FILE NAME: Oil Industry and American Petroleum Institute (API)

DATE: 1953 June-Dec

DOC#: API031

DOCUMENT DESCRIPTION: Letters, Memos, Reports, Financial Reports & Other Relevant Documents from June-Dec, 1953

June 8th, 1953

Dr. Robert A. Kehoe
University of Cincinnati
The Kettering Laboratory
College of Medicine
Cincinnati 19, Ohio

Dear Boosten Kehoe:

Pursuant to the action taken at the Medical Advisory Committee meeting on September 25, 1952, we are enclosing the Institute's check in the amount of $5,000 payable to the University of Cincinnati as our contribution towards the skin physiology project for the twelve-month period ending June 30, 1954.

Very truly yours,

DVBiln
Enclosure
cc: Dr. T. H. Frank
Mr. Lacey Walker

MEMO TO MR. WALKER:

This expenditure is to be charged against the Medical Research Fund.

API 05616

June 5th, 1953

Dr. Robert A. Kehoe
University of Cincinnati
The Kettering Laboratory
College of Medicine
Cincinnati 19, Ohio

Dear Doctor Kehoe:

Pursuant to the understanding reached by our letters of October 28 and November 5, 1947, we are enclosing the Institute's check in the amount of $8,500 payable to the University of Cincinnati as our contribution towards the development of information on fluorine and fluorine compounds for the twelve-month period ending June 30, 1954.

Very truly yours,

DVS:hm
Enclosure
cc: Dr. F. H. Frank
Mr. Leroy Walker

MEMO TO MR. WALKER:

This expenditure is to be charged against the Medical Research Fund.

API 05617

June 24, 1953

Dr. Robert A. Kehoe
University of Cincinnati
The Kettering Laboratory
College of Medicine - Eden Avenue
Cincinnati 19, Ohio

Dear Doctor Kehoe:

Enclosed you will find four copies of the continuation agreement covering API Medical Research Project M-2 for the fiscal year ending June 30, 1954. These have been signed on behalf of the Institute.

Upon the return of two executed copies we shall send the initial payment of $40,000.

Very truly yours,

DVS:km
Enclosures (4)

API 05618

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

KETTERING LABORATORY
LLEGE OF MEDICINE—SOEN AVENUE
CINNATI 19, OHIO

CABLE ADDRESS KETLAB, CINCINNATI
TELEPHONE: CAPITOL 1414

Mrs Shamo
Please file

June 26, 1953

Mr. D. V. Stroop, Director
Department of Technical Services
American Petroleum Institute
50 West 50th Street
New York City 20

Dear Mr. Stroop:

I herewith acknowledge with thanks receipt of the following checks, covering expenditures for the year, beginning June 30, 1953:

Investigation of skin physiology	$ 5,000.00
Investigation of fluorine compounds	2,500.00

Very truly yours,

E. R. Fortlage

E. R. Fortlage, Secretary to
Dr. Kehoe

ef

API 05619

AMERICAN PETROLEUM INSTITUTE
50 WEST 50TH STREET
NEW YORK 20, N. Y.

June 30, 1953

Board of Directors
University of Cincinnati
Cincinnati 19, Ohio

Gentlemen:

This communication is authority to continue work on investigation of the toxicity and mode of action of certain petroleum products for the year ending June 30, 1954, according to the terms of the agreement dated January 8, 1946, and on the basis of a maximum budget for operating expenses of $78,283.

Upon receipt of your approval of the continuation of the project with this maximum budget we shall pay you the sum of $40,000. The balance of $38,283, less the unexpended balance in the fund on June 30, 1953, will be paid on January 1, 1954.

It is understood that any balance in the fund on June 30, 1954 will be returned to the American Petroleum Institute, and that no excess over the amount of the budget is to be obligated or spent without written authorization.

Very truly yours,

AMERICAN PETROLEUM INSTITUTE

By Frank C. Porter
President

By
Secretary

Accepted and Approved:

UNIVERSITY OF CINCINNATI
Through its Board of Directors

By_____

By_____

API 05620

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

THE KETTERING LABORATORY
COLLEGE OF MEDICINE—EDEN AVENUE
CINCINNATI 19, OHIO

CABLE ADDRESS KETLAB, CINCINNATI
TELEPHONE. CAPITOL 1414

July 9, 1953

Mr. D. V. Stroop, Director
Department of Technical Services
American Petroleum Institute
50 West 50th Street
New York City 20

Dear Mr. Stroop:

I herewith acknowledge with thanks receipt of American Petroleum Institute's check in the amount of $40,000.00, covering expenditures to be made on their behalf.

Very truly yours,

E. R. Fortlage

E. R. Fortlage, Secretary to
Dr. Kehoe

ef

API 05621

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

THE KETTERING LABORATORY
COLLEGE OF MEDICINE—EDEN AVENUE
CINCINNATI 19, OHIO

CABLE ADDRESS: KETLAB, CINCINNATI
TELEPHONE: CAPITOL 1414

August 26, 1953

Mr. D. V. Stroop, Director
Department of Technical Services
American Petroleum Institute
50 West 50th Street
New York City 20

Dear Mr. Stroop:

I hasten to correct an error made in my letter of August 25. The amount of American Petroleum Institute's check of July, 1953 should have read $40,000.00.

Very truly yours,

E. R. Fortlage

E. R. Fortlage, Secretary to
Dr. Kehoe

ef

August 27, 1953

Miss E. R. Furlaga
The Kettering Laboratory
College of Medicine
Eden Avenue
Cincinnati 19, Ohio

Dear Miss Furlaga:

This will acknowledge receipt of your letter of August 25, 1953, and to correct the typographical error in the amount of the check which was ($0,000, instead of the ($10,000 stated in your letter.

Very truly yours,

EWH:jb
cc: With copies of Furlaga letter to
S. H. Prank, M.D.
G. H. Hamilton, M.D.
Marshall Clinton, M.D.
Kleiber Davis, M.D.
R. F. Dalgarno, M.D.

API 05623

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

THE KETTERING LABORATORY
COLLEGE OF MEDICINE—EDEN AVENUE
CINCINNATI 19, OHIO

August 25, 1953

CABLE ADDRESS: KETLAB, CINCINNATI
TELEPHONE: CAPITOL 1414

Mr. D. V. Stroop, Director
Department of Technical Services
American Petroleum Institute
50 West 50th Street
New York City 20

Dear Mr. Stroop:

I am sending you herewith, for your information, a statement of expenditures made on behalf of the American Petroleum Institute for the second quarter of 1953. (This statement does not include American Petroleum Institute's check in the amount of ~~$10,000.00,~~ received on July 9, 1953.) I believe that this statement will be self-explanatory, but if you have any questions or comments, Doctor Kehoe would appreciate your bringing them to his attention.

Very truly yours,

E. R. Fortlage

E. R. Fortlage, Secretary to
Dr. Kehoe

ef

Enc.

API 05624

UNIVERSITY OF CINCINNATI
KETTERING LABORATORY

ACCOUNT OF THE AMERICAN PETROLEUM INSTITUTE

FOR 2nd Quarter 1953

SALARIES (Based on Proportion of Time Actually Spent on Project)

Direct Salaries	10,645.48	
Indirect Salaries		
Histopathological Preparation	258.00	
Other Services	11,051.25	21,954.73

MISCELLANEOUS EXPENSE

Purchase of Animals	278.40	
Special Laboratory Supplies	346.20	
Travel	712.55	
Overhead (Proportion of Heat, Gas, Electricity, Steam, Telephone, General Laboratory Supplies, Postage, Annuities, Pensions, Maintenance, etc.	7,202.84	8,539.99
TOTAL		30,494.72

Balance Available for Further Work at End of	27,044.10	
Balance Due Kettering Laboratory at End of		
Receipts	. . . .	
Expenditures 2nd Quarter 1953	30,494.72	
Balance Available for Further Work at End of		
Balance Due Kettering Laboratory at End of 2nd Quarter	3,450.62	

Form 1230 KET LAB. 3M 8-52

API 05625

EXPLANATORY NOTES ON TABULAR SUMMARY OF BIOLOGICAL EXPERIMENTS

September 1, 1953

In a critical review of the individual data sheets on the experiments, each test has been classified according to the degree of confidence put by the investigators in the apparent potency of the material as indicated by the rate of induction of tumors. In the cases in which it was felt that the state of health of the animals, as measured by growth curves and survival rates, was not sufficiently good, the tabulated potency, P_{MC}, has been set down in parentheses.

Normally, any given sample of oil was applied to two or more groups of mice, each group containing 6 to 10 animals. If there were significant differences in the apparent state of health of the different groups, the "Average Latent Period for Tumor Induction" was calculated using the data on times of appearance of tumors from those groups in which the growth and rate of survival approached that of control animals. The figures associated with this procedure have been indicated in the columns on "Original Number of Mice" and "Final Effective Number of Mice" in the Tables, in that the total numbers of animals used initially and the corresponding effective numbers are indicated in parentheses, while the numbers used in the calculations are shown directly above.

The "Average Latent Periods" have been recalculated by a slightly modified method and are shown in the Table with the 5 percent fiducial limits, which signify that the statistical probability is only 1 in 20 that the true mean time of tumor induction lies beyond these limits. When there were indications,

from the growth or mortality data, that the experimental procedure was affecting the health of the animals to some extent but not so severely as to render the results ambiguous, the Average Latent Period was put in parentheses, but the value of the potency, P_{MC}, was not so qualified.

Summarizing, the experiments have been classified into three grades indicated in the Tables as follows:

GRADE	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION	RELATIVE CARCINOGENIC POTENCY, P_{MC}
A (normal growth and survival)	___	___
B (some symptoms of abnormal conditions, but reliable estimate of potency possible)	(___)	___
X (reliability of results uncertain)	(___)	(___)

For Information Only - Not for Publication

API Research Project MC-1

TABULAR SUMMARY

OF

CURRENT AND COMPLETED

BIOLOGICAL EXPERIMENTS

September 1, 1953

The Kettering Laboratory
in the
Department of Preventive Medicine and Industrial Health
College of Medicine
University of Cincinnati
Cincinnati, Ohio

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* Experiments which are complete, including micropathology, are indicated by an asterisk in the body of the tables.

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INDEX TO TABLE I

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760mm.)			
					<750° (%)	750-925° (%)	>925° (%)	E.P. (°F.)
Non-catalytic cracking of virgin gas oil	2	Cracked sidestream	21.2	33/100° SSU				
"	6	Cracked residuum	5.2		33	26	41	-
"	59	Cracked residuum	8.5	33/100° SSU		32		-
"	65	Cracked residuum	6.6	163.5/100° SSU	43.8	29.9	26.3	-
"	72	Cracked residuum	9.6	37.1/122° SSF	35	37.5	27.5	-
"	94	Cracked residuum	10.4	31.7/122° SSF	35	48	17	-
"	108	Cracked residuum	2.3	1530/130° SSU	32	25.5	41.9	-
Non-catalytic cracking of catalytic gas oil	20	Cracked residuum	4.7	132/122° SSF	51	33	16	-
Dilution of No. 20	20-1	50% oil No.20, 50% dodecyl-benzene						

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA: STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./wks.)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%FL in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
2	C3H 1	100	20	7[1]	0/75	-	-
6 *	CFW 3	100	20 (30)	18 (21)	72/30 (76/30)	(25.2±3.5)	$0.08^{+.01}_{-.02}$
59	C3H 3	100	20	11	82/69	(53.2±8.7)	$(0.04^{+.01}_{-.02})$
65	C3H 3	100	20	9	89/29	(23.6±3.3)	$(0.12^{+.01}_{-.03})$
72*	C3H 3	100	20	15	73/18	(15.1±1.8)	$(0.22^{+.03}_{-.05})$
94	C3H 3	100	6 (20)	5 (9)	80/39 (67/39)	(31.0±13.6)	$(0.09^{+.08}_{-.05})$
108	C3H 3	100	20	7	71/28	(24.0±5.6)	-
108	C3H 3	5	7 (19)	6 (13)	100/52 (92/52)	(36.1±12.5)	$0.07^{+.03}_{-.04}$
20 *	CFW 3	100	20	15	100/22	(15.0±1.8)	$(0.15^{+.06}_{-.03})$
20	C3H 3	100	20	10	90/21	(17.4±2.1)	-
20-1*	CFW 3	100	20	17	100/25	(16.1±2.7)	$0.15^{+.07}_{-.05}$

[1] Number alive after 63 weeks.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760mm.)			
					<750° (%)	750-925° (%)	>925° (%)	E.P. (°F.)
Non-catalytic cracking of catalytic gas oil	23	FCC gas oil feed	26.7	55.5/100° SSU	78.5	20.6	.9	838
"	24	Cracked residuum from No. 23	5.9	51.9/210° SSU	32.3	34.6	33.1	-
"	29	TCC gas oil feed	15.7	70/100° SSU	73	27	-	860
"	30	Cracked residuum from No. 29	8.5	10/210° SSF	36	38	26	-
"	34	Houdry gas oil feed	28.0	47.5/100° SSU		9		815
"	35	Cracked residuum from No. 34	2.7	2320/100° SSU	35	28	37	-
"	38	Total cracking charge; combination unit	16.1	2333/100° SSU	32.2	23.3	43.1	-
"	39	Cracked residuum from No. 38	7.8	177/122° SSF	31.0	19.8	48.4	-
"	44	FCC decanted oil feed	15.2	241/100° SSU	31.1	54.2	13.6	-
"	45	Cracked residuum from No. 44	-1.7	179/122° SSF	20.4	33.4	39	-

