ACUTE INHALATION TOXICITY STUDIES ON FOUR [redacted] MIXTURES

[redacted]

Haskell Laboratory Report No. 115-76

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INTRODUCTION

The toxicity data available on [redacted] is limited. Because of potential exposure situations to these materials at Parkersburg and Chambers Works, the subsequent acute inhalation studies were initiated at Haskell Laboratory. These studies were aimed at providing a preliminary data base for evaluating the potential hazard of the [redacted]

Materials Tested		Haskell Nos.	Samples Ready for Testing	Submitted by
I. [redacted]	Low Boilers	I. 9544	11/24/76	[redacted] Organic Chemicals Department, Jackson Laboratory
II. [redacted]	Composite	II. 9542		
III. [redacted]	Crude	III. 9545		
IV. [redacted]	Composite	IV. 9543		

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[redacted]

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I. [redacted] Low Boilers

A. Generation Procedure

The test material was fed through a micrometer valve, from an inverted gas cylinder, to provide a constant drip rate into an isothermal flask heated to 60°C. Instantaneous evaporation occurred and the resultant vapors were swept into a 20-liter battery jar, containing the test animals, by a 5 liter/minute house air stream. Three exposures, each of four hours in duration, were conducted at various concentration levels. Each exposure utilized 10 male ChR-CD rats ranging in initial body weight from 240 to 300 grams.

B. Analytical Procedure

A Hewlett Packard 5710A gas chromatograph, equipped with a flame ionization detector, was used for sample analysis. A ten foot by one-eighth inch stainless steel column, packed with 10% SE-30 on Chromasorb® W, was used at 70°C. Analysis was performed on the largest peak (n = 1) in the chromatogram. Comparison was made by monitoring the n = 1 component in standards and converting to the total low boiler concentration. One milliliter gaseous injections were employed in the analyses.

C. Results

The data for the three exposures is presented below:

TWA Concentration (mg/liter of low boilers)	Fractional Mortality (# deaths/ten animals)	Clinical Signs
25	0/10	Hyperemia, labored respiration
72	0/10	Hyperemia, labored respiration
140	0/10	Hyperemia, labored respiration

Practically no weight loss was observed in any test animal and all animals gained weight at a regular rate during the 14-day post-exposure recovery period.

D. Summary

The approximate lethal concentration (ALC) for the [redacted] Low Boiler Mixture (H#9544) is > 140 mg/liter for rats exposed for four hours. This value suggests that H#9544 is "practically non-toxic" on an acute inhalation basis.

II. [redacted] Composite

A. Generation Procedure

Chamber atmospheres were generated by two different techniques. One method was to syringe drive the mixture through a one-quarter inch Teflon® tube submerged in a heated mineral oil bath. The resulting vapors were swept into a 20-liter battery jar by a 5 liter/minute house air stream. The chamber air composition achieved in this manner was similar to the weight percent composition in the sample solution. This might simulate an exposure at high process temperatures.

A second generation technique employed was to force house air through a fritted disc immersed in the telomer solution (heated to 40°C). The resulting air mixture achieved using the method is similar to the equilibrium vapor composition expected in normal storage situations. No dilution air was added in this case.

Employing both generation techniques, five four-hour exposures, each using 10 male ChR-CD rats, were conducted. Rats tested ranged in initial body weight from 240 to 270 grams.

B. Analytical Method

A Varian 600B gas chromatograph, equipped with a flame ionization detector, was used for sample analysis. A six-foot by one-eighth inch stainless steel column, packed with 10% FFAP on Chromasorb® W, was employed. Samples were trapped in ethanol using midget impingers. Since chamber air composition varies with the generation technique, all concentrations are reported on the basis of the n = 3 component concentration (See Appendix A).

C. Results and Discussion

With syringe drive generation, the n = 3 component levels remained relatively stable throughout the exposure, whereas, the "high-boiling" components of the sample precipitated out as a dust of varying concentration and particle size distribution. This factor probably contributed heavily to the non-linearity in the dose-response data in the accompanying table.

Using the bubbler generation technique, all of the extremely low boiling components of the sample appeared during the first 30 to 60 minutes of exposure and then disappeared (as evidenced by gas chromatographic monitoring). Stable levels of low boilers are not achieved by this generation technique.

The following table tabulates the results achieved using both generation techniques.

