

30277-101

REPORT DOCUMENTATION PAGE		1. REPORT NO. HSM-99-73-55	2. NA	PB82230236 	
4. Title and Subtitle Bioassay of Coke Oven Coal Tar Carcinogenic Activity, Final Report					
7. Author(s) Bingham, E.			6. NA		
3. Performing Organization Name and Address Information Not Given			8. Performing Organization Rept. No. NA		
12. Sponsoring Organization Name and Address NIOSH Cincinnati, Ohio			10. Project/Task/Work Unit No. NA		
			11. Contract(G) or Grant(G) No. (C) 99-73-55 (G)		
			13. Type of Report & Period Covered Contract Report		
15. Supplementary Notes NA			14. NA		

16. Abstract (Limit 200 words)

The carcinogenicity of coke oven coal tar was investigated. C3H-mice were treated dermally twice a week with 50 milligrams of various benzo(a)pyrene (50328) (BaP) solutions in toluene, whole coal tar containing different amounts of BaP, the light oil coal tar fraction, or coal tar with the light oil removed. The mice were examined periodically for tumors and skin lesions, and were killed for autopsy when carcinoma was diagnosed. The carcinogenicity of whole coal tar with 0.6 percent BaP and the light oil fraction removed was greater than that of a 0.6 percent BaP solution in toluene. The potency of the BaP solution accounted for 71 percent of the carcinogenic activity of the tar in the absence of the light oil fraction and for 77 percent of the activity when the light oil fraction was present. Dilution of BaP solutions with toluene reduced the potency of the compound more than similar dilution of coal tar solutions. Threshold BaP doses for animals given BaP in toluene and those given coal tar were 0.0006 and 0.00006 milligram, respectively. The authors suggest that coal tar contains additional carcinogens whose potency is masked in the presence of high BaP concentrations or that act as carcinogens.

7. Document Analysis a. Descriptors

Laboratory=animals, Hydrocarbons, Polynuclear-compounds, Carcinogenic-potency, Carcinogenesis, Toxicology

b. Identifiers/Open-Coded Terms

REPRODUCED BY:
U.S. Department of Commerce
National Technical Information Service
Springfield, Virginia 22161