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA							
	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
23*	CFW 3	100	20	20	100/19	12.5±1.3	$0.24^{+.11}_{-.08}$
23*	C3H 2	100	20	18	94/28	(18.5±2.9)	$0.25^{+.09}_{-.06}$
24*	CFW 3	100	19	18	100/15	(9.5±1.5)	> 0.5
29*	C3H 1	100	20	19	84/30	(23.8±3.7)	$0.40^{+.11}_{-.14}$
30*	C3H 1	100	10 (20)	8 (13)	100/33 (92/33)	(24.5±4.8)	$0.35^{+.05}_{-.12}$
34*	CFW 3	100	20	19	84/32	(23.2±3.3)	$0.09^{+.01}_{-.02}$
35	CFW 3	100	20	13	100/20	(16.7±1.5)	0.13±.02
38	CFW 3	100	19	13	62/58	(45.1±12.6)	$(0.05^{+.01}_{-.02})$
39	CFW 3	100	29	18	56/24	(21.9±2.7)	-
44	C3H 1	100	20	16	94/40	(31.1±3.8)	$(0.25^{+.04}_{-.08})$
45	C3H 1	100	10 (20)	8 (9)	88/41 (89/41)	(34.2±5.4)	$(0.21^{+.02}_{-.07})$

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760			
					< 750° (%)	750-925° (%)	>925° (%)	
Non-catalytic cracking of catalytic gas oil	46	FCC gas oil feed	23.6	56.7/100° SSU	87.9	12.1	0	7
"	47	Cracked residuum from No. 46	9.6	140/100° SSU	76	15.5	8.5	
"	54	Total cracking charge	33.0	7.8/122° SSF	93.9	4.1	2.0	
"	55	Cracked residuum from No. 54	4.2	18.8/122° SSF	55.9	26.1	18	
"	61	Cracked residuum	6.3	73.6/100° SSU	66.8	18.2	15	
"	63	Houdry gas oil feed	25.6	25.7/100° SSU	48.5	37.6	13.9	
"	64	Cracked residuum from No. 63	19.9	31.8/100° SSU	52.5	31.8	15.7	

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

	BIOLOGICAL DATA							
API SAMPLE NUMBER	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%F.L. in wks)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
46*	CFW 3	100	20	15	100/24	(17.9±1.5)	$0.11^{+.02}_{-.01}$
47	CFW 3	100	20	14	93/17	(13.0±1.6)	$0.22^{+.10}_{-.06}$
54	CFW 3	100	20	16	100/36	(25.0±2.9)	0.07±.01
55*	CFW 3	100	9 (19)	8 (15)	89/19 (87/21)	(13.3±2.2)	$0.21^{+.15}_{-.07}$
61	CFW 3	100	20	17	88/26	(15.2±3.8)	$(0.22^{+.15}_{-.12})$
63*	C3H 3	100	20	18	89/26	(20.3±1.9)	(0.14±.02)
63	C3H 3	100	12 (19)	12 (15)	100/19 (100/19)	(15.7±2.0)	$0.19^{+.04}_{-.03}$
63	C3H 2	100	20	18	100/33	(23.4±2.6)	$0.17^{+.05}_{-.03}$
64*	C3H 3	100	20	13	100/23	(16.8±1.9)	$(0.17^{+.03}_{-.02})$

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760mm.)			
					<750° (%)	750-925° (%)	>925° (%)	E. (°
Non-catalytic cracking of catalytic gas oil	91	FCC gas oil feed	20.4	57.8/100° SSU	80.1	17.9	2.0	8
"	92	Cracked residuum from No. 91	6.1	102.5/100° SSU	70.5	27	2.5	
"	93	Cracked residuum	7.9	49.4/100° SSU	87	4.5	8.5	
Steam cracking	86	Cracked residuum	3.5	5000/100° SSU	51.9	28.4	18[1]	8
Viscosity breaking	18	Cracked residuum from No. 17	3.1	1123/210° SSU	23.7	24	52.3	
"	66[2]	Cracked residuum	6.5	18/210° SSF	22.1	29	48.9	
"	67[2]	Cracked sidestream from fractionator producing No. 66	15.6	81/100° SSU	84.6	10.7	4.7	
Dubbs coking	52[2]	Cracked sidestream	21.0	43.5/100° SSU	95.2	2.5	2.3	
"	53[2]	Blowdown oil	10.5	203/100° SSU	61.3	23.3	15.4	

[1] Distillation stopped when cracking occurred.

[2] Feed to unit included catalytically cracked components.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

	BIOLOGICAL DATA							
API SAMPLE NUMBER	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
91*	C3H 2	100	20	19	95/23	(16.4±2.1)	(0.28 $^{+.06}_{-.05}$)
92	C3H 2	100	13 (20)	11 (14)	91/23 (79/23)	(15.4±4.1)	(0.33 $^{+.14}_{-.11}$)
93	C3H 3	100	20	18	94/40	(29.0±2.8)	(0.09 $^{+.01}_{-.02}$)
86	C3H 1	100	10 (20)	8 (17)	100/36 (100/49)	(35.0±1.2)	0.17±.01
18*	CFW 3	100	10	9	56/30	(30.1±11.3)	(0.07±.03)
66	C3H 2	100	20	19	100/37	29.3±2.0	0.12±.01
67	C3H 2	100	10 (20)	9 (13)	89/17 (77/17)	11.8±3.2	0.13 $^{+.26}_{-.13}$
52	CFW 3	100	10 (20)	8 (15)	100/36 (87/36)	(18.9±7.9)	0.10 $^{+.27}_{-.04}$
53	CFW 3	100	20	20	100/15	10.2±1.2	0.53 $^{?}_{-.21}$

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760			
					<750° (%)	750-925° (%)	>925° (%)	E. (°
Batch coking	87	Cracked sidestream	14.9	500/100° SSU				
Delayed coking	28	Cracked sidestream	15.3	361/100° SSU		42.4		-
"	74	Total furnace charge(including recycle)	12.5	198/122° SSF	22.3	32.5	45.2	
"	33	Cracked sidestream from No. 74	16.8	131.4/100° SSU	60	38.1	1.9	
"	84	Cracked sidestream	30.2	55/100° SSU	79	19.9	1.1	
"	90	Cracked sidestream	30.5	40.6/100° SSU	90.2	9.2	.6	
"	96	Cracked sidestream	33.2	43.7/100° SSU	77.7	22.2	.1	
"	97	Total furnace charge(including recycle)	16.6	386/100° SSU	57.8	32.2	10	
"	98	Cracked sidestream from No. 97	31.0	38.1/100° SSU	100			
"	103	Cracked sidestream	25.2	135/100° SSU	43.9	35.1	20.4	

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA: STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
87	C3H 2	20	20	11	91/30	(23.8±5.0)	$(0.18^{+.04}_{-.06})$
28*	CFW 3	100	10 (20)	10 (19)	100/15 (84/15)	(10.8±1.6)	$0.40^{?}_{-.15}$
28	C3H 1	100	13 (20)	13 (19)	85/33 (84/51)	(26.2±4.2)	$0.31^{+.04}_{-.10}$
74	C3H 2	100	14 (20)	12 (16)	100/47 (94/47)	(35.8±5.3)	$0.11^{+.02}_{-.04}$
33*	CFW 3	100	20	18	95/15	10.3±1.3	$0.51^{+}_{-0.22}$
33*	C3H 1	100	20	19	95/30	(19.4±3.4)	$0.51^{+.10}_{-.18}$
84	C3H 3	100	20	19	95/24	16.8±2.0	$0.17^{+.04}_{-.02}$
90	C3H 3	100	20	17	100/38	(23.3±3.3)	$(0.13^{+.01}_{-.04})$
96[1]	C3H 3	100	20	15	93/27	(17.7±3.1)	$(0.17^{+.03}_{-.04})$
97	C3H 3	100	20	15	87/22	(17.9±2.2)	$(0.17^{+.01}_{-.04})$
98	C3H 3	100	20	11	73/39	(29.5±7.0)	$(0.11^{+.02}_{-.05})$
103	C3H 3	100	20	17	94/23	(15.9±1.8)	$(0.20^{+.02}_{-.04})$

[1] The pattern of response to the irritational effects of this oil was similar to that observed with dodecylbenzene.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760m			
					<750° (%)	750-925° (%)	>925° (%)	E. (°F
Delayed coking	41	Wax tailings, 50% benzene	1.2	131/240° SSF	9.6	49.8	40.6	-
Naphtha reforming	19	Cracked residuum	17.0	39.7/100° SSU	91	8.95	0	91
"	58	Cracked residuum from kerosene feed	6.3	117/122° SSF	85	14.3	0	86
"	76	Cracked residuum	30.6	31/130° SSU	~91	8		86
Polyforming	13	Cracked residuum	10.1	154/100° SSU	63	15	22[1]	89
"	37	Cracked residuum	11.2	60.2/100° SSU	66	15	19[1]	86
"	69	Cracked residuum	15.9	43/130° SSU	75.1	8.3	16.6	-
Hydroforming	49	Cracked residuum	10.1	37.3/100° SSU	~95	3.5		~9
"	77	Cracked residuum	22.8	~28/100° SSU	100			
T. C. C.	3	Cracked sidestream	33.2	32.7/100° SSU				
"	60	Cracked sidestream	24.9	40/100° SSU	100			

[1] Distillation stopped when cracking occurred.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA: STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
41	C3H 2	100	20	13	85/25	(23.1±2.0)	$(0.17^{+.13}_{-.02})$
19*	CFW 3	100	10 (30)	7 (13)	86/37 (92/37)	(26.9±6.4)	(0.07±.02)
58	CFW 3	100	20 (30)	18 (24)	89/30 (88/31)	(22.4±4.0)	0.09±.02
76	CFW 3	100	10 (29)	9 (28)	100/30 (96/52)	24.7±3.5	0.07±.01
13*	CFW 3	100	20 (30)	13 (16)	92/29 (94/38)	(25.6±3.3)	$(0.07^{+.02}_{-.01})$
13	CFW 2	100	30	28	89/61	(31 7'5.4)	$0.10^{+.02}_{-.03}$
37	CFW 3	100	20 (30)	13 (17)	100/46 (94/46)	(25.4±5.1)	0.07±.02
69	CFW 3	100	10 (20)	10 (18)	80/29 (78/30)	(24.1±5.1)	$(0.09^{+.01}_{-.03})$
49	C3H 1	100	20	19	84/41	(35.9±2.6)	$0.18^{+.01}_{-.03}$
77	CFW 3	100	10 (20)	10 (19)	100/38 (89/41)	(29.3±4.8)	$(0.07^{+.01}_{-.02})$
3	C3H 1	100	20	0[1]	0/62	-	-
60*	CFW 3	100	10 (20)	8 (14)	63/48 (57/48)	(43.4±11.1)	(0.04±.01)

[1] Number alive after 63 weeks.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760mm)			
					<750° (%)	750-925° (%)	>925° (%)	E.P. (°F.)
T. C. C.	109	Cracked sidestream	24.1	46.1/100° SSU				
"	7	Cracked residuum	20.2	34.5/100° SSU	~100			
"	9	Cracked residuum	18.4	37.1/100° SSU	97	2.33	-	780
"	10	Cracked residuum	11.6	117/100° SSU	56.7	36.6	6.7	-
"	31	Cracked residuum	16.0	14.8/122° SSF	63	35.6		870
"	36	Cracked residuum	21.9	90/100° SSU		48		892
"	40	Cracked residuum	19.8	72.6/100° SSU	77.2	22.2	.65	860
"	71	Cracked residuum	22.8	59/100° SSU	77	21.5	1.5	845
"	78	Cracked residuum	16.1	126.8/100° SSU	45.7	44.3	10	-
"	82	Cracked residuum	13.6	126/130° SSU	25.7	51.5	22.8	-

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

	BIOLOGICAL DATA						
API SAMPLE NUMBER	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION 5%EL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
109[1]*	C3H 3	100	6 (20)	6 (15)	100/21 (93/25)	14.0±4.9	$0.22^{+.20}_{-.07}$
7	C3H 1	100	20	9	11/55	-	-
9*	C3H 3	100	10	9	100/47	(36.2±4.5)	0.06±.01
9*	CFW 3	100	10 (20)	10 (16)	100/40 (100/41)	(28.4±4.1)	$0.07^{+.01}_{-.02}$
10*	C3H 1	100	10 (20)	9 (17)	100/39 (94/39)	(24.6±7.0)	$(0.40^{+.07}_{-.19})$
10	CFW 1	100	10 (20)	8 (10)	88/20 (90/31)	(17.3±3.8)	$(0.41^{+.24}_{-.15})$
31	C3H 1	100	20	17	100/32	(22.0±2.8)	$0.40^{+.03}_{-.11}$
36	C3H 1	100	20	16	94/44	(34.9±4.3)	$0.22^{+.06}_{-.07}$
40	C3H 1	100	10 (20)	5 (9)	100/42 (100/42)	(34.1±7.4)	$(0.18^{+.09}_{-.05})$
71	C3H 1	100	20	20	90/22	(16.6±1.7)	$0.55^{+.06}_{-.08}$
71	C3H 1	20	20 (33)	19 (32)	90/37 (91/52)	(27.1±4.8)	$0.31^{+.04}_{-.11}$
71	C3H 1	5	19	15	0/9	-	-
78	C3H 1	100	9 (19)	9 (16)	89/19 (88/20)	(14.3±2.9)	$0.65^{+.25}_{-.15}$
82	C3H 1	100	10 (20)	10 (20)	90/33 (95/34)	(24.1±6.4)	$0.33^{+.14}_{-.08}$