	Analytical TWA Concentration (mg/liter of n=3 component)	Fractional Mortality (# deaths/ ten animals)	Clinical Symptoms and Comments
Syringe drive generation	2.8	0/10	None
	37.5	3/10	Salivation and labored respiration. Cloud of white dust filled chamber and covered walls. All deaths occurred during exposure.
	17.3		
Bubbler generation	95	0/10	Yellow discoloration of rat fur correlated with low boiler appearance in gas chromatograms (in first 30 to 60 minutes). Labored respiration, salivation, hyperemia and red nasal discharge were also observed.
	122		

D. Summary

In four-hour exposures, [redacted] Composite (H#9542) was administered to rats using two different generation techniques. With syringe drive, where high boilers precipitated out in the lines and chamber as a dust, the ALC for H#9542 is about 17 mg/liter (n = 3 concentration). Under such conditions, this ALC value suggests that the [redacted] Composite is "slightly toxic" on an acute inhalation basis.

Using the bubbler generation method, where the very low boilers come off early in the exposure, the [redacted] Composite appears to be "practically non-toxic" to rats exposed for four hours as indicated by an ALC > 122 mg/liter (n = 3 concentration).

III. [redacted] Crude

A. Generation Procedure

The test material was syringe driven through a Teflon® tube immersed in a 160°C oil bath. The vaporized [redacted] then entered a 10 liter/min. house air stream and was delivered to a 20-liter battery jar containing ten male ChR-CD rats ranging in initial body weight from 240 to 300 grams. Three exposures were run at different concentration levels.

B. Analytical Procedure

A Varian 600B gas chromatograph, equipped with a flame ionization detector, was employed for sample analysis. A three-foot by one-eighth inch stainless steel column packed with 10% SE-30 on Chromasorb® W was used at room temperature. One milliliter gas samples were directly injected into the column.

C. Results

The data from these exposures is presented in the following table:

Analytical TWA Concentration (mg/liter BL Olefin)	Fractional Mortality (# deaths/ten animals)	Clinical Signs
45.8	0/10	None
204	0/10	None
433	0/10	None

D. Summary

The ALC for [redacted] Crude (H#9545) is greater than 433 mg/liter for rats exposed for four hours. Under our test conditions, this material is considered to be "relatively harmless" on an acute inhalation basis.

IV. [redacted] Composite

A. Generation Procedure

In light of the problems experienced with syringe driving such mixtures (reference the [redacted] Composite discussion), the bubbler method of generation was employed in this test. Chamber concentrations were varied by adjusting the ratio of air bubbled through the telomer solution to the amount of dilution air or by altering the telomer solution temperature. This method of generation more closely approximates the equilibrium vapor composition one would expect over a liquid.

B. Analytical Procedure

The procedure employed was identical to that used for [redacted] Composite. The only variation was that the column oven was programmed from 50-80°C at 4°C/min.

C. Results and Discussion

Similar to the [redacted] Composite bubbler exposures, high concentrations of low boiling components were observed immediately upon start up of exposure and gradually disappeared over the first hour of exposure (See Figure 1). Test results are presented in the table below:

Exposure	Analytical TWA Concentration (mg/liter of n = 3 component)	[redacted] Sol'n. Temp. (°C)	Fractional Mortality (# deaths/10 rats)	Clinical Signs
1	2.0	50-70	0/10	†
2	6.8	50-70	0/10	†
3	7.7	50-70	2/10	†
4	4.8	130-140	0/10	*
5	6.0	130-140	2/10	*
6	7.6	130-140	0/10	*
7	8.7	130-140	2/10	*
8	(12.5)	130-140	(8/10)	*
8a	(12.5)	130-140	(0/10)	None

All mortalities occurred during exposure and within the time period that the low boilers were present in highest concentrations. For illustration, during exposure #8 at 12.5 mg/liter, eight of ten rats died during the first 45 minutes of exposure. The two remaining rats, removed from the chamber at 45 minutes, started recovering from effects immediately and suffered only mild weight loss. Ten new rats, placed in the chamber (Exposure # 8a) at 45 minutes, were used to complete the remainder of the four-hour exposure. No adverse clinical signs were noted in the new rats, suggesting that the early deaths of the other rats were due to the presence of the low boilers.

The effect of solution temperature on exposed rats appeared to be minimal. At similar concentrations, comparable fractional mortalities were obtained at both temperature ranges - 50-70°C and 130-140°C.