c. COSATI Field/Group

L Availability Statement

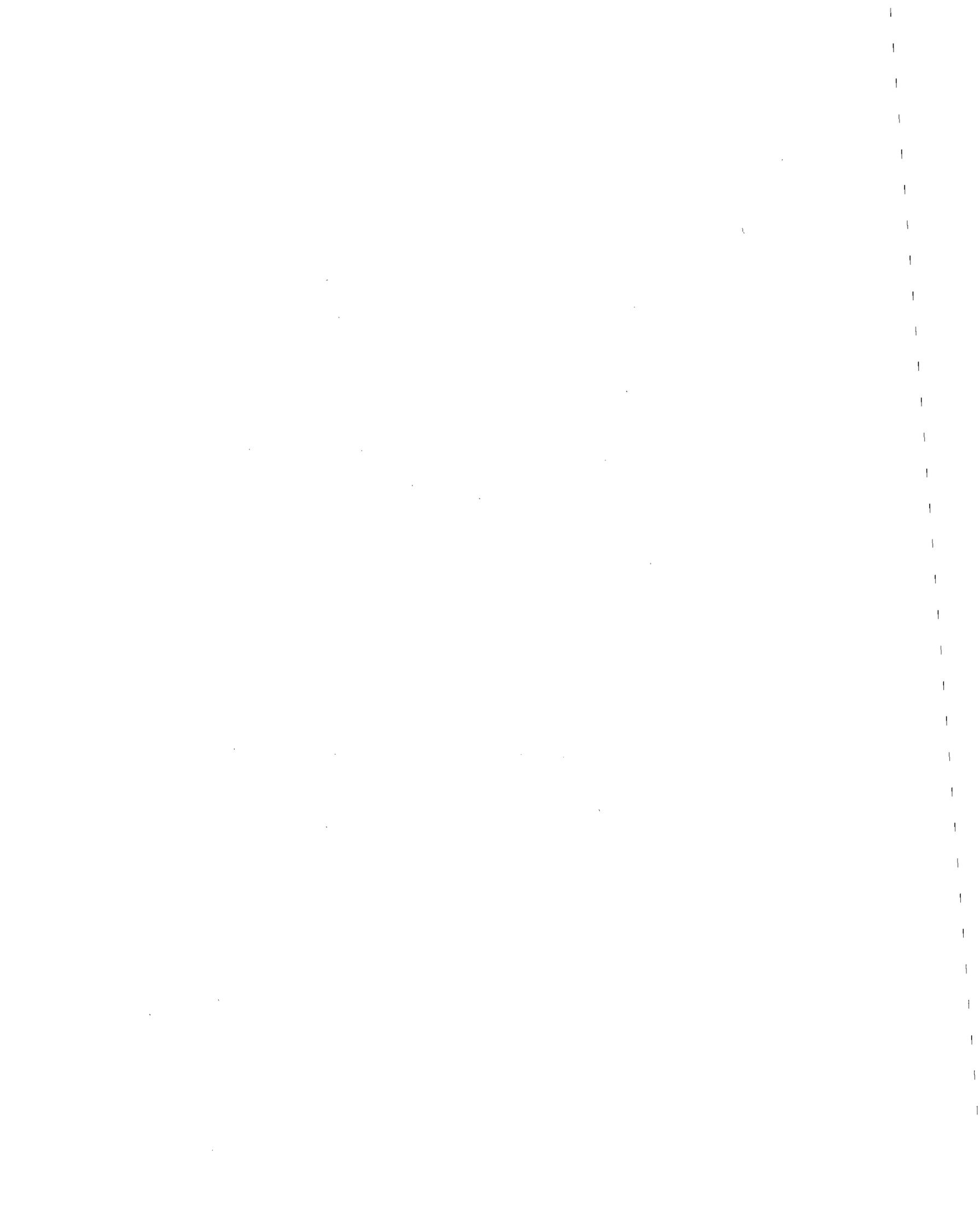
Available to Public

19. Security Class (This Report)
NA

21. No. of Pages

20. Security Class (This Page)

22. Price



Final Report

Bioassay of Coke Oven Coal Tar Carcinogenic Activity - HSM 99-73-55

Eula Bingham, Ph.D. - Principal Investigator

The purpose of this contract is two-fold:

1. To determine the carcinogenic potential of a representative coke oven coal tar by topical application to the skin of mice.
2. To define the threshold of carcinogenic activity in the mouse skin test for the known carcinogen benzo(a)pyrene and the complex organic mixture containing benzo(a)pyrene, coal tar. Should this threshold be the same for both, it would constitute substantial evidence that benzo(a)pyrene may be used as an index for carcinogenic activity in the coal tar sample. The data generated from this study could be used as criteria for recommendation of an industrial air standard.

Method

Mice (C3H males) were acclimatized for two weeks prior to beginning the experiment. They were toe numbered, assigned to one of the test groups using a randomization procedure, and housed in groups of five to a stainless steel cage. Food and water were provided ad libitum.

The solutions were applied, with either a microliter pipette or a previously calibrated glass dropper, twice weekly to the intrascapular region of the backs. Hair was removed from the backs of the mice using electric clippers prior to application of the solution and periodically as regrowth occurred. The mice were observed for the appearance of tumors and other skin lesions which were recorded weekly. When a papillomatous lesion 1mm^3 was seen the mouse was kept under observation. When the papilloma progressed and it was diagnosed grossly as a

carcinoma, the mouse was sacrificed and autopsied. Selected histopathologic examination of tumors were made to confirm the gross diagnosis of tumors.

Results

As can be seen from the tables and graphs, the carcinogenic potency of whole coal tar, containing 0.6% benzo(a)pyrene (B(a)P) and with the light oil fraction removed, was greater than a standard solution of 0.6% B(a)P in toluene. (To determine the carcinogenic potency of a solution we followed the method of Horton, Trosset, and Denman. They developed a graphic technique of converting carcinogenic activity of various types of solutions into a value called P_{MC} that enabled one to compare relative carcinogenic activities of a solution.) The potency of the B(a)P solution accounts for 71% of the potency of the tar. When the light oil fraction is recombined with the coal tar the potency of the B(a)P solution is approximately 77% of the tar figure.

Dilution of the coal tar (with light oils removed) and a standard solution of B(a)P with toluene, reduces the potency of the B(a)P solution more than the coal tar solution. This may suggest that there are, in the coal tar, additional carcinogens whose potency is masked when such high levels of B(a)P are present in whole tar; or it may indicate the presence of cocarcinogens. Either may be the case.

The data also suggest that there may be a threshold value for B(a)P and coal tar. No tumors developed in mice receiving a weekly dose of 0.0006 mg B(a)P in toluene. The dose that produced no tumors in the coal tar animals was equivalent to 0.00006 mg.

