge (around the nose and eyes). Lung weights (absolute and relative) were substantially higher for the test animals compared to negative controls. Notable necropsy findings included lung adhesions (in one), abnormal tracheal contents, lung discoloration, lung consolidation and liver discoloration.

Upon microscopic evaluation of the lungs, there were relatively high incidences of hemorrhage (also seen in controls), perivascular infiltrates, bronchopneumonia (in 3) and interstitial pneumonitis.

B. UCONE Lubricant Exhibiting Moderate Toxicity

50-HB-660

UCONE Lubricant 50-HB-660 (CAS No. 9038-95-3) is a polyalkylene glycol and has a molecular weight of 1700. Structurally, it has the formula $C_4H_9(OCH_2CH_2)_x(OCH_2CH(CH_3))_yOH$. This slightly viscous liquid is completely soluble in water.

Endotracheal injection during the first study caused death of male rats at dosages of 0.2 ml/kg and higher (using concentrations of 10X and higher in saline). Although death of one male at the 0.2 ml/kg level required 5 days, the time to death at higher dosages (0.5 to 2.0 ml/kg) was only one minute. Neither of 2 male rats died after receiving 0.1 ml/kg endotracheally (using a 5.0X dilution).

Fifteen male rats all survived administration of 0.1 ml/kg (5.0X dilution) of 50-HB-660 in the second study. After an initial weight loss on the day after dosing, a consistent weight gain pattern was evident at 2 through 14 days. No signs of toxicity were observed. Absolute lung weights appeared to be similar to those of saline controls. Lung weights as percentage of body weights were slightly higher than negative control values. Other than a few instances of consolidation, there was little remarkable gross pathology. Histopathologic examination revealed pulmonary hemorrhage (similar incidence to controls), a few eosinophilic concretions, several foci of emphysema, perivascular infiltrates, interstitial pneumonitis and medial hyperplasia of pulmonary arteries.

C. UCONE Lubricants Exhibiting Low Toxicity

LB-1145

UCONE Lubricant LB-1145 (CAS No. 9003-13-8) is a polyalkylene glycol which has an approximate molecular weight of 2050. Its structural formula is $C_4H_9(OC_3H_6)_nOH$ and it has high viscosity. LB-1145 is, at most, slightly soluble in water.

Endotracheal administration of undiluted sample at a dosage of 2.0 ml/kg did not kill either of 2 rats in the first study. This dosage was the maximum amount given in the endotracheal study.

Fifteen male rats were dosed with 2.0 ml/kg of undiluted LB-1145 in the definitive (second) endotracheal study. All survived. Piloerection and tremors were observed within several minutes after dosing. Body weights were slightly depressed for the first day after dosing, but consistent gains were apparent at 2 days through 14 days. The weight gains were only slightly less than negative controls. Comparison of absolute and relative lung weights to those of saline control animals revealed substantially higher values for the test rats. This effect was apparent at each sacrifice period. Necropsy revealed no significant gross lung lesions. Microscopic findings included perivascular infiltrates (similar in incidence to controls), interstitial pneumonitis (slightly higher than incidence in controls) and a relatively high incidence of medial hyperplasia of pulmonary arteries.

LB-3000

UCON® Lubricant LB-3000 (CAS No. 9003-13-8) is a polyalkylene glycol. It has a molecular weight range of 3000 to 4000. Structurally, its general formula is $C_4H_9(OC_3H_6)_nOH$. LB-3000 is a viscous liquid which exhibits low solubility in water.

In the first study, one of 2 rats died at 30 minutes following a dose of 2.0 ml/kg of undiluted sample. Using a 50X dilution, another 2 rats were dosed with 1.0 ml/kg. Both survived.

In the second study, there were no deaths or other signs of toxic effect among 15 male rats receiving 1.0 ml/kg of LB-3000 (as a 50X dilution). After an initial mean weight decrease, steady weight gain was apparent after 2 days and was similar to saline control animal weight values. Lung weights, expressed as absolute weight and as percentage of body weights were similar to corresponding control figures. There were no remarkable gross pathologic findings. Microscopically, there were relatively numerous instances of perivascular lung infiltrates, interstitial pneumonitis and medial hyperplasia of the pulmonary arteries.

D. Control Materials

24-L-60N

TERGITOL® 24-L-60N is a nonionic surfactant with an average molecular weight of 510. It is composed of a mixture of C-12 and C-14 linear alcohols which are ethoxylated with an average of 7.0 moles of ethylene oxide. This viscous liquid is soluble in water.

In initial testing, 0.01 ml/kg and 0.02 ml/kg (using 0.5X and 1.0X dilutions, respectively) killed male rats. Endotracheal doses of 0.005 ml/kg of 24-L-60N did not kill either of 2 animals. Times to death for rats at the higher levels were less than 2 minutes.