D. Summary

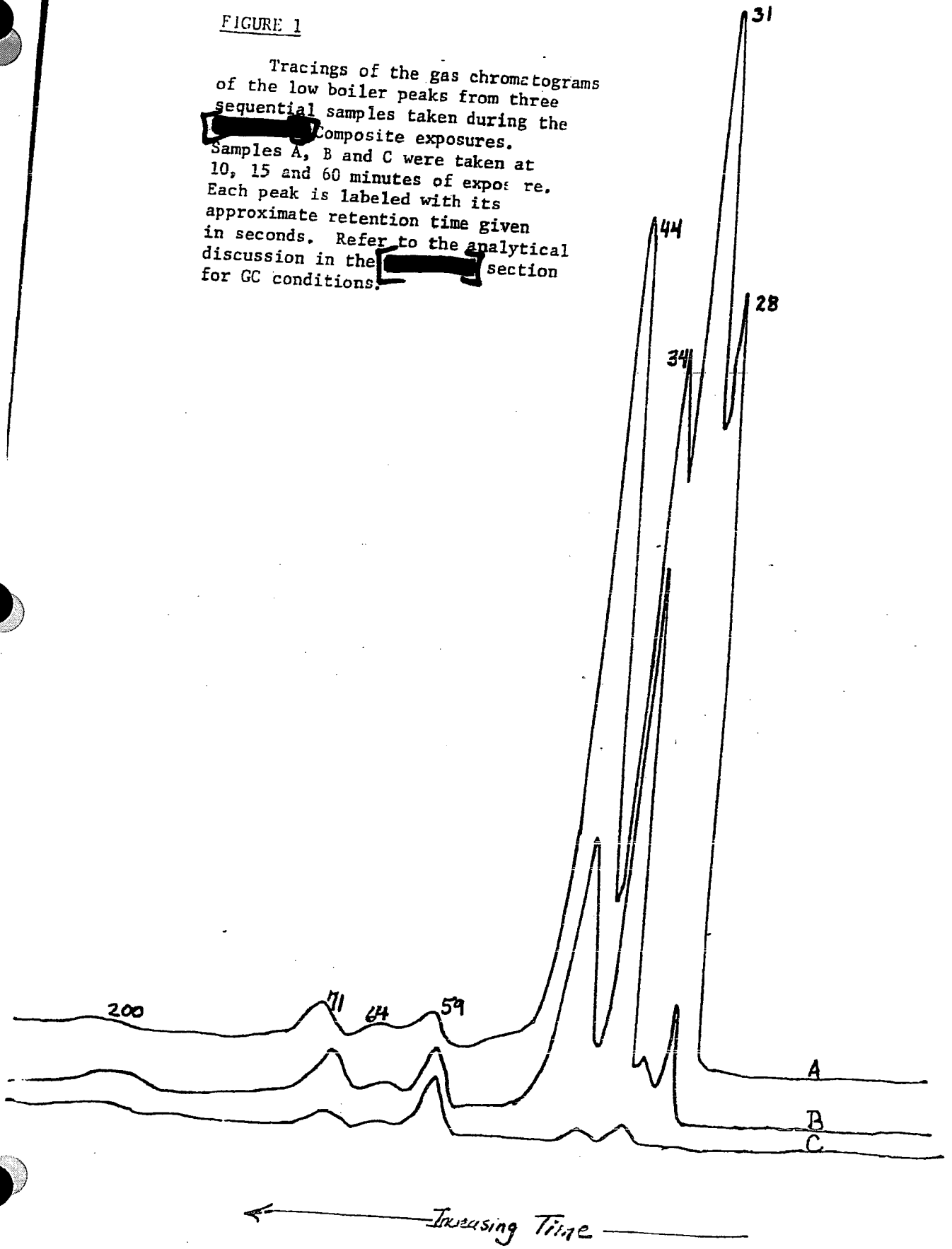
Under these experimental conditions, [redacted] Composite (H#9543) has a four-hour ALC of about 6.0 mg/liter (n = 3 component concentration). This value is considered "moderately toxic" on an acute inhalation basis.

† Mild to moderate salivation, early signs of labored respiration, hyperemia, and red discharge around the nose and eyes.

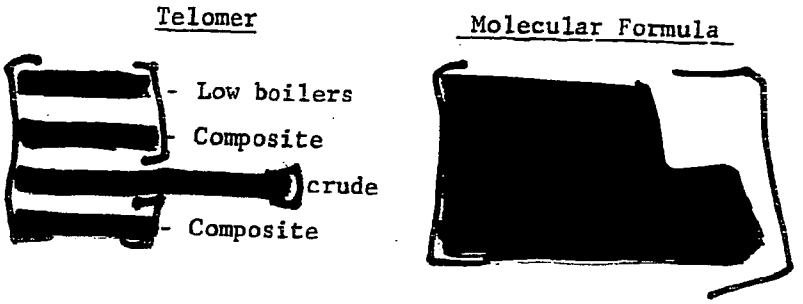
* Profuse salivation, lacrimation (and later, red discharge from the eyes), red nasal discharge, convulsions, and light to moderate yellow fur discoloration.