Eula Bingham, Ph.D., Principal Investigator
William Barkley, B.S., Sr. Research Associate
Jane Agee, B.S., Jr. Research Associate

Material	Dosage	Final Results		Final Effective Number	Percentage of Mice Developing Tumors	Mice with		Average Time of Appearance of Tumors (weeks)	P _{me}
		Duration of Experiment	Number of Mice Started in Experiment			Malignant	Benign		
1% B(a)P in toluene	50 mg 2/wk	61 weeks	30	30	100.0%	30	0	23.2 ± 0.860 _{SE} Conf. Lim. 95% 1.758 21.442-24.958	0.15
1% Coal Tar in toluene approx. 0.6% B(a)P	50 mg 2/wk	32	30	30	100.0%	28	2	17.7 ± 0.586 _{SE} Conf. Lim. 95% 1.197 16.503 - 18.897	0.21
1% Light Oil + 0.6% B(a)P 20:80	50 mg 2/wk	44	50	50	100.0%	50	0	24.6 ± 0.517 _{SE} Conf. Lim. 95% 1.055 23.565-25.675	0.13
1% Light Oil + Coal Tar approx. 0.6% B(a)P 20:80	50 mg 2/wk	37	50	48	100.0%	46	2	20.6 ± 0.422 _{SE} Conf. Lim. 95% 0.861 19.764-21.486	0.17
0.06% B(a)P in toluene	50 mg 2/wk	83	70	61	96.7%	41	18	44.2 ± 0.877 _{SE} Conf. Lim. 95% 1.791 42.429-46.011	0.05
0.06% Coal Tar in Toluene approx. 0.06% B(a)P	50 mg 2/wk	37	70	70	100.0%	68	2	22.9 ± 0.310 _{SE} Conf. Lim. 95% 0.633 22.310-23.576	0.15
0.006% B(a)P in toluene	50 mg 2/wk	92	100	83	8.4%	4	3	55.6 ± 4.466 _{SE} Conf. Lim. 95% 10.928 44.643-66.500	0.02

* Supported by NIOSH Contract # HSM-99-73-55
and ES-00159 Center for Study of the Human Environment

Material	Dosage	Duration of Experiment	Number of Mice Started in Experiment	Final Effective Number	Percentage of Mice Developing Tumors	Mice with		Average Time of Appearance of Tumors (weeks)	P _{MC}
						Malignant	Benign		
al Tar in Toluene prox. 0.006%	<u>50 mg</u> 2/wk	87 (weeks)	100	97	95.9%	77	16	47.3+1.060 ^{SE} Conf. Lim. 95% 2.164	0.04
								45.126-49.455	
0006% B(a)P in luene	<u>50 mg</u> 2/wk	92	100	66	0.0%	0	0	0.0 + 0.000 Conf. Lim. 95% 0.000	---
al Tar in Toluene prox. 0.0006% B(a)P	<u>50 mg</u> 2/wk	93	100	76	51.3%	20	19	72.9+1.219 Conf. Lim. 95% 2.490	0.002
								70.434-75.413	
00006% B(a)P in luene	<u>50 mg</u> 2/wk	88	100	60	0.0%	0	0	0.0 + 0.000 Conf. Lim. 95% 0.000	---
al Tar in Toluene prox. 0.00006% a)P	<u>50 mg</u> 2/wk	92	100	56	0.0%	0	0	0.0 + 0.000 Conf. Lim. 95% 0.000	---
ght Oil	<u>50 mg</u> 2/wk	91	100	60	0.0%	0	0	0.0 + 0.000 Conf. Lim. 95% 0.000	---

*Supported by NIOSH contract # HSM-99-73-55
and ES-00159 Center for Study of the Human Environment

Comparison of Potencies*
of Various Carcinogenic Solutions

	P_{MC}	Per Cent Activity Assigned to B(a)P
0.6% B(a)P in Toluene diluted with Light Oil (80:20)	0.13	76.5
Coal Tar (0.6% B(a)P) diluted with Light Oil (80:20)	0.17	
0.6% B(a)P in Toluene	0.15	71.4
Coal Tar (0.6% B(a)P)	0.21	
0.06% B(a)P in Toluene (diluent-Toluene)	0.05	33.0
Coal Tar (0.06% B(a)P (diluent-Toluene)	0.15	