[1] The pattern of response to the irritational effects of this oil was similar to that observed with dodecylbenzene.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760m			
					<750° (%)	750-925° (%)	>925° (%)	E. (°F
F. C. C.	4	Cracked sidestream	21.6					
"	23	Cracked sidestream	26.7	55.5/100° SSU	78.5	20.6	.9	83
"	46	Cracked sidestream	23.6	56.7/100° SSU	87.9	12.1	0	78
"	88	Cracked sidestream	22.5	78/100° SSU	69.3	30.2	.5	9
"	89	Cracked sidestream	27.0	51/100° SSU	100			7
"	91	Cracked sidestream	20.4	57.8/100° SSU	80.1	17.9	2.0	8
"	101	Cracked sidestream	24.8	40.1/100° SSU	89.7	9.1	.3	7
"	102	Cracked sidestream	23.5	53.1/100° SSU	99	1		7
"	104	Cracked sidestream	25.8	60.4/100° SSU		7.6		

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

		BIOLOGICAL DATA						
API SAMPLE NUMBER	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%FL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
4	C3H 1	100	20	5[1]	0/69	-	-
23*	CFW 3	100	20	20	100/19	12.5±1.3	$0.24^{+.11}_{-.05}$
23*	C3H 2	100	20	18	94/28	(18.5±2.9)	$0.25^{+.05}_{-.06}$
46*	CFW 3	100	20	15	100/24	(17.9±1.5)	$0.11^{+.02}_{-.01}$
88	C3H 2	100	20	18	94/26	(17.0±2.4)	$(0.25^{+.07}_{-.04})$
89	C3H 3	100	30	28	89/21	(13.2±2.0)	$0.28^{+.04}_{-.08}$
91*	C3H 2	100	20	19	95/23	(16.4±2.1)	$(0.28^{+.06}_{-.05})$
101[2]	C3H 3	100	20	6	100/12	(10.3±.8)	-
102[2]	C3H 2	20	6 (18)	6 (16)	100/27 (69/43)	22.6±3.3	$0.17^{+.05}_{-.03}$
102[2]	C3H 2	100	18	15	93/32	(23.8±3.4)	$0.19^{+.01}_{-.06}$
104[2]	C3H 2	100	20	19	89/26	22.4±1.6	$0.17^{+.02}_{-.01}$
104[2]	C3H 2	20	13 (20)	12 (12)	75/53 (75/53)	(39.0±10.1)	$0.11^{+.01}_{-.06}$

[1] Number of animals alive after 63 weeks.

[2] The pattern of response to the irritational effects of this oil was similar to that observed with dodecylbenzene.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760mm.)			
					<750° (%)	750-925° (%)	>925° (%)	E.P. (°F.)
F. C. C.	8	Cracked residuum	11.1	110.3/100° SSU	75	22		890
Dilution of No. 8	8-4	50% oil No. 8, 50% (white oil + West Texas residuum						
"	8-16	50% oil No. 8, 50% sec.-amylbenzene						
"	8-21	50% oil No. 8, 50% colorless fraction from No. 8 obtained by chromatography on silica gel						

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA: STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
8	C3H 3	100	10	9	89/7	(5.4±1.0)	$1.06^{+.68}_{-.30}$
8	C3H 2	100	20	17	94/14	(8.5±2.4)	$(0.77^{+.51}_{-.29})$
8	CFW 2	100	19	17	100/14	7.5±1.8	>0.6
8	C3H 2	20	15	13	92/20	(16.6±1.8)	$0.28^{+.03}_{-.04}$
8	C3H 1	100	10 (20)	10 (16)	100/32 (100/32)	(21.4±5.2)	$(0.47^{+.08}_{-.21})$
8	C3H 1	100	12 (18)	10 (16)	100/25 (100/31)	(18.9±3.8)	$(0.44^{+.16}_{-.10})$
8*	C3H 1	100	20	17	94/24	(15.9±2.7)	$0.61^{+.13}_{-.18}$
8	C3H 1	20	13 (20)	12 (19)	100/50 (100/50)	(36.4±6.5)	$0.20^{+.02}_{-.08}$
8	C3H 1	20	40	32	97/42	(31.7±2.2)	$0.23^{+.02}_{-.05}$
8	C3H 1	50	40	34	91/40	(27.5±2.2)	$0.29^{+.04}_{-.07}$
8	C3H 1	50	14 (20)	12 (18)	100/32 (100/32)	20.3±3.9	$0.40^{+.14}_{-.09}$
8	C3H 1	5	33 (40)	27 (33)	96/48 (88/48)	(35.0±3.1)	$0.20^{+.01}_{-.05}$
8-4	C3H 3	100	20 (30)	14 (20)	100/23 (90/23)	(18.3±1.9)	$(0.17^{+.01}_{-.04})$
8-16	C3H 1	100	20	19	100/52	(34.4±3.9)	$0.22^{+.04}_{-.07}$
8-21	C3H 1	100	13 (20)	11 (15)	100/27 (87/43)	(20.9±3.0)	$0.43^{+.04}_{-.12}$

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760			
					<750° (%)	750-925° (%)	>925° (%)	E (°
F. C. C.	12	Cracked residuum	18.1	71/100° SSU				
"	26	Cracked residuum	7.3	344.2/100° SSU	61.3	34.1	4.6	
"	42	Cracked residuum	14.2	139.8/100° SSU	28.6	63.6	7.8	
"	43	Cracked residuum	24.2	Pour Point 110°	24.5	67.8	7.7	
"	(44)	Cracked residuum	15.2	241/100° SSU	31.1	54.2	13.6	
"	48	Cracked residuum	6.0	91.7/100° SSU	47.1	37.3	15.6	
"	68	Cracked residuum	9.8	81/130° SSU	43.3	44.9	11.8	
"	73	Cracked residuum	17.5	16.9/122° SSF	21	62	17	
"	85	Cracked residuum	8.1	216/100° SSU	42.6	47.8	9.6	

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA: STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
12	CFW 1	100	18	17	88/34	(19.0±5.3)	$0.46^{+.08}_{-.24}$
12[1]	CFW 3	100	15	14	100/14	(10.7±.9)	$0.42^{+.26}_{-.11}$
26	C3H 1	100	20	19	100/20	(14.3±1.3)	$0.65^{+.09}_{-.08}$
42	C3H 1	100	20	18	94/34	(23.3±2.7)	$(0.38^{+.02}_{-.10})$
43	C3H 1	100	20	15	100/37	(33.0±2.5)	$0.20^{+.02}_{-.03}$
(44)	C3H 1	100	20	16	94/40	(31.1±3.8)	$(0.25^{+.04}_{-.08})$
48	C3H 1	100	20	13	100/36	(31.5±2.2)	$(0.22^{+.01}_{-.04})$
68	C3H 1	100	20	15	100/17	(14.8±.9)	$(0.62^{+.06}_{-.05})$
73	C3H 1	100	10 (20)	7 (12)	100/22 (83/22)	(18.6±1.9)	$0.45^{+.07}_{-.06}$
73	C3H 1	100	20	19	100/31	(24.4±2.5)	$0.31^{+.04}_{-.05}$
85*	C3H 1	100	20	18	100/25	(18.1±1.6)	0.47±.06

[1] Hair clipped.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760 <750° (%)	750-925° (%)	>925° (%)	R (°
Houdry	11	Cracked residuum	4.3	71/100° SSU	84	16	0	8
"	34	Cracked residuum	28.0	47.5/100° SSU		9		8
"	50	Cracked residuum	21.3	64/100° SSU	85	15	0	8
"	51	Cracked residuum	25.7	67/100° SSU	83	17	0	8
"	63	Cracked residuum	25.6	25.7/100° SSU	48.5	37.6	13.9	
"	81	Cracked residuum	22.7	40/210° SSU	40.8	52.6	6.6	
Cycloversion	22	Cracked residuum	25.6	84/100° SSU	49.5	44.2	6.3	

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

			BIOLOGICAL DATA					
API SAMPLE NUMBER	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
11*	C3H 3	100	20	18	94/19	(15.0±2.2)	$(0.22^{+.03}_{-.05})$
34*	CFW 3	100	20	19	84/32	(23.2±3.3)	$0.09^{+.01}_{-.02}$
50	CFW 3	100	20	16	100/21	(15.0±1.7)	$(0.15^{+.06}_{-.03})$
51	CFW 3	100	20	18	83/19	(13.8±2.0)	$(0.22^{+.05}_{-.08})$
63*	C3H 3	100	20	18	89/26	(20.3±1.9)	(0.14±.02)
63	C3H 3	100	12 (19)	12 (15)	100/19 (100/19)	(15.7±2.0)	$0.19^{+.04}_{-.03}$
63	C3H 2	100	20	18	100/33	(23.4±2.6)	$0.17^{+.05}_{-.03}$
81	C3H 1	100	10 (20)	10 (20)	100/35 (100/36)	(25.9±4.9)	$0.31^{+.09}_{-.10}$
81	C3H 1	100	36	32	91/41	(30.7±2.2)	$0.23^{+.03}_{-.04}$
81	C3H 1	20	31 (40)	28 (31)	97/52 (94/52)	(37.7±3.1)	$(0.18^{+.03}_{-.05})$
22	CFW 3	100	10 (20)	7 (14)	100/17 (100/17)	(10.8±3.1)	$0.40^{+?}_{-.22}$

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760			
					<750° (%)	750-925° (%)	>925° (%)	E. (°
Solvent extraction	16	Phenol extract from Coastal 900-X	9.7	352/210° SSU		62		9
"	17	Duosol extract from California waxy residuum, 50% in sec.-amyl-benzene	7.1	2276/210° SSU	3	28.7	68.3	
"	27	Phenol extract from San Joaquin naphthenic distillate	11.0	173/100° SSU	80	19	0	
"	70	Nitro-benzene extract from Barbers Hill 60/80	15.7	99.4/210° SSU	.5	85.3	14.2	
"	75	SO_2 extract from TCC gas oil	14.4	38.3/100° SSU	100			
Distillation	25	700°+ bottoms from F.C.C. heavy cycle gas oil	24.3	115/100° SSU	49	45	6	
Dilution of No. 25	25-1	50% oil No.25 50% (White oil + West Texas residuum)	21.1	320.6/122° SSU				

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA: STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{BC}
16*	CFW 3	100	10	6	67/73	(68.3±16.0)	(0.03±.01)
16*	C3H 3	100	10	7	43/70	(78.6±24.3)	-
17*	CFW 3	100	10 (20)	8 (12)	87/62 (67/62)	(35.4±16.7)	$(0.06^{+.04}_{-.03})$
27*	CFW 3	100	10 (20)	9 (12)	89/17 (83/17)	(11.4±3.0)	$0.33^{+?}_{-.16}$
70	C3H 3	100	6 (20)	5 (14)	100/42 (93/44)	(31.2±11.5)	$0.09^{+.04}_{-.05}$
75	CFW 3	100	20	13	77/51	(38.6±7.2)	(0.05±.01)
25*	C3H 3	100	30	19	95/19	(13.4±1.4)	$0.25^{+.03}_{-.05}$
25-1*	C3H 3	100	30	26	92/40	(27.0±3.7)	$0.10^{+.01}_{-.03}$

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SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	SPECTRUM TYPE[1] OR PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760			
					<750° (%)	750-925° (%)	>925° (%)	B. (°F
Straight run distillation	1	Distillate # 11896	31.9	37/100° SSU				
"	56	Waxy Midcontinent distillate, Type B (.5)	29.9	87/100° SSU	52.4	41.6	(2.0)	83
"	79	San Joaquin naphthenic distillate, Type C (2.2)	16.6	63.9/210° SSU	~13	86.2		85
"	105	West Texas paraffin distillate, Type B (.5)	28.9	54.3/100° SSU	72.9	23.4	3.3	
"	114	Type B (.63)	24.6	235/100° SSU				
"	115	Type C (.58)	23.2	234/100° SSU				
"	5	Residuum from Wilmington crude # 11885	12.8	572/122° SSF	26	26	48	

[1] See page 8 of Section A of report dated April 5, 1952, for discussi of the classification of Straight Run Distillates by Spectrum Type.

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SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA: STRAIN OF MOUSE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
1	C3H 1	100	20	1[1]	0/72	-	-
56	CFW 6	100	20	15	87/22	(15.3±2.9)	-
56*	CFW 3	100	10 (20)	8 (17)	100/20 (88/22)	(15.4±3.2)	$0.15^{+.11}_{-.05}$
56[2]	C3H 3	100	20	20	5/11	-	-
56	C3H 3	20	20	20	0/15	-	-
79*	C3H 2	100	10 (20)	7 (14)	86/57 (71/57)	(39.2±15.4)	$(0.14^{+.01}_{-.10})$
105[3]	C3H 3	100	14 (20)	13 (17)	85/33 (88/33)	(23.2±4.4)	$0.11^{+.04}_{-.03}$
114	C3H 3	100	20	14	0/28	-	-
114	C3H 3	20	20	14	7/43	-	-
115	C3H 3	20	20	20	5/26	-	-
5	C3H 1	100	20	0[1]	0/56	-	-

[1] Number of animals alive after 63 weeks.

[2] Hair clipped.