FIGURE 1

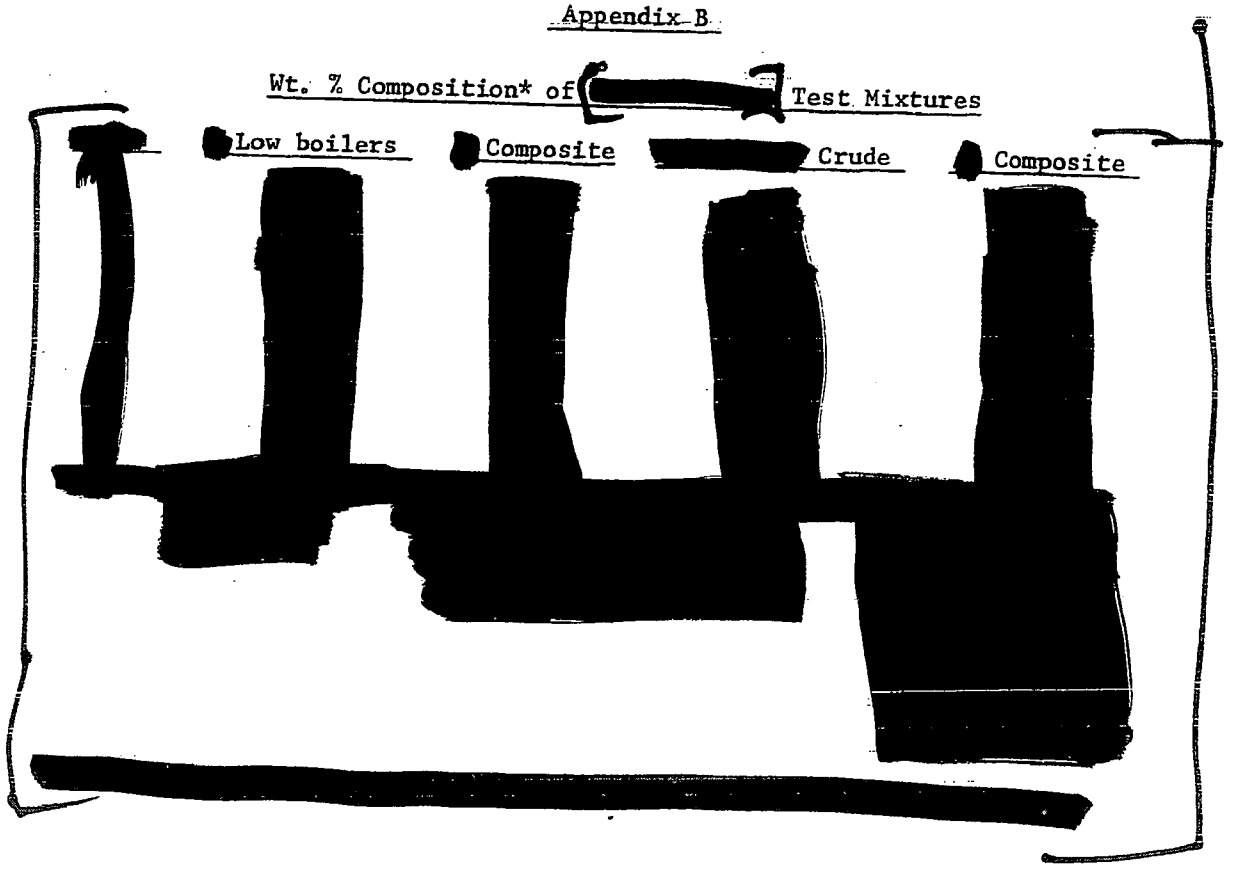
Tracings of the gas chromatograms of the low boiler peaks from three sequential samples taken during the [redacted] Composite exposures. Samples A, B and C were taken at 10, 15 and 60 minutes of exposure. Each peak is labeled with its approximate retention time given in seconds. Refer to the analytical discussion in the [redacted] section for GC conditions.



Appendix A



Appendix B



* Reported by [redacted] Organic Chemicals Department

** See Appendix A.