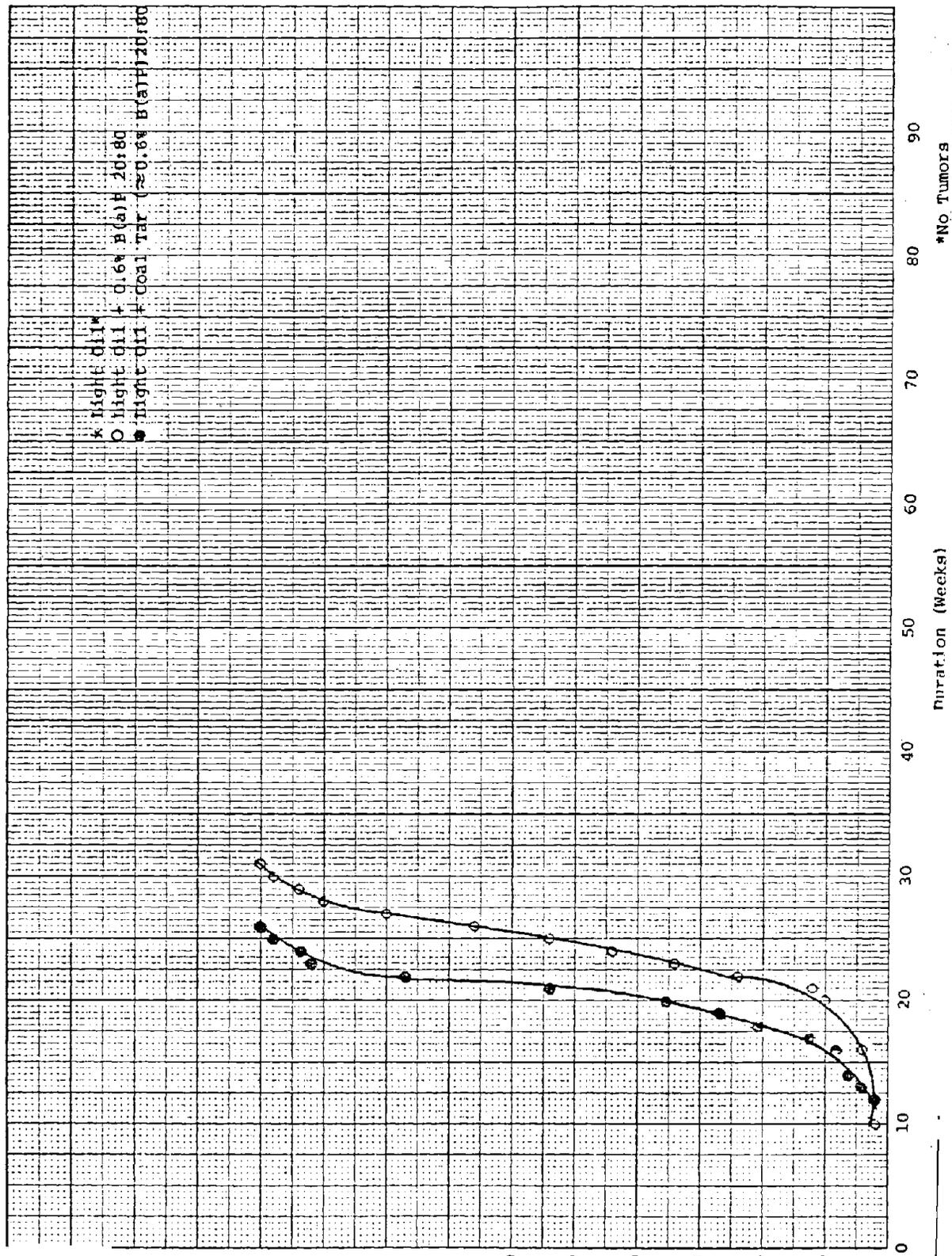
*Potency is presented as P_{MC} according to method of A.W. Horton, D. T. Denman, R. P. Trosset. "Carcinogenesis of the Skin. II The Accelerating of Aliphatic and Related Hydrocarbons". Cancer Research, Vol. 17:758-766, 1957.

A Comparison of the Tumor Incidence in Mouse Skin Bioassays of Coal Tar Samples
and Equivalent B(a)P Doses in Toluene

<u>Solution</u>	<u>Dose of BaP Per Week, Mg</u>	<u>Duration of Experiment*</u>	<u>Total Dose Mg</u>	<u>Number of Mice</u>	<u>% of Mice Bearing Tumors</u>
Coal Tar	0.6 = 100 mg Tar	23	2300 mg	30	100
0.6% B(a)P	0.6	29	17.4 mg	30	100
Coal Tar Diluted with Toluene	0.06 = 10 mg Tar	29	290 mg	70	100
0.06% B(a)P	0.06	65	3.9 mg	70	96.7
Coal Tar Diluted with Toluene	0.006 = 1 mg Tar	80	80 mg	100	95.9
0.006% B(a)P	0.006	80	0.48 mg	100	8.4
Coal Tar Diluted with Toluene	0.0006 = 0.1 mg Tar	80	8 mg	100	51.3
0.0006% B(a)P	0.0006	80	0.048 mg	100	0
Coal Tar Diluted with Toluene	0.00006 = 0.01 mg Tar	80	0.8 mg	100	0
0.00006% B(a)P	0.00006	80	0.0048	100	0
Light Oil	-	80	-	50	0
Light Oil + Coal Tar (20:80)	0.48 = 80 mg Tar	26	2080	50	100
Light Oil + 0.6% B(a)P (20:80)	0.48	31	14.9	50	100