[3] The pattern of response to the irritational effects of this oil was similar to that observed with dodecylbenzene.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	SPECTRUM TYPE[1] OR PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760 <750° (%)	750-925° (%)	>925° (%)	R. (°
Fractional distillation	110-1	Type B (.004)	61.0	.95/70°F.[2]	100			
"	111-4	Type B (1.62)	23.0	17/140°F.[2]				
"	111-4a	75% No. 111-4 25% Benzene	22.7					
"	111-5a	Crude residuum (<5% Benzene)	15.4	112/100°F.[2]				
Dilution of No. 111-4	111-6	50% No. 110-1 50% No. 111-4						
"	111-7	50% No. 111-4 50% No. 112-1						
Fractional distillation	112-1	Type B (.016)	65.9	.896/70°F.[2]	100			
"	112-3	Type B (.045)	39.7	3.4/140°F[2]				
Lubricating oil	99	Type C (.5)	20.0	475/100° 52/210° SSU	~38			
"	100	Type B (.3)	29.5	307/100° 53/210° SSU	~0			
"	100-1	0.2% Antioxidant[3] in No. 100						
"	100-2	0.5% Antioxidant, 2,6-di-tert.-butyl-4-methylphenol, in No. 100						

[1] See page 8 of Section A of report dated April 5, 1952 for discussion of the classification of Straight Run Distillates by spectrum type.

[2] Kinematic viscosity (centistokes).

[3] Same type additive as that contained in API-99.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA: STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
110-1	C3H 3	20	20	19[1]	0/55	-	-
111-4*	C3H 3	20	19	17	88/22	(17.6±1.6)	$0.17^{+.02}_{-.03}$
111-4a	C3H 3	5	20	20	0/3	-	-
111-5a	C3H 3	5	20	20	0/5	-	-
111-6*	C3H 3	20	13 (19)	13 (19)	77/31 (58/31)	(26.0±4.5)	0.10±.03
111-7*	C3H 3	20	7 (20)	7 (17)	100/27 (76/44)	22.4±3.5	$0.11^{+.04}_{-.02}$
112-1	C3H 3	20	20	17[1]	0/58	-	-
112-3[3]	C3H 3	20	20	18[1]	0/58[2]	-	-
99	C3H 3	100	14 (20)	11 (16)	91/36 (94/47)	(31.0±4.5)	$0.07^{+.02}_{-.01}$
100	C3H 3	100	20	19[1]	0/80	-	-
100-1	C3H 3	100	20	20	0/3	-	-
100-2	C3H 3	100	20	19	0/42	-	-

[1] Number of animals alive after 36 weeks.

[2] Two papillomas appeared at 20 weeks but regressed.

[3] The pattern of response to the irritational effects of this oil was similar to that observed with dodecylbenzene.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760			
					<750° (%)	750-925° (%)	>925° (%)	E.P. (°F
Wax pressing	32	Dewaxed paraffin distillate fraction from Lima crude						
"	57	Dewaxed oil from No. 56	28.7	91.3/100° SSU	80	19.5	.5	8
MEK - Benzol solvent dewaxing	43-1	Dewaxed oil from F.C.C. decanted oil No. 43	12.9	195/100° SSU	29.5	57	13.5	
Filtration dewaxing of No. 8	8-3	Filtrate oil, 85% of original (.94% S)	11.3		65	21.4	13.4	
Desulfurization of 8-3 by catalytic hydrogenation	21	Hydrogenated heavy gas oil (.15% S)	18.1	50.1/100° SSU	74	20	6	
Acid treating	62	Hydrolyzed acid sludge	14.2	7277/100° SSU		58		8
Effect of viscosity on tumor induction	114	Straight run distillate, see page 18 of Appendix	24.0	235/100° SSU				
"	114-1	95% API-114, 5% alkylpolystyrene	25.4	1756/100° SSU				
Retorting of oil shale	116	Crude shale oil	19.4	294.9/100° SSU				

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA: STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./wks.)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%FL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
32	CFW (3-6)[1]	100	10 (20)	8 (15)	100/40 (87/44)	(31.5±4.3)	-
57*	CFW 6	100	20	17	100/25	(16.9±2.0)	-
43-1*	C3H 1	100	10 (20)	10 (19)	100/24 (95/25)	(19.5±2.2)	0.43±.08
43-1	C3H 2	20	20	19	0/5	-	-
8-3*	C3H 3	100	20	20	90/17	(11.2±1.7)	$(0.36^{+.07}_{.11})$
21	C3H 3	100	20	20	100/13	(9.4±1.1)	$(0.43^{+.08}_{.11})$
62	C3H 3	100	10 (20)	9 (16)	33/79 (25/79)	(98.3±26.5)	-
114	C3H 3	20	20	14	7/43	-	-
114	C3H 3	100	20	14	0/28	-	-
114-1	C3H 3	20	20	15	33/46	-	-
114-1	C3H 3	100	20	13	0/28	-	-
116	C3H 3	100	30	20	25/19[2]	-	-

[1] Three applications per week for 14 weeks, six applications per week thereafter.

[2] Painting discontinued after 13 weeks.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	PRODUCT	ANALYTICAL DATA					
			GRAVITY	VISCOSITY	DISTILLATION (2mm. corr. to 760			
					<750° (%)	750-925° (%)	>925° (%)	E. (°
Fuel oil blending	113	Industrial fuel oil	8.3	30/122° SSF	43	20	37	
"	118	Catalytically cracked residuum component of API-119			35.2	45.5	10.5	
"	119	10% API-118, 90% light catalytic cycle oil (b.450 - 600°)	23.3	38.8/100° SSU				

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA							
	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
113[1]	C3H 3	20	7 (27)	7 (22)	100/25 (77/27)	(18.8±3.8) (22.1±2.5)	$0.16 \pm .04$
113[2]	C3H 3	20	14 (27)	10 (16)	100/28 (88/28)	(17.5±3.4) (19.7±2.7)	$0.16^{+.06}_{-.03}$
113[3]	C3H 3	20	20 (27)	20 (25)	100/25 (100/25)	(18.1±1.6) (18.1±1.5)	$0.16 \pm .02$
113[3]	C3H 2	20	7 (27)	7 (22)	100/24 (91/40)	22.5±.6 (26.6±3.5)	$0.18^{+.02}_{-.01}$
113[3]	C3H 1	20	27	20	95/45	(35.0±2.6)	$0.19^{+.01}_{-.04}$
113[3]	C3H 3	100	27 (40)	27 (36)	100/23 (100/25)	(16.3±1.3) (17.5±1.3)	$0.18^{+.02}_{-.01}$
113[3]	C3H 3	5	26 (39)	26 (38)	100/26 (92/34)	(16.9±1.5) (18.9±2.1)	$0.17 \pm .02$
113[3]	C3H 3	1	20	18	78/54	~46.1	~0.04
113[3]	C3H 3	20	20	18	100/27	(19.2±2.1)	$0.17^{+.01}_{-.04}$
113[4]	C3H 3	20	20	20	100/26	(18.3±2.1)	$0.15^{+.03}_{-.02}$
118	C3H (2/month)	100	24 (30)	21 (24)	100/50 (100/50)	(34.9±4.3)	$0.46^{+.02}_{-.17}$
119	C3H (2/month)	100	29	25	40/54	-	-
119	C3H (2/week)	100	22 (27)	19 (23)	95/27 (96/30)	21.6±1.5	$0.18^{+.02}_{-.01}$

[1] Approximate age of mice at start of experiment, 27 weeks.
[2] Approximate age of mice at start of experiment, 23 weeks.
[3] Approximate age of mice at start of experiment, 20 weeks.
[4] Approximate age of mice at start of experiment, 14 weeks.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	P R O D U C T	ESTIMATED CORRECTED BOILING RANGE (in °F. at 760 mm.)
Fractional distillation	8-6[1]	0 - 9.3% fraction from API-8	435 - 560
"	8-7[1]	9.3 - 19.4% fraction from API-8	560 - 630
"	8-8[1]	19.4 - 30.3% fraction from API-8	630 - 695
"	8-9[1]	30.3 - 39.8% fraction from API-8	695 - 710
"	8-10[1]	39.8 - 49.6% fraction from API-8	710 - 765
"	8-11[1]	49.6 - 59.2% fraction from API-8	765 - 800
"	8-12[1]	59.2 - 69.1% fraction from API-8	800 - 830
Diels-Alder reaction	8-12a[1]	non-adduct from reaction (95.4% of 8-12)	
Fractional distillation	8-13[1]	69.1 - 78.5% fraction from API-8	830 - 850
"	8-14[2]	78.5 - 80.8% fraction from API-8	850 - 875
"	8-15[1]	Residue; 80.8 - 100%	> 875
"	8-18	Proportionate reblend of distillation fractions, 8-6 through 8-15	

[1] 50% solution in benzene.

[2] 33.3% solution in benzene.

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TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA: STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%F.L.in wks)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
8-6	C3H 2	100	20	14[1]	0/66	-	-
8-7	C3H 2	100	20	16[1]	0/74	-	-
8-8	C3H 2	100	20	16[1]	0/74	-	-
8-9*	C3H 2	100	20	18	56/62	(58.8±13.4)	-
8-10*	C3H 2	100	20	16	94/44	31.2±3.4	$0.10^{+.03}_{-.01}$
8-11*	C3H 2	100	20	20	90/33	(24.6±2.5)	$0.15^{+.03}_{-.02}$
8-12*	C3H 2	100	20	14	93/28	(19.5±3.1)	$0.23^{+.05}_{-.06}$
8-12a*	C3H 2	100	16	16	100/26	(17.6±2.1)	$0.25^{+.03}_{-.05}$
8-13*	C3H 2	100	20	14	79/25	(22.1±2.5)	$(0.20^{+.02}_{-.05})$
8-14*	C3H 2	100	20	12	25/21	(26.1±4.7)	-
8-15*	C3H 2	100	20	13	92/35	(28.0±2.6)	$(0.14^{+.01}_{-.03})$
8-18	C3H 1	100	10 (15)	10 (14)	90/18 (87/39)	13.3±2.5	$0.72^{+.25}_{-.16}$

[1] Number of animals alive after 45 weeks.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	P R O D U C T
Diels-Alder reaction	8-23a	Crystalline material from 1st chromatographic fraction of Class A[1] adduct regenerate, .34% in benzene
"	8-23b	non-crystalline residues from 1st and 2nd chromatographic fraction, 1.5% in benzene
"	8-23c	Crystalline material from 2nd chromatographic fraction of Class A[1] adduct regenerate, .34% in benzene
"	8-23d	3rd chromatographic fraction of Class A[1] adduct regenerate, 0.8% in benzene
"	8-23e	4th chromatographic fraction of Class A[1] adduct regenerate, .57% in benzene
"	8-23f	5th chromatographic fraction of Class A[1] adduct regenerate, .57% in benzene
"	8-23g	Class B[1] adduct regenerate, 1.5% in benzene
"	8-23h	Total Class A[1] adduct regenerate, 2.2% in benzene
Solvent extraction with conc. H_2SO_4	8-19	Extract from API 8-10 and 8-11, 50% benzene
"	8-20	Raffinate from API 8-10 and 8-11, 50% benzene
"	23-1	Extract from API-23, 20% benzene
"	23-2	Raffinate from API-23, 20% benzene
Fractionation of API-12	12-7	Non-adduct of Diels-Alder reaction on raffinate from sulfuric extraction of aromatic fraction b.130-180° at .2 mm. (~680-800°F./760 mm.), 70% benzene

[1] Class A adduct was that normally soluble in 5% aqueous NaOH; Class B adduct was not soluble in either 5% aqueous NaOH or benzene after hydrolysis.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA							
	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks)	RELATIVE CARCINOGENIC POTENCY, PMC
8-23a	C3H 3	15	20	17	0/54[2]	-	-
8-23b	C3H 3	15	20	11	100/51	~ 38.1	~ 0.05
8-23c	C3H 3	12	10	6	0/54[3]	-	-
8-23d	C3H 3	15	14 (20)	13 (18)	100/36 (100/38)	29.4±2.7	0.08±.01
8-23e	C3H 3	15	9	8	13/46[4]	-	-
8-23f	C3H 3	15	20	16	0/54[4]	-	-
8-23g	C3H 3	15	14	13	92/50	43.5±4.2	0.04±.01
8-23h	C3H 3	15	13	12	100/43	(35.2±3.4)	$0.07^{+.01}_{-.02}$
8-19	C3H 2	100	9	9	22/32[1]	-	-
8-20	C3H 2	100	6 (9)	6 (9)	83/25[1] (67/28)	(22.8±5.0)	$0.18^{+.06}_{-.05}$
23-1*	C3H 2	100	20	19	90/26	(18.2±3.1)	$0.28^{+.02}_{-.09}$
23-2*	C3H 2	100	20	19	100/44[1]	(25.7±3.1)	$0.16^{+.01}_{-.04}$
12-7	C3H 2	20	20	18	33/46[5]	-	-

[1] Painting discontinued after 26 weeks; [2] 30 weeks; [3] 37 weeks; [4] 32 weeks; [5] 43 weeks.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	P R O D U C T
Air oxidation (cobalt naphthenate catalyst)	83	Two hour oxidation product
"	83-1	Four hour oxidation product
Chromatography	8-5	Aromatics of No. 8 from Silica Gel
"	8-13a	First aromatic fraction,[2] 2%[1], of API 8-13
"	8-13b	Second aromatic fraction, 2.4%[1], of API 8-13
"	8-13c	Third aromatic fraction, 8.7%[1], of API 8-13
"	8-13d	Fourth aromatic fraction, 5.6%[1], of API 8-13
"	8-13e	Fifth aromatic fraction, 5.6%[1], of API 8-13
"	8-13f	Sixth aromatic fraction, 2%[1], of API 8-13
"	8-13g	Seventh aromatic fraction, 16.9%[1], of API 8-13
"	8-13h	Eighth aromatic fraction, 2.4%[1], of API 8-13
"	8-13i	Ninth aromatic fraction, 6.9%[1], of API 8-13
"	8-17	Reblend of chromatography fractions of API-8
"	12-2	Non-aromatics (cut with 20% heptane)
"	71-1	See page 34 of Section A-4 of report dated April 5 1952 for description
"	71-2	Proportionate reblend of all fractions from chromatography of API-71
"	8-24	Non-aromatics of No. 8 from alumina

[1] Tested at this percentage by weight in benzene.