In definitive testing (second study), 15 male rats all survived doses of 0.005 ml/kg (0.25X dilution). No signs were apparent through the time of scheduled sacrifice. Body weights appeared to be somewhat depressed after one day, but showed relatively consistent increases thereafter. They were only slightly less than control values. Lung weight figures (absolute and relative) did not differ substantially from those of saline controls. There were very few gross lesions observed during necropsy and those were not considered significant. Upon microscopic evaluation of the lungs, there were instances of alveolar histiocytosis, interstitial pneumonitis and medial hyperplasia of the arteries. These were the only lesions that were more common in positive control rats than in negative controls.

Saline

Physiological saline is a 0.9X solution of sodium chloride (CAS No. 7647-14-5) in water (CAS No. 7731-18-5).

Previous studies at BRRC have demonstrated that rats survive endotracheal doses of 2.0 ml/kg of saline with no obvious effects.

In the second study, 15 male rats received 2.0 ml/kg of saline. All survived. Mean rat weights were somewhat inconsistent through 3 days, but steady increases were apparent at 7 to 14 days. Necropsy revealed a few instances of lung discoloration and one liver lesion. Microscopic evaluation of lung tissue showed the presence of hemorrhages, perivascular infiltrates, interstitial pneumonitis, interstitial fibrosis (one case) and medial hyperplasia of the arteries.

DISCUSSION

Evaluation of the results of the endotracheal study is facilitated by the tabulation of lethal dose, lung weight and histologic data. The following list presents these data by family in order of increasing molecular weight.

Summary of Doses, Lung Weight Effects and Histopathology from UCONO Endotracheal Study

Material Tested	Mol. Wt.	Water Solubility	Minimum Lethal Dose, ml/kg; 1st Study	Dosage Level, ml/kg; 2nd Study (Conc.)	Mean Lung Wt., % of Body Wt.	Incidence of Histologic Changes
LB-65	360	low	0.01	0.005 (0.25X)	1.406	low
LB-1145	2050	low	>2.0	2.0 (100X)	1.651	moderate
LB-3000	3000-4000	low	2.0	1.0 (50X)	1.442	moderate
50-HB-260	940	high	0.05	0.02 (1.0X)	1.370	low
50-HB-660	1700	high	0.2	0.1 (5.0X)	1.503	moderate
50-HB-2000	2600	high	-0.05	0.02 (1.0X)	1.951	high
50-HB-5100	4000	high	-0.05	0.02 (1.0X)	1.952	high
24-L-60N	510	high	0.01	0.005 (0.25X)	1.413	moderate
Saline	-	-	(>2.0)	2.0 (100X)	1.408	low

In the first study, the test and control materials were evaluated for lethality. The most toxic UCONO Lubricants were LB-65, 50-HB-260, 50-HB-2000 and 50-HB-5100. The first 2 of these have relatively low molecular weights (< 1000) with low or high water solubility. Lubricants 50-HB-2000 and 50-HB-5100 have much higher molecular weights, but are very soluble in water. TERCITOL 24-L-60N, the positive control material, was also highly toxic. It is a highly water soluble material with a low molecular weight. Moderate toxicity resulted from a single endotracheal dose of 50-HB-660. This material has a moderately high molecular weight and is highly soluble in water. The least toxic lubricants were those with high (> 2000) molecular weight and low water solubility. These were LB-3000 and LB-1145.

In the second study, most groups of animals exhibited an initial weight depression, persisting for one or 2 days, followed by relatively steady weight increase. Notable exceptions included those materials that produced death of rats before their scheduled sacrifice: UCONO Lubricants 50-HB-2000 and 50-HB-5100. Mean body weights for these groups remained well below beginning

weights throughout the observation period. Two other lubricants, LB-1145 and 50-HB-660, appeared to depress body weights slightly (compared to saline control animals), although fairly steady weight gains were noted. Other test materials and the positive control produced minimal, if any, weight effects.

There were no signs of toxicity observed for most of the materials tested. Exceptions were 2 lubricants that caused substantial signs and their death in the second study (50-HB-2000 and 50-HB-5100) and a third (LB-1145) which caused moderate, but reversible, signs. Death from the first 2 materials occurred after 3 to 7 days.

Lung weights appeared to be most severely increased by 50-HB-2000 and 50-HB-5100. Lungs were moderately heavy, compared to saline controls, following doses with 50-HB-660 and LB-1145. Other groups of animals had mean lung weights that were similar to those of controls.

While the lungs of several test animals exhibited gross color changes, similar changes were also evident in negative controls. Otherwise, few test materials produced remarkable gross changes. There were scattered instances of emphysema, consolidation tracheal infiltrates and edemations observed among rats treated with 50-HB-2000, 50-HB-5100 or 50-HB-660.