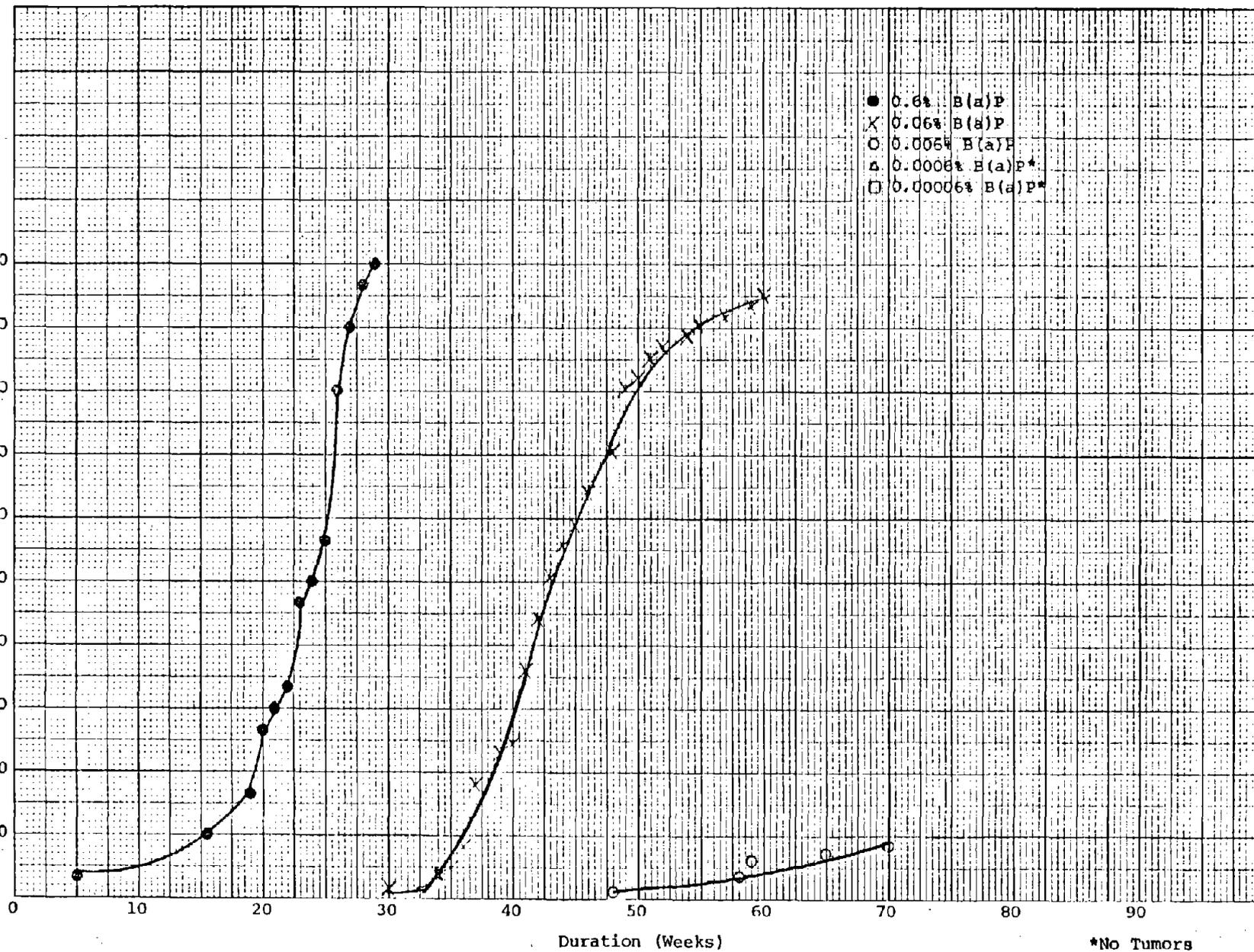
*Treatment stopped when all mice developed tumors or at 80 weeks.

Tumor Incidence from Topical Application of Light Oil



*No Tumors

Tumor Incidence from Topical Application of B(a)P



8

Tumor Incidence from Topical Application of Coal Tar