[2] Proceeding colorless non-aromatic fraction, 48% of API-8-13, proved to be a non-accelerating solvent when diluted 50% with benzene. See API-266 on page 37.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA: STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (% EL. in wks)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
83	C3H 2	100	20	14	100/17	(12.7±1.7)	$(0.42^{+.05}_{-.09})$
83-1	C3H 2	100	20	16	94/17	(12.4±1.6)	$(0.40^{+.08}_{-.06})$
8-5	C3H 1	100	20	12	92/22	(18.7±1.8)	$0.44^{+.07}_{-.05}$
8-5	CFW 1	100	20	19	79/28	(21.2±5.6)	$0.26^{+.17}_{-.07}$
8-13a	C3H 3	20	15	12	0/30	-	-
8-13b	C3H 3	20	15	12	0/30	-	-
8-13c	C3H 3	20	15	13	69/30	~ 27.4	~ 0.09
8-13d	C3H 3	20	15	8	87/29	~ 24.1	~ 0.10
8-13e	C3H 3	20	15	7	43/29	-	-
8-13f	C3H 3	20	15	12	25/25	-	-
8-13g	C3H 3	20	15	9	100/27	(21.0±2.8)	$(0.14^{+.02}_{-.04})$
8-13h	C3H 3	20	15	12	92/29	~ 24.7	~ 0.10
8-13i	C3H 3	20	15	10	70/29	~ 25.3	~ 0.10
8-17	C3H 1	100	10 (20)	8 (17)	100/17 (94/30)	(12.4±2.3)	$0.80^{+.27}_{-.18}$
12-2	CFW 3	100	20	15[1]	0/83[2]	-	-
71-1	C3H 1	20	30	30	83/64	(39.0±5.6)	$0.18^{+.04}_{-.06}$
71-1	C3H 1	100	15	14	100/16	(11.1±1.5)	$0.93^{+.23}_{-.15}$
71-2	C3H 1	20	30	28	93/59	(34.6±5.0)	$0.22^{+.03}_{-.08}$
8-24	C3H 3	50	30	22	0/40	-	

[1] Number of animals alive after 33 weeks.
[2] Painting discontinued after 41 weeks.

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

PROCESS	API SAMPLE NUMBER	P R O D U C T
Distillation (1 plate vacuum)	12-4	Aromatics b. 510-740°F. (corrected)
"	12-5	Aromatics b. ~900-1000°F. (5 g./100 ml. benzene)
"	12-6	Aromatics residue; b. > 1000°F. (5 g./100 ml. benze

TABLE I

SKIN PAINTING EXPERIMENTS ON HIGH BOILING SAMPLES

API SAMPLE NUMBER	BIOLOGICAL DATA						
	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%F.L.in wks)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
12-4*	CFW 3	100	10 (20)	10 (16)	60/34 (56/34)	(27.2±13.2)	$(0.09^{+.09}_{-.05})$
12-5	CFW 3	100	10 (20)	6 (12)	100/34 (92/34)	(23.6±5.8)	$0.07^{+.04}_{-.01}$
12-6	CFW 3	100	10 (20)	8 (12)	75/39 (67/33)	(32.2±12.1)	$0.05^{+.04}_{-.01}$

TABLE II

CONCENTRATION STANDARDS WITH METHYLCHOLANTHRENE IN BENZENE

API SAMPLE NUMBER	CONCENTRATION (g./100g.)	DOSAGE PER APPLICATION (mg.)	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE OF METHYLCHOLANTHRENE (mg./standard area[1]/week)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% EL. in wks.)	STARTING DATE
228	0	100	C3H 3	0	20	18[2]	0/101	-	12/4/50
201	0.011	100	C3H 3	0.033	10	9	44/71	72.6±9.2	7/20/49
203	0.086	100	C3H 3	0.258	10	9	100/34	26.2±3.4	5/20/49
203	0.086	100	C3H 3	0.258	20	20	85/35	29.9±2.2	10/9/50
219*	0.114	100	C3H 3	0.342	30	28	96/35	24.0±2.4	4/14/50
243*	0.148	100	C3H 3	0.444	20	20	100/24	17.9±2.0	7/28/51
243	0.148	20	C3H 3	0.444	20	19	100/26	18.2±2.1	10/1/51
204	0.171	100	C3H 3	0.513	10	10	100/21	15.7±1.6	5/20/49

1. Area covered by 0.1 gram Benzene.
2. Number of animals alive after 36 weeks.

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TABLE II

CONCENTRATION STANDARDS WITH METHYLCHOLANTHRENE IN BENZENE

API SAMPLE NUMBER	CONCENTRATION (g./100g.)	DOSAGE PER APPLICATION (mg.)	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE OF METHYLCHOLANTHRENE (mg./standard area[1]/week)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% EL. in wks.)	STARTING DATE
204	0.171	20	C3H 3	0.513	20	20	100/21	16.6±1.2	9/26/52
204	0.171	20	C3H 3	0.513	20	20	100/21	16.4±1.1	9/26/52
204	0.171	20	C3H 3	0.513	20	20	100/21	14.1±1.8	10/28/52
205	0.342	100	C3H 3	1.026	10	10	100/14	11.0±1.9	5/20/49
206	0.685	100	C3H 3	2.055	10	10	100/16	6.7±4.2	7/20/49
238	0.228	20	C3H 2	0.456	20	20	100/27	18.7±2.3	10/2/51
268	0.286	20	C3H 2	0.572	20	19	100/21	(17.6±1.1)	2/13/53
205	0.342	100	C3H 2	0.684	20	20	100/20	15.1±1.5	6/9/50

1. Area covered by 0.1 gram Benzene.

API 05676

TABLE II

CONCENTRATION STANDARDS WITH METHYLCHOLANTHRENE IN BENZENE

API SAMPLE NUMBER	CONCENTRATION (g./100g.)	DOSAGE PER APPLICATION (m.)	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE OF METHYLCHOLANTHRENE (mg./standard area[1]/week)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%EL. in wks.)	STARTING DATE
227*	0.114	100	C3H 1	0.114	20	19	87/49	44.6±2.5	3/22/50
205*	0.342	100	C3H 1	0.342	10 (20)	10 (19)	100/28 (100/35)	21.0±3.4 (22.4±2.7)	6/13/50
209	0.514	20	C3H 1	0.514	20	20	100/24	18.3±1.9	10/4/51
220	1.027	100	C3H 1	1.027	20	20	100/18	9.7±1.6	5/3/50

1. Area covered by .1 gram Benzene.

API 05677

TABLE II

CONCENTRATION STANDARDS WITH METHYLCHOLANTHRENE IN BENZENE

API SAMPLE NUMBER	CONCENTRATION (γ/1.04 c.)	VOLUME APPLIED (cc.)	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE OF METHYLCHOLANTHRENE (mg./std. area[1]/wk.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (S.E. in wks.)	STARTING DATE
228	0	100	CFW 3	0	20	16[2]	0/62	-	12/4/50
210	0.023	100	CFW 3	0.069	10 (20)	7 (14)	86/47 (79/53)	(25.9±11.3)	2/3/50
203	0.086	100	CFW 3	0.258	10	9	100/23	(17.1±3.5)	3/20/49
203	0.086	100	CFW 3	0.258	10 (20)	7 (16)	100/31 (75/31)	(22.5±4.3)	10/9/50
213*	0.114	100	CFW 3	0.342	10 (20)	10 (16)	100/20 (100/33)	(16.1±2.3)	1/14/50
204	0.171	100	CFW 3	0.513	10	9	100/16	(11.9±2.7)	3/20/49
205	0.342	100	CFW 3	1.026	10	10	100/24	(14.3±4.1	3/20/49
205	0.342	100	CFW 1	0.342	19	17	100/30	(21.9±3.0)	9/13/50
206	0.685	100	CFW 1	0.685	20	17	100/27	(19.5±2.5)	9/13/50

1. Area covered by 0.1 c. benzene.
2. Number of animals still alive after 33 weeks.

API 05678

TABLE II

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF METHYLCHOLANTHRENE IN SEC.-AMYLBENZENE TO THE SKIN OF MICE

API SAMPLE NUMBER	CONCENTRATION (g./100 g.)	STRAIN OF MICE	NUMBER OF APPLICATIONS[1] PER WEEK	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
224*	0	CFW	3	30	23	17/59	-	-
223	0.087	CFW	3	10 (20)	9 (18)	89/46 (83/46)	32.3 ± 10.2	$0.05^{+.03}_{-.02}$
223	0.087	C3H	3	20	16	81/46	40.8 ± 3.8	$0.05 \pm .01$
222	0.174	CFW	3	19	19	100/33	23.6 ± 2.2	$0.08^{+.01}_{-.02}$
222	0.174	C3H	3	10 (20)	10 (20)	100/28 (100/44)	23.9 ± 2.5	$0.10^{+.02}_{-.01}$

1. Dosage per application was 100 mg.

API 05679

TABLE II

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF METHYLCHOLANTHRENE IN VARIOUS SOLVENTS TO THE SKIN OF MICE

API SAMPLE NUMBER	STARTING DATE	CARCINOGEN[1]	SOLVENT	CONCENTRATION (g./100 g. solvent)	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./wks.)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in weeks)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
218	2/3/50	MC	API-5[2]	0.306	C3H 3	100	20	17	100/30	(24.9±1.4)	$0.10^{\pm.01}$
218	2/3/50	MC	API-5	0.306	CFW 3	100	10 (20)	9 (16)	89/25 (81/29)	(21.6±3.8)	$0.08^{+.03}_{-.01}$
246	3/22/52	MC	API 112-1[3]	0.209	C3H 3	20	20	20	100/22	15.1±1.2	$0.20^{+.03}_{-.02}$
246	4/11/52	MC	API 112-1	0.209	C3H 3	20	20	18	100/21	15.0±1.4	$0.20^{+.03}_{-.02}$
248	4/11/52	MC	API 110-1[3]	0.204	C3H 3	20	20	20	100/22	(16.7±1.2)	$0.18^{+.01}_{-.02}$
281	11/12/51	MC	Cottonseed oil	0.041	C3H 3	100	38	37	62/69	49.0±4.4	$0.03^{\pm.01}$

1. 20-Methylcholanthrene (MC).
2. Wilmington Residuum; see page 18 of Table I for description.
3. See page 19 of Table I for description.

API 05680

TABLE II

CONTROL EXPERIMENTS WITH VARIOUS SOLVENTS

API SAMPLE NUMBER	SOLVENT	NUMBER OF APPLICATIONS[4] PER WEEK	STRAIN OF MICE	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	INCIDENCE OF GROSS CARCINOMA (percent/weeks)	STARTING DATE
80	White oil	3	C3H	30	26[1]	0/78	0/78	8/7/51
95	White oil	3	CFW	33	26[2]	0/78	0/78	7/28/51
221*	Dodecyl-benzene	3	C3H	20	18	33/37	0/52	5/5/50
221[3]	Dodecyl-benzene	3	C3H	30	0	0/14	0/14	2/27/53
224*	Sec.-amyl-benzene	3	CFW	30	23	17/59	0/71	7/14/50
228	Benzene	3	C3H	20	18[1]	0/101	0/101	12/4/50
228	Benzene	3	CFW	20	16[2]	0/62	0/62	12/4/50
241	Distilled water	3	C3H	40	30[1]	0/78	0/78	7/28/51
241	Distilled water	3	CFW	17	12[2]	0/70	0/70	7/28/51

1. Number of animals alive after 36 weeks.
2. Number of animals alive after 33 weeks.
3. Age of animals at start of experiment, 54 weeks.
4. Dosage per application was 100 mg.

API 05681

TABLE III

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF SYNTHETIC CARCINOGENS[1] IN DODECYLBENZENE[2] TO THE SKIN OF MICE

API SAMPLE NUMBER	CONCENTRATION (g./100g.)	STRAIN OF MICE	NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./wks.)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%F.L. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
221*	0	C3H	3	100	20	18	33/37	-	-
221[3]	0	C3H	3	100	30	0	0/14	-	-
226	0.006	CFW	3	100	20	17	41/54	-	-
226*	0.006	C3H	3	100	10 (20)	8 (12)	63/38 (50/40)	35.2±11.1	-
225*	0.011	CFW	3	100	10 (20)	8 (14)	100/54 (79/54)	43.3±16.1	$0.04^{+.02}_{-.01}$
225*	0.011	C3H	3	100	20	15	87/43	34.0±4.0	0.06±.01
213*	0.046	CFW	3	100	20	15	100/18	10.5±1.7	$0.45^{+?}_{-.19}$
211	0.114	CFW	3	100	8	7	100/17	11.5±2.9	$0.31^{+?}_{-.14}$
211	0.114	C3H	3	100	20	20	100/22	10.9±2.0	$0.32^{+.11}_{-.07}$
208	0.149	C3H	3	100	30	30	100/15	10.3±.7	$0.35^{+.04}_{-.03}$

1. The carcinogen was methylcholanthrene in every case except API-245, in which case 3,4-benzpyrene was used.
2. Product obtained by alkylation of benzene with the propylene tetramer (aluminum chloride catalyst).
3. Age of mice at start of experiment, 54 weeks.
4. No gross or microscopic evidence of invasive malignancy.