Microscopically, there were numerous lesions apparent among animals receiving the test substances, as well as those receiving only saline. Analysis here is limited to only those instances in which the incidence of histologic change was higher than those apparent in negative controls. The most severe effects were seen from 50-HB-2000 and 50-HB-5100, the materials that caused death during the second study. Especially evident were congestion, edema, alveolar histiocytosis, hemorrhage and emphysema. Other lesions found in these 2 groups and, to a moderate degree in 50-HB-660, LB-3000, LB-1145 or TERGITOL® 24-L-60N, included perivascular infiltrates and interstitial pneumonitis. Relatively few lesions developed after treatment with LB-65 or 50-HB-260, except for medial hyperplasia of the pulmonary arteries (seen in all test groups). Overall, UCON® Lubricants producing the most lung damage were, in general, those with high water solubility.

CONCLUSIONS

Following single endotracheal injection to rats, the most toxic materials, based on lethality, were UCON® Lubricants LB-65, 50-HB-260, 50-HB-2000 and 50-HB-5100. Toxicity was similar to that from the positive control, TERGITOL® 24-L-60N. The LB-65 and 50-HB-260 produced only minimal (if any) gross and microscopic lung changes, probably a reflection of the low doses administered. Conversely, 50-HB-2000 and 50-HB-5100 caused substantial effects on body weight, lung weight and lung pathology (gross and microscopic). These effects were worse than those seen from 24-L-60N and occurred from near lethal (or lethal) doses.

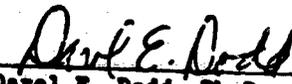
Moderate toxicity resulted from treatment with UCON® Lubricant 50-HB-660 both in terms of lethality and pulmonary lesions. Lower toxicity was apparent following endotracheal administration of LB-3000 and LB-1145. However, moderate microscopic lung lesions were apparent. The LB-1145 also produced

moderate signs of toxicity, weight depression and lung weight effects. Generally, overall toxicity of LB-3000 and LB-1145 was similar to that from the TERCITOL®[®], but occurred from much higher doses.

It is concluded that aspiration of certain of the UCON® Lubricants, even in small amounts, must be avoided. This appears to be especially important when handling lubricants of the 50-8B series (highly soluble in water) and those with low molecular weight.

Revised and Approved by:


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Study Director Date


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Acknowledgements:

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Table 1

Test and Control Materials

Material	Quantity	Source	Date Received	Identification	Description	BRC Sample No.
Saline	1 gal.	RIGCA Chem. Arlington, TX	March 28, 1988	Cat. #7210 Lot #H211	Transparent, colorless, low viscosity liquid	51-122
TERGITOL® 24-L-60N	1 gal.	UCC, S. Chas.	December 2, 1987	71-CMH-31-A	Milky-colored viscous liquid	50-534
UCOME Lubricant LB-65	100 ml	UCC, Tarrytown, NY	August 18, 1988	None	Transparent, colorless, slightly viscous liquid	51-355
UCOME Lubricant LB-1145	100 ml	UCC, Tarrytown, NY	August 18, 1988	None	Transparent, colorless, viscous liquid	51-356
UCOME Lubricant LB-3000	100 ml	UCC, Tarrytown, NY	August 18, 1988	None	Transparent, colorless, viscous liquid	51-357
UCOME Lubricant 50-HB-260	100 ml	UCC, Tarrytown, NY	August 18, 1988	None	Transparent, colorless, slightly viscous liquid	51-358
UCOME Lubricant 50-HB-660	100 ml	UCC, Tarrytown, NY	August 18, 1988	None	Transparent, colorless, slightly viscous liquid	51-359
UCOME Lubricant 50-HB-2000	100 ml	UCC, Tarrytown, NY	Sept. 2, 1988	None	Transparent, colorless, viscous liquid	51-377
UCOME Lubricant 50-HB-5100	100 ml	UCC, Tarrytown, NY	Sept. 2, 1988	None	Transparent, colorless, viscous liquid	51-378

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Table 2

Male Rat Mortality Data From Initial Endotracheal Injections

Material	Dosage	Concentration (in Saline)	Dead/Dosed
TERGITOL® 24-L-60R	0.02 ml/kg	1.0%	2/2
	0.01 ml/kg	0.5%	1/1
	0.005 ml/kg	0.25%	0/2
UCON® LB-65	2.0 ml/kg	100%	3/3
	0.5 ml/kg	25%	2/2
	0.02 ml/kg	1.0%	1/1
	0.01 ml/kg	0.5%	1/1
	0.005 ml/kg	0.25%	0/2
	0.002 ml/kg	0.1%	0/1
UCON® LB-1145	2.0 ml/kg	100%	0/2
UCON® LB-3000	2.0 ml/kg	100%	1/2
	1.0 ml/kg	50%	0/2
UCON® 50-HB-260	2.0 ml/kg	100%	2/2
	0.5 ml/kg	25%	2/2
	0.1 ml/kg	5.0%	3/3
	0.05 ml/kg	2.5%	2/2
	0.02 ml/kg	1.0%	0/2
	0.01 ml/kg	0.5%	0/2
	0.005 ml/kg	0.25%	0/2
UCON® 50-HB-660	2.0 ml/kg	100%	2/2
	0.5 ml/kg	25%	2/2
	0.2 ml/kg	10%	1/2
	0.1 ml/kg	5.0%	0/2
UCON® 50-HB-2006	0.2 ml/kg	10%	2/2
	0.1 ml/kg	5.0%	2/2*
	0.05 ml/kg	2.5%	2/2*
UCON® 50-HB-5100	0.5 ml/kg	25%	2/2*
	0.2 ml/kg	10%	2/2*
	0.1 ml/kg	5.0%	2/2*
	0.05 ml/kg	2.5%	1/2*

*Delayed times to death observed.

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Table 3
Summary of Weights and Signs of Toxicity for Male Rats Subjected to Endotracheal Injection

Material	Dosage ml/kg	Concen- tration (%)	Mean Wt. (G) ± S.D. (Number of Animals Weighed)							Signs of Toxicity
			0 Day	1 Day	2 Days	3 Days	7 Days	14 Days		
Saline	2.0	100%	265 ±	264 ±	279 ±	278 ±	295 ±	330 ±	None noted.	
			9.4 (15)	11.6 (3)	6.7 (3)	15.8 (3)	11.6 (6)	12.2 (3)		
YERGITOL 24-L-60N	0.005	0.25%	263 ±	260 ±	274 ±	269 ±	291 ±	313 ±	None noted.	
			5.7 (15)	5.2 (3)	5.7 (3)	6.7 (3)	14.7 (6)	28.4 (3)		
UCON LB-65	0.005	0.25%	258 ±	250 ±	266 ±	271 ±	294 ±	333 ±	None noted.	
			10.0 (15)	3.1 (3)	10.4 (3)	0.60 (3)	14.7 (6)	8.7 (3)		
UCON LB-1145	2.0	100%	256 ±	252 ±	263 ±	260 ±	284 ±	314 ±	Piloerection at 2 to 5 min; tremors at 2 to 7 min.	
			9.8 (15)	4.6 (3)	6.0 (3)	13.0 (3)	13.2 (6)	4.4 (3)		
UCON LB-3000	1.0	50%	258 ±	253 ±	256 ±	271 ±	292 ±	325 ±	None noted.	
			10.2 (15)	9.6 (3)	8.1 (3)	4.4 (3)	22.7 (6)	50.7 (3)		
UCON 50-HB-260	0.02	1.0%	262 ±	250 ±	273 ±	276 ±	300 ±	330 ±	None noted.	
			11.3 (15)	7.2 (3)	10.5 (3)	4.2 (3)	15.0 (6)	20.0 (3)		
UCON 50-HB-660	0.1	5.0%	256 ±	245 ±	258 ±	259 ±	275 ±	297 ±	None noted.	
			9.4 (15)	5.2 (3)	10.8 (3)	6.6 (3)	20.0 (6)	30.4 (3)		

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Table 3 (Continued)
Summary of Weights and Signs of Toxicity for Male Rats Subjected to Intratracheal Inhalation

Material	Dosage ^a ml/kg	Concen- tration (%)	Mean Wt. (G) ± S.D. (Number of Animals Weighed)					Signs of Toxicity
			0 Day	1 Day	2 Days	3 Days	7 Days	
UCOM9 50-NB-2000	0.02	1.0%	259 ±	251 ±	262 ±	235 ±	202 ±	Sluggishness, emaciation, labored breathing, piloerection, red crust on perianasal and periorcular fur at 3 to 5 days; lacrimation in 1 at 3 days. Death of 3 at 3 to 5 days.
			11.6 (15)	8.7 (3)	5.5 (3)	4.2 (2)	6.4 (2)	
UCOM9 50-NB-5100	0.02	1.0%	259 ±	256 ±	249 ±	225	204	Sluggishness, labored breathing, piloerection, emaciation, red crust on perianasal and periorcular fur at 3 to 5 days; red tearing in 1 at 4 days. Death of 7 at 3 to 5 days.
			9.9 (15)	8.1 (3)	10.1 (3)	(1)	(1)	

^aDosage expressed on the basis of contained sample, not as dilution in saline.

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