API 05682

TABLE III

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF CARCINOGENS[1] IN DODECYLBENZENE[2] TO THE SKIN OF MICE

API SAMPLE NUMBER	CONCENTRATION (g./100g.)	STRAIN OF MICE	NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./wks.)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%F.L.in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
249	0.172	C3H	3	20	20	18	89/14	10.4 ± 1.4	$0.34^{+.09}_{-.06}$
249	0.172	C3H	3	100	13 (20)	13 (16)	100/12 (100/12)	9.1 ± 1.2	$0.42^{+.11}_{-.07}$
212	0.344	C3H	3	100	10 (20)	10 (19)	100/14 (100/18)	10.2 ± 2.1	$0.35^{+.15}_{-.08}$
245[1]	0.172	C3H	3	100	20	18	100/19	11.3 ± 2.0	$0.30^{+.11}_{-.06}$
245[1]	0.172	C3H	3	20	15	13	100/31	17.0 ± 3.7	$0.17^{+.07}_{-.04}$
245[1]	0.172	C3H	3	5	10 (15)	9 (11)	100/23 (100/23)	16.4 ± 2.7	$0.17^{+.06}_{-.03}$

1. The carcinogen was methylcholanthrene in every case except API-245, in which case 3,4-benzpyrene was used.
2. Product obtained by alkylation of benzene with propylene tetramer (aluminum chloride catalyst).

API 05683

TABLE III

EXPERIMENTS ON ACCELERATION OF CARCINOGENESIS BY SPECIFIC SOLVENTS[1]

API EXPERIMENT NUMBER	DESCRIPTION OF EXPERIMENT: MATERIALS APPLIED TO MICE DURING FIRST SIX WEEKS OF EXPERIMENT	DESCRIPTION OF EXPERIMENT: MATERIALS APPLIED TO MICE DURING SEVENTH WEEK TO END OF EXPERIMENT	STRAIN OF MICE	NUMBER OF APPLICATIONS[6] PER WEEK	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)[3]	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%FL in wks)[3]
221*	DDB	DDB	C3H	3	20	18	33/37	-
9*	API-9[2]	API-9	CFW	3	10 (20)	10 (16)	100/40 (100/41)	28.4±4.1
9*	API-9	API-9	C3H	3	10	9	100/47	36.2±4.5
221-9*	DDB	API-9	C3H	3	20	20	100/21	14.0±2.1
221-9	DDB	API-9	C3H	3	14 (20)	11 (14)	100/22 (100/22)	14.2±2.6
253-9	PDD	API-9	C3H	3	7 (20)	6 (17)	100/20 (94/26)	12.8±4.8
57*	API-57[2,4]	API-57	CFW	6	20	17	100/25	16.9±2.0
221-57*	DDB	API-57	CFW	6	20	18	100/16	8.0±1.9
208	API-208[5]	API-208	C3H	3	30	30	100/15	10.3±.7
221-208	DDB	API-208	C3H	3	20	20	100/14	7.2±1.4

1. Dodecylbenzenes obtained by alkylation of benzene with 12-carbon olefins; DDB obtained with propylene tetramer; 2-phenyldodecane (PDD) obtained with 1-dodecene.
2. See Table I for description.
3. Time measured from date of initial painting with carcinogenic material.
4. Hair clipped.
5. See Table II for description.
6. Dosage per application was 100 mg.

API 05684

TABLE III

EXPERIMENTS ON ACCELERATION OF CARCINOGENESIS BY SPECIFIC SOLVENTS[1]

API EXPERIMENT NUMBER	DESCRIPTION OF EXPERIMENT: MATERIALS APPLIED TO MICE DURING FIRST SIX WEEKS OF EXPERIMENT	SINGLE APPLICATION[2] IN SEVENTH WEEK	NINTH WEEK TO END OF EXPERIMENT	STRAIN OF MICE	NUMBER OF APPLICATIONS[8] PER WEEK	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)[7]	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%FL in wks.)[7]
229	Nil	API-229[3,4]	Nil	C3H	-	40	40	12/13	-
230 *	Nil	API-229[4]	DDB	C3H	3	40	36	94/34	12.8±2.8
231	Nil	API-8[4,5]	Nil	C3H	-	45	34[6]	0/64	-
232	Nil	API-8[4]	DDB	C3H	3	45	34	56/26	-
236	DDB	API-8	DDB	C3H	3	30	26	31/30	-
237	DDB	API-229	DDB	C3H	3	40	38	87/22	11.2±2.5
239	Nil	API-8[4]	water	C3H	3	30	21[6]	0/79	-
240	Nil	API-8[4]	white oil, API-80	C3H	3	30	18[6]	0/79	-

1. Dodecylbenzenes obtained by alkylation of benzene with 12-carbon olefins; DDB obtained with propylene tetramer; 2-phenyldodecane (PDD) obtained with 1-dodecene.
2. Single application followed by two week interval before further treatment of mice.
3. Solution of 0.5 g. 9,10-dimethyl-1,2-benzanthracene in 100 ml. sec.-amylbenzene.
4. Hair clipped.
5. See Table I for description.
6. Number of animals alive after 63 weeks.
7. Time measured from date of initial painting with carcinogenic material.
8. Dosage per application was 100 mg.

API 05685

TABLE III

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF BENZPYRENE IN VARIOUS SOLVENTS TO THE SKIN OF C3H MICE

API SAMPLE NUMBER	STARTING DATE	SOLVENT	CONCENTRATION (g./100ml.)	NUMBER OF APPLICATIONS PER WEEK	DOSAGE OF SOLUTION PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./wks.)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in weeks)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
2hh	3/14/51	Benzene	0.15	3	100	7 (20)	7 (20)	100/33 (100/33)	22.1 ± 5.8 (25.1 ± 2.5)	$0.12^{+.06}_{-.04}$ $0.10^{+.01}_{-.02}$
244	9/1953	Benzene	0.15	3	20	20				
264	12/19/52	API-80[1]	0.15	3	100	20	19	100/31	(25.5 ± 1.3)	$0.10\pm.01$
264	12/19/52	API-80	0.15	3	20	20	18	100/31	(25.4 ± 1.5)	$0.10^{+.01}_{-.02}$
258	11/6/52	API-80	0.20	1	50	30	20	85/41	~ 36.0	~ 0.17
257	11/6/52	API-8-24 (fraction[2] of API-8)	0.20	1	50	20	16	88/41	~ 35.7	~ 0.17
246	1/16/53	fraction of API-8-19 diluted 50% with benzene	0.15	3	100	15	13	62/30	~ 28.7	~ 0.08

1. Technical white oil, viscosity ~100 SSU/100°.
2. Colorless fraction from chromatography; see pages 24 and 22 for description.

API 05686

TABLE III

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF BENZPYRENE IN VARIOUS SOLVENTS TO THE SKIN OF C3H MICE

API SAMPLE NUMBER	STARTING DATE	SOLVENT	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE OF SOLUTION[1] PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./wks.)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in weeks)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
276-1	2/13/53	Fraction b.520-600° F./760 mm. from distillation of API-80	C3H 3	(20-50)[2]	(12-6)[2]	6	100/22	(16.6±3.4)	$0.18^{+.06}_{-.05}$
276-2	2/13/53	Fraction b.600-630° F./760 mm. from distillation of API-80	C3H 3	(20-50)[2]	(12-6)[2]	6	100/22	(17.4±4.5)	$0.20^{+.05}_{-.08}$
276-3	2/13/53	Fraction b.630-645° F./760 mm. from distillation of API-80	C3H 3	(30-50)[2]	(12-6)[2]	5	100/22	(18.1±3.3)	$0.17^{+.01}_{-.04}$
276-4	2/13/53	Fraction b.645-655° F./760 mm. from distillation of API-80	C3H 3	(30-50)[2]	(12-6)[2]	6	67/26	~ 25.5	~ 0.09
276-5	2/13/53	Fraction b.655-700° F./760 mm. from distillation of API-80	C3H 3	100	15	15	87/27	~22.9	~ 0.11
276-6	6/12/53	Silica gel chromatography of distillation residue b. > 720°F./760 mm. of API-80	C3H 3	50	15	15	0/10	-	-

1. Concentration of benzpyrene in solution was 0.15 g./100 ml. solvent.
2. After 4 weeks the dosage was increased to 50 mg. and the number of mice was reduced to 6.

API 05687

TABLE VII

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF BENZPYRENE IN VARIOUS SOLVENTS TO THE SKIN OF C3H MICE

API SAMPLE NUMBER	STARTING DATE	SOLVENT	NUMBER OF APPLICATIONS PER WEEK	DOSAGE OF SOLUTION[1] PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS T.I./wks.	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
		SATURATED FRACTIONS FROM CATALYTICALLY CRACKED RESIDUUM							
277-1	3/9/53	Fraction b.430-500°F./760mm. from distillation of colorless fraction of API-71[2]	3	30	8	7	100/17	(13.5±2.2)	$0.23^{+.07}_{-.04}$
277-3	3/9/53	Fraction b.550-565°F./760mm. from distillation of colorless fraction of API-71[2]	3	20	6	6	83/18	12.7±8.7	$0.26^{+?}_{-.14}$
277-4	3/9/53	Fraction b.580-600°F./760mm. from distillation of colorless fraction of API-71[2]	3	40	8	8	88/19	~16.1	~0.18
277-5	3/9/53	Fraction b.600-620°F./760mm. from distillation of colorless fraction of API-71[2]	3	50	8	8	75/24	~20.5	~0.13

1. Concentration of benzpyrene in solution was 0.15 g./100 ml. solvent.
2. Colorless fraction of API-71 obtained by chromatography on silica gel.

API 05688

TABLE III

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF BENZPYRENE IN VARIOUS SOLVENTS TO THE SKIN OF C3H MICE

API SAMPLE NUMBER	STARTING DATE	SOLVENT	NUMBER OF APPLICATIONS PER WEEK	DOSAGE OF SOLUTION[1] PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS T.I./wks.	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
		PARAFFINS							
269	3/9/53	Cetane (chromatographed on silica gel)	3	50	15	11	36/10	-	-
278	7/24/53	n-decane	3	50	20	20	0/4	-	-
		CYCLOPARAFFINS							
263	12/19/52	Cyclohexyldecane, API-256	3	20	20	19	95/20	~ 13.1	~ 0.25
279	9/1953	7-cyclohexyltridecane, PSC-504	3	40	8				
		ALKYLNAPHTHALENES							
265	2/5/53	Dibutylmethylnaphthalene	3	20	15 (20)	11 (16)	100/22 (100/25)	(16.3±2.1)	$0.18^{+.04}_{-.03}$
272	6/12/53	Monoamylnaphthalenes, b. 570°F./760 mm.	3	40	6	6	0/10	-	-
273	6/12/53	Diamylnaphthalenes, b.630-690°F./760 mm.	3	50	9	7	14/10	-	-

1. Concentration of benzpyrene in solution was 0.15 g./100 ml. solvent.

API 05689

TABLE III

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF BENZPYRENE IN VARIOUS SOLVENTS TO THE SKIN OF C3H MICE

API SAMPLE NUMBER	STARTING DATE	SOLVENT	NUMBER OF APPLICATIONS PER WEEK	DOSAGE OF SOLUTION[1] PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS T.I./wks.	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in weeks)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
		ALKYLBENZENES							
275	6/12/53	Triisopropylbenzene	3	50	11	8	0/9	-	-
262	11/19/52	1-phenyldecane, API-255	3	20	19	19	95/16	(9.8 ± 1.5)	$0.37^{+.12}_{-.07}$
245	12/3/51	Dodecylbenzene[2]	3	100	20	18	100/19	(11.3 ± 2.0)	$0.30^{+.11}_{-.06}$
245	11/21/52	Dodecylbenzene	3	20	15	13	100/31	(17.0 ± 3.7)	$0.17^{+.07}_{-.04}$
245	11/21/52	Dodecylbenzene	3	5	10 (15)	9 (11)	100/23 (100/23)	(16.4 ± 2.7)	$0.17^{+.06}_{-.03}$
259	11/21/52	20% Dodecylbenzene in API-80	3	100	15	13	100/32	(26.7 ± 1.5)	$0.10^{+.01}_{-.02}$
260	11/21/52	5% Dodecylbenzene in API-80	3	100	15	15	100/33	28.1 ± 1.6	$0.08 \pm .01$

1. Concentration of benzpyrene in solution was 0.15 g./100 ml. solvent.
2. Product from alkylation of benzene with propylene tetramer (aluminum chloride catalyst).

API 05690

TABLE III

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF BENZPYRENE IN VARIOUS SOLVENTS TO THE SKIN OF C3H MICE

API SAMPLE NUMBER	STARTING DATE	SOLVENT	NUMBER OF APPLICATIONS PER WEEK	DOSAGE OF SOLUTION[1] PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./wks.)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in wks.)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
		ALKYLBENZENES							
274-8	6/12/53	Fraction b.450-500°F./760mm. from distillation of alkylbenzene[2]	3	40	8	7	0/9	-	-
274-13	6/12/53	Fraction b.555-560°F./760mm. from distillation of alkylbenzene	3	50	9	9	78/9	≈ 8.6	≈ 0.46
267-1	1/31/53	Fraction b.603-642°F./760mm. from distillation of alkylbenzene (PDDB)[3]	3	20	15	11	91/27	≈ 22.5	≈ 0.11
267-3	1/31/53	Fraction b.655-683°F./760mm. from distillation of PDDB	3	20	15	12	42/28	-	-
267-5	1/31/53	Fraction b.664-730°F./760mm. from distillation of PDDB	3	20	15	12	33/29	-	-
267-8	1/31/53	Fraction b.659-760°F./760mm. from distillation of PDDB	3	20	15	13	46/28	-	-

1. Concentration of benzpyrene in solution was 0.15 g./100 ml. solvent.
2. Product of alkylation of benzene with propylene polymer.
3. Residual by-product of commercial alkylation of benzene with propylene tetramer.

API 05691

TABLE III

EXPERIMENTS TO DETERMINE WHETHER CERTAIN MATERIALS HAVE IRRITATIONAL PROPERTIES OF THE TYPE EVIDENCED BY DODECYLBENZENE

API SAMPLE NUMBER	DESCRIPTION OF EXPERIMENT	IRRITATION LIKE DODECYL-BENZENE	SEVERITY OF EARLY ACANTHOSIS AND HYPERKERATOSIS	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	NUMBER OF MICE
221	Dodecylbenzene[3]	yes	heavy	C3H 3	100	20
221	Dodecylbenzene	yes	heavy	C3H 3	100	30[1]
221-1	11-42% fraction obtained from chromatography of No. 221 on alumina	yes	heavy	C3H 3	20	3
221-2	42-84% fraction obtained from chromatography of No. 221 on alumina	yes	heavy	C3H 3	20	3
221-3	20% Dodecylbenzene in API-80[2]	no	nil	C3H 3	100	6
221-4	40% Dodecylbenzene in API-80	no	nil	C3H 3	100	7
221-5	60% Dodecylbenzene in API-80	yes	medium	C3H 3	100	7
221-6	80% Dodecylbenzene in API-80	yes	heavy	C3H 3	100	6
253	2-phenyldodecane	yes	medium	C3H 3	100	20
254	1-phenyldodecane	yes	slight	C3H 3	20	7

1. Age of mice at start of experiment, 54 weeks.
2. See page 32 of Table II for description.
3. Product from alkylation of benzene with propylene tetramer (aluminum chloride catalyst).

API 05692

TABLE III

EXPERIMENTS TO DETERMINE WHETHER CERTAIN MATERIALS HAVE IRRITATIONAL PROPERTIES OF THE TYPE EVIDENCED BY DODECYLBENZENE

API SAMPLE NUMBER	DESCRIPTION OF EXPERIMENT	IRRITATION LIKE DODECYL-BENZENE	SEVERITY OF EARLY ACANTHOSIS AND HYPERKERATOSIS	STRAIN OF MICE AND NUMBER OF APPLICA-TIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	NUMBER OF MICE
255	1-phenyldecane	yes	medium	C3H 3	20	7
256	1-cyclohexyldecane	yes	slight	C3H 3	20	7
280	α-methylnaphthalene	yes	medium	C3H 3	100	5
71-3a	Material from cold trap of distillation of API-71-3[1](0-2.5%)	yes	medium	C3H 3	100	3
71-3b	Fraction b.465-530°F./760 mm. from distillation of API-71-3(2.5-6%)	yes	heavy	C3H 3	100	3
71-3c	Fraction b.530-610°F./760 mm. from distillation of API-71-3(6-11%)	yes	medium	C3H 3	100	3
71-3d	Fraction b.610-670°F./760 mm. from distillation of API-71-3(11-18.7%)	no	nil	C3H 3	100	3
71-3e	Fraction b.670-690°F./760 mm. from distillation of API-71-3(18.7-26%)	no	nil	C3H 3	100	3
221	Dodecylbenzene	yes	heavy[2]	rabbit 3	300	2

[1]. Colorless fraction obtained by chromatography of API-71, TCC residuum.

[2] Severe crusting comparable to that in mice but occurring between the 9th and 15th week (approximately double the time required for the mice).

API 05693

TABLE III

EXPERIMENTS TO DETERMINE WHETHER CERTAIN MATERIALS HAVE IRRITATIONAL PROPERTIES OF THE TYPE EVIDENCED BY DODECYLBENZENE

API SAMPLE NUMBER	DESCRIPTION OF EXPERIMENT	IRRITATION LIKE DODECYL-BENZENE	SEVERITY OF EARLY ACANTHOSIS AND HYPERKERATOSIS	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	NUMBER OF MICE
276-1,2	Solutions of benzpyrene in fractions b. 520-630° of technical white oil	yes	slight	C3H 3	20	12
276-3	Solution of benzpyrene in fraction b.630-645° of technical white oil	yes	very slight	C3H 3	30	12
276-4	Solution of benzpyrene in fraction b.645-655° of technical white oil	no	(scaling only)	C3H 3	30	12
276-5	Solution of benzpyrene in fraction b.655-700° of technical white oil	no	nil	C3H 3	100	15
276-6	Solution of benzpyrene in fraction b. >720° of technical white oil	no	nil	C3H 3	50	15
269	Solution of benzpyrene in Cetane	yes	heavy	C3H 3	50	15

API 05694

TABLE IV

EXPERIMENTS INVOLVING A LIMITED NUMBER OF APPLICATIONS OF CARCINOGENIC MATERIALS

API SAMPLE NUMBER	DESCRIPTION	STRAIN OF MICE AND NUMBER OF APPLICATIONS PER WEEK	DOSAGE PER APPLICATION (mg.)	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./wks.)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%F.L. in wks.)
43-1[1]	Dewaxed oil from MEK-Benzol dewaxing of F.C.C. decanted oil No. 43	C3H 2	20	20	19	0/6	-
43-1[2]	"	C3H 2	20	20	18	0/6	-
43-1[3]	"	C3H 2	20	20	20	0/6	-
71[1]	T.C.C. cracked residuum	C3H 2	20	20	20	0/6	-
71[2]	"	C3H 2	20	19	19	0/6	-
71[3]	"	C3H 2	20	20	20	0/6	-
83-2	Aromatics by chromatography from API-83[4] plus 30.6% by weight of sec.-amylbenzene	C3H 1	100	13 (20)	12 (18)	83/145[5] (83/45)	34.6±8.4
276-1, 2, 3, 4	0.15 g. benzpyrene /100 ml. of fractions of API-80 b. 520 to 655°	C3H 3	20	24 (6 each)	13	0/28[6]	-

[1] Painting continued until last animal dies.
[2] Painting of all animals discontinued at time first animal in group developed a papilloma.
[3] Painting of each animal discontinued at time of appearance of papilloma in the individual animal.
[4] See page 24 for description.
[5] Painting discontinued after 19 treatments.
[6] Painting discontinued after 11 treatments.

API 05695

TABLE V

EXPERIMENTS ON THE RETARDATION OF TUMOR FORMATION BY WASHING - CFW MICE

API EXPERIMENT NUMBER	CARCINOGENIC OIL APPLIED	NUMBER OF APPLICATIONS[2] PER WEEK	HAIR CLIPPED	PERIOD OF EXPOSURE TO OIL BEFORE REMOVAL BY WASHING	WASHING AGENT	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%F.L. in wks)
8	8[1]	1	no	Control (no washing)	none	10 (20)	9 (13)	100/26 (92/26)	13.3±4.6
300	8	1	no	10 min.	soap solution	9	0	0/81	-
301	8	1	no	1 hour	soap solution	10	7	14/36	-
302*	8	1	no	4 hours	soap solution	9	8	63/70	(61.6±26.2)
12	12[1]	3	yes	Control (no washing)	none	15	14	100/14	10.7±.9
303	12	3	yes	1 hour	soap solution	15	14	100/40	27.3±3.6
304*	12	3	yes	9 hours	soap solution	15	11	100/21	17.1±1.3

1. See Table I for description.
2. Dosage per application was 100 mg.

API 05696

TABLE V

EXPERIMENTS ON THE RETARDATION OF TUMOR FORMATION BY WASHING - CFW MICE

API EXPERIMENT NUMBER	CARCINOGENIC OIL APPLIED	NUMBER OF APPLICATIONS[3] PER WEEK	HAIR CLIPPED	PERIOD OF EXPOSURE TO OIL BEFORE REMOVAL BY WASHING	WASHING AGENT	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5%FL. in wks.)
305	8[1]	3	yes	20 min.	detergent solution	20	14	93/51	41.9±3.8
306	8	3	yes	1 hour	detergent solution	20	17	94/44	34.0±2.9
307	8	3	yes	1 hour	white oil-detergent[2]	20	20	85/33	26.6±2.3
308	8	3	yes	20 min.	white oil	20	15	100/52	31.9±4.9
113	113[1]	3	yes	Control (no washing)	none	20	18	94/36	(16.3±5.0)
309	113	3	yes	1 hour	detergent solution	19	14	43/67	-
310	113	3	yes	4 hours	detergent solution	20	13	54/57	-
311	113	3	yes	4 hours	white oil-detergent[2]	20	12	83/52	45.3±4.6

1. See Table I for description.
2. White oil rinse followed by washing with detergent solution.
3. Dosage per application was 100 mg.

API 05697

TABLE V

EXPERIMENTS ON THE RETARDATION OF TUMOR FORMATION BY WASHING - C3H MICE

API EXPERIMENT NUMBER	CARCINOGENIC OIL APPLIED	NUMBER OF APPLICATIONS[1] PER WEEK	HAIR CLIPPED	PERIOD OF EXPOSURE TO OIL BEFORE REMOVAL BY WASHING	WASHING AGENT	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (50%T.I. in wks)
56[2]	56[3]	3	yes	Control (no washing)	none	20	20	0/16	-
56	56	3	yes	Control (no washing)	none	20	20	15/16	-
314	56	3	yes	7 hours	detergent solution	20	19	0/16	-
113	113[3]	3	no	Control (no washing)	none	27 (40)	27 (36)	100/23 (100/25)	16.3±1.3 (17.5±1.3)
315	113	3	yes	7 hours	detergent solution	20	20	0/16	-
316	none	3	yes	none	detergent solution	20	20	0/16	-
317	none	3	yes	none	white oil-detergent[4]	20	20	0/16	-

1. Dosage per application was 100 mg. except where otherwise indicated.
2. Dosage per application was 20 mg.
3. See Table I for description.
4. White oil rinse followed by washing with detergent solution.

API 05698

TABLE V

EXPERIMENTS ON THE RETARDATION OF TUMOR FORMATION BY WASHING - CFW MICE

API EXPERIMENT NUMBER	DESCRIPTION OF EXPERIMENT	NUMBER OF APPLICATIONS[1] PER WEEK	HAIR CLIPPED	ORIGINAL NUMBER OF MICE	FINAL EFFECTIVE NUMBER OF MICE	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (%EL. in wks)
312	Barrier cream applied 9:00 AM API-8 applied 11:00 AM Removal of oil by by washing with detergent solution 12:00 AM	3	yes	10 (20)	7 (10)	71/45 (70/45)	($42.3^{+}6.0$)
313	Barrier cream applied 9:00 AM API-8 applied 11:00 AM API-8 applied 2:00 PM Removal of oil by washing with detergent solution 4:30 PM	3	yes	20	13	100/31	$24.6^{+}2.7$

1. Dosage per application was 100 mg.

API 05699

MEMORANDUM

September 1, 1953

SUBJECT: RECEIPTS, EXPENDITURES, AND ALLOCATIONS -- API MEDICAL RESEARCH FUND

Contributions Received

1945	$ 28,900.00	
1947	27,800.00	
1948	98,300.00	
1949	64,340.00	
1950	94,840.00	
1951	97,460.00	
1952	104,285.00	
1953	79,056.00	
TOTAL		$594,981.00

Expenditures Made Prior to September 1, 1953

Harvard University			
Toxicological Reviews	$ 40,253.73		
Cutting Oil Study	2,500.00		
		? 42,753.73	
University of Cincinnati			
Carcinogenicity	436,506.91		
Fluorine Study	14,000.00		
Physiology of Skin	12,500.00		
		463,006.91	
Philip Drinker		? 15,300.00	
Miscellaneous		512.17	
TOTAL EXPENDITURES			521,572.31
BALANCE ON DEPOSIT SEPTEMBER 1, 1953			$ 73,408.19

ESSO LABORATORIES
STANDARD OIL DEVELOPMENT COMPANY
P. O. BOX 51, LINDEN, N. J.

MEDICAL RESEARCH DIVISION
ROBERT E. ECKARDT, PH D., M D.
DIRECTOR
HORACE W. GERARDE, PH D., M D.
HEAD TOXICOLOGIST

INDUSTRIAL HYGIENE SECTION
NATHAN V. HENDRICKS, CH.E.
HEAD OF SECTION
FRANKLIN W. CHURCH, M.S.
GEORGE M. WILKENING, M.S.
INDUSTRIAL HYGIENISTS

September 22, 1953

Dr. Pfeffer Davis
Phillips Petroleum Company
Bartlesville, Oklahoma

Dear Dr. Davis:

As new Chairman of the RPA Committee, I have prepared the attached report summarizing the activities of the Kettering Laboratory as I see them to the present time. It would be my intention to present this to the Subcommittee on Carcinogenicity meeting in Houston as a formal report of our RPA Committee to the Subcommittee. Because of the unavailability of time to obtain approval from each of the RPA Committee members, I am unable to claim this as a full RPA Committee report. However, I plan to arrive in Houston at about two o'clock Monday afternoon, September 28th, and have a reservation at the Shamrock Hotel beginning in the evening. I would be happy to go over this report with any and/or all members of the RPA Committee that evening in order to introduce any corrections or suggestions that might seem warranted, or, if the Committee so decides, to abandon this report altogether. For any members of the RPA Committee who will not be in Houston Monday evening, I would suggest that they write me their criticisms and suggestions at the Shamrock Hotel and they will be taken into consideration at the discussions which the rest of the Committee will hold that evening.

I am sending three copies of this report to Dr. Horton with the suggestion that if he has any comments which he feels I should have included in this report, or if he disagrees with our interpretation of the work of the Kettering Laboratory, he will be in a position to advise me of the opinion of the Laboratory Monday evening in Houston. The two extra copies of the report being sent to Dr. Horton are for Dr. Kehoe and Dr. Phair.

I realize that this report cannot be a complete summary of all of the work done by the Kettering Laboratory, otherwise it would have to be too long, but I do feel that it represents, at least in my mind, the important observations which have been made thus far by the Kettering Laboratory, and in the summary emphasizes the important points that should be pursued in the work of the Laboratory. It is my hope that our RPA Committee, if not wishing to accept this report, will deem it advisable to prepare a report somewhat similar to this one which can be submitted to the Subcommittee on Carcinogenesis at the Houston meeting. If it is agreeable with this Committee and with you, it would be my plan to read this report

before the Subcommittee on Tuesday morning and then to have copies made available to each of the members of the Subcommittee on Carcinogenesis following the Houston meeting. Furthermore, it would be my suggestion that the Subcommittee may wish to consider sending a report similar to this to the Medical Advisory Committee with the suggestion that it be forwarded to the Safety Committee of the Board of Directors of the API.

As I have indicated above, the report which I am sending to you now should be considered only as my own rough draft of such a report, representing only my ideas and subject to the approval of the other members of the RPA Committee. I trust that our RPA Committee will be able to come to some agreement on this report Monday evening in Houston prior to the meeting of the Subcommittee on Carcinogenesis.

Sincerely,

R. E. ECKARDT, M. D.

REE:llk

Attachment

cc with attachment: Dr. C. H. Hine
Dr. E. K. Linder
Dr. M. H. Newquist
Mr. E. J. Adams
Dr. L. G. Beard, Jr.
Mr. B. M. Henderson
[illegible]
Dr. A. Wesley Horton (3)
Mr. E. V. Stroop

[illegible]

REPORT OF RPA COMMITTEE SUBMITTED ON SEPTEMBER 29, 1953,

TO SUBCOMMITTEE ON CARCINOGENESIS, API MEDICAL ADVISORY COMMITTEE

SUMMARY OF THE API PROJECT ON CARCINOGENESIS AT KETTERING LABORATORY

The original program of carcinogenic work at Kettering Laboratory grew out of the results obtained from testing a series of 8 oils. The conclusion of this work, reported on November 5, 1948, was that all 8 oils affected the skin. Two of them produced mild irritation, two produced a few verrucous papillomata, one produced papillomas and two questionable cancers, two produced a definite cancer each, and one was highly carcinogenic.

As a result of these preliminary studies, the Kettering Laboratory undertook a more extensive research program under the auspices of the API Medical Advisory Committee designed to 1) survey refining processes and materials which might represent potential hazards from the cancer standpoint, 2) biological testing of indicated oils and tars, 3) chemical research to determine the nature of the carcinogenic components and to develop analytical techniques for their determination, and, 4) an epidermiological program to develop sound information regarding the actual incidence of cancer among employees of the petroleum industry and to determine the efficacy over a period of years of the various safety programs which have been or are being set up by individual oil companies.

To implement this program, it was suggested that materials from a number of processes be studied, in accordance with the outline on pages 2 and 3 of the Kettering report dated October 27, 1950.

Non-accelerating Solvents

In order to have a reference standard to which the results of tests of these oils could be referred, the laboratory undertook a study of the carcinogenicity of solutions of methyl cholanthrene in benzene. For reasons related to well known dose-response phenomena it was decided to use the average latent period for tumor production as a measure of carcinogenicity, the average latent period being defined as the length of time required to reach 50% tumor indices.

In the course of this work with reference standards, it soon became apparent that C3H mice gave fairly reproducible results, whereas CFW mice gave less reproducible results. It was, therefore, decided to standardize the mouse strain and to use only C3H mice in subsequent tests, even though a considerable number of tests on oils with CFW mice had already been started or completed.

In addition, it became apparent that if too strong a solution of methyl cholanthrene is painted on the C3H mice too frequently, the health of the mice, as determined by non-tumor mortality and weight curves, is impaired, and, apparently, their ability to produce tumors is impaired at the same time. In addition, other factors which influence the health of the mice, such as infections, infestations with lice, etc., are also reflected in non-tumor mortality and growth rates, and will seriously affect tumor production. Thus unhealthy animals from any cause do not produce tumors as readily as healthy animals, and the average latent period is prolonged in the unhealthy animals. Since the average latent period is taken as a measure of carcinogenicity, it is obvious that the apparent carcinogenicity of a material could be profoundly influenced by the health of the animals, and misleading results thereby obtained.

The above observations led to the necessity of painting mice once, twice, or three times per week depending on the strength of solution being used, and to the establishment of three or more separate standard curves depending on the frequency of painting. The most recent report from the Kettering Laboratory, however, has shown that these three curves can be united into a single curve when they are expressed in terms of the dose of carcinogen applied per unit area of skin per week. This has necessitated measuring the area of skin covered by a solution of methyl cholanthrene in a solvent. Within limits this has been found to be constant for each solvent tested. The solvents thus far tested have been benzene, hydro-peroxide, free amyl benzene, cotton seed oil, technical white oil and fractions of refinery streams. The effect of these solvents is their effect on the spreading of the solution. Thus if the same amount of the same concentration of methyl cholanthrene in two different solvents were to be painted on the skin 3 times a week, the dose per unit area need not be the same. If one solvent caused the solution to spread over twice the area of the other solvent, the dose per unit area in the first case would be half that in the second case, and the average latent period for the two solutions would be different, leading to different P_{MC} values for the two solutions. The P_{MC} value refers only to concentration of methyl cholanthrene in benzene, and serves only as a reference standard. What this work implies is that it will be necessary in carcinogenic work to determine not only the frequency of application and the amount applied per application, but also the area covered by this amount.

Accelerating Solvents

What has been said above applies only to solutions of pure carcinogens in non-accelerating solvents. In the course of the work at the Kettering Laboratory it was observed that certain solvents, in addition to having an effect on the area of spread of the solution also have a specific effect on the carcinogenicity of the solution. Thus it was found that different concentrations of methyl cholanthrene in some solvents, even though they spread over the same area, have essentially the same average latent period. According to the above, this should not be the case since the dose per unit area should be different. In this case the area remains constant, the amount applied per application remains constant, but the concentration varies, and hence dose per unit area varies. Theoretically, therefore, the average latent period should vary, but actually this was not found to be the case. The explanation for this effect is that the solvent exerts some specific accelerating action on carcinogenesis. To summarize these two concepts, it may be well to give some equations. Thus dose per unit area per week may be defined as follows:

$$d = \frac{mgm \times c \times f}{a}$$

where mgm = mgm of solution applied per application

c = concentration

f = number of applications per week

a = area covered

In the simplest case of 2 non-accelerating solvents with different spreading, mgm, c, and f were constant but a varied, thereby influencing d. In the second case, mgm, f, and a were constant but c varied and hence d also was variable,

but this did not influence average latent period. Hence two situations exist, one in which the rate of tumor formation is related directly to d, the other in which it is not. To date dodecyl benzene and normal hexadecane have been found to be accelerating solvents, although gasoline is not.

An interesting observation recently made is that if dodecyl benzene is applied once to the skin, and then serial biopsies taken, holes in the epithelium can be observed microscopically but not grossly. It has been postulated by the Kettering Laboratory that these holes provide foci of rapidly regenerating epithelium which may be responsible for the accelerating action observed.

Refinery Streams

As a result of the above information of a fundamental nature developed over the past several years, the Kettering Laboratory now believes that carcinogenic refinery streams may be divided into two main classes:

1). Those streams or materials in which P_{MC} is related to d.

2). Those streams or materials in which P_{MC} is not related to d.

In the first group fall those materials such as catalytically cracked residua in which carcinogen concentration is so high or accelerators relatively so low that the carcinogen concentration becomes of first importance as a measure of tumor activity in [illegible] the second group, characterized by medium distillates, the carcinogen [illegible] and the accelerator concentration relatively so high [illegible] are more important in producing tumors of the mouse [illegible] than the carcinogens.

The laboratory has developed information which indicates that the accelerators are present in those refinery streams boiling from 450-650°F., while carcinogens are present in those streams boiling above 650-700°F. Thus in mixtures which

have a wide boiling range, say from 450-1000°F., the carcinogenicity of the mixture may not be dependent alone on the amount of 700°F. + material present, but also on the amount and nature of the 450-650°F. fraction.

In partial support of this concept, the laboratory has analyzed a series of refinery streams for their benzpyrene content, in accordance with a method developed in Pittsburgh, and have related the determined benzpyrene content to the P_{MC} (appendix II of January - September, 1953, Progress Report). These determinations indicate that the % BP/P_{MC} ratio essentially divides into two groups, those that run from 0.30 and higher, and those that run from 0.10 and lower. The first group of materials falls in the first class of refinery materials, and the second group into the second class. In three instances (API[6], 71 and 91) this ratio lay between 0.1 and 0.3, and these three oils may warrant further study.

Tables of P_{MC}

In the newly distributed tables of P_{MC} values distributed on September 1, 1953, essentially three types of results are given:

1). Those in which both the average latent period and the P_{MC} values are given in parentheses. It is the feeling of the laboratory that these results are open to serious errors in their accuracy due to uncontrollable variables in the biological experiments such as poor health, toxicity of applied materials, etc.

[illegible] in which the average latent period is enclosed in parentheses but the P_{MC} value is not. These are pretty good experiments from a biological standpoint, but the laboratory still has some reservations about the accuracy.

3). Those in which neither the average latent period nor the P_{MC} value are enclosed in parentheses. These experiments are believed to be as good a biological experiment as it is possible to obtain.

Of the samples in these tables for which a P_{MC} value is given, 57 fall into the first group, 93 fall into the second group, and 27 fall into the third group. It is the feeling of this writer (and I hope the remaining members of the RPA Committee) that the 150 samples which fall into type 1 and 2 results can be repeated and brought into a type 3 experiment. Since much of the validation of the theories of the laboratory is dependent upon accurate P_{MC} values, it is highly desirable that these P_{MC} values be made as accurate as biological experimentation will permit.

Another serious defect of these tables is that in some experiments, animals have been eliminated from the experiment because the laboratory believed that biologically it was unsound to include them. In several cases the results are based on as few as 6 animals. It is to be desired that no results will be reported unless a minimum number of 20 animals are included in the experiment. The Committee recognizes the validity of throwing out some animals, but feels that where this has been done the experiment should be repeated to include at least 20 animals.

Other Observations

The l[illegible] determined that washing is an effective way of reducing the carci[illegible]ity of an oil to the skin of the mouse. In general, the sooner the oil is washed off the better. Limited experiments with white oil wash and barrier creams are difficult to interpret, but the laboratory feels that a white oil rinse prior to washing, or the use of barrier creams in association with washing, may offer advantages greater than with washing alone.

Epidemiology

The epidemiological data is accumulating in the laboratory, with some 1200 cases now having been reported. No definite trends are as yet discernible but it was not anticipated that any such trends would be discernible prior to at least 5 years experience. It is hoped that the support which the General Committee, Division of Refining has given to the epidemiological study will stimulate renewed reporting of cases with sufficient medical and occupational histories to permit some early correlations to be made about 1956.

Summary

1. The RPA Committee believes that the Kettering Laboratory is performing important work in the field of carcinogenesis of refinery streams and materials. They believe that although a great many practical answers have already been obtained, the work should be pursued because the work of the laboratory promises to provide many fundamental answers to questions which now exist concerning industrial and occupational carcinogenesis.

2. It is believed that the work with non-accelerating solvents which relates the carcinogenic response of a solution of pure carcinogen to the dose applied per unit area per week to the skin is of extreme fundamental importance. The Committee urges that additional work be conducted to establish firmly the curve which expresses this relationship.

3. It is [illegible] that the work with accelerating solvents is also of extreme [illegible] importance and that this should be pursued vigorously in an attempt to develop a complete understanding of the relative role of carcinogens and accelerators in refinery streams and materials.

4. Since much of the correlation of chemical analyses with biological potency is dependent upon the accuracy of P_{MC} values, the Committee laments the fact that many of the P_{MC} values thus far reported are based on data which the laboratory recognizes as not having been obtained from the best biological experiment possible. The Committee suggests, therefore, that the laboratory devote considerable effort to repeating those experiments in an effort to develop P_{MC} values that are based on the soundest possible biological experiment.

5. The Committee believes that the work with washing techniques and protective creams may provide intensely practical guides to refinery hygiene practice and suggests that this work be pursued as new approaches appear to the laboratory.

6. The Committee recognizes that the epidemiological studies cannot be expected to produce significant results until at least 1956, and, therefore, urges that renewed efforts at adequate case and occupational history reporting be made during the next several years. It believes that adequate medical staffs can do most to insure the success of this program, and in this connection it acknowledges the stimulus that the General Committee, Division of Refining has given to the attainment of this objective.

7. The laboratory has already determined that a number of refinery streams and materials have a relatively high degree of carcinogenicity. Although data obtained with mice cannot be directly transposed to humans, there is sufficient data in occupational cancer experience to indicate that the petroleum industry cannot take lightly the observations of the laboratory on the carcinogenicity of these refinery streams and materials.

8. The Committee recognizes that the laboratory at best can determine from its biological and chemical work only the relative carcinogenicity of various refinery streams and materials. The determination of the hazard is

dependent upon factors of extent, frequency, duration, and length of exposure. As recognized by the laboratory in Dr. Kehoe's talk to the members of the General Committee, Division of Refining the determination of the hazard is at present a function of the individual petroleum companies. Adequate medical and industrial hygiene staffs are essential in these individual companies if they are adequately to appraise the hazard. The Committee supports Dr. Kehoe's plea that petroleum company managements recognize this truism and make plans for the development of such adequate medical and industrial hygiene staffs.

9. It is apparent that the laboratory has accumulated sufficient data that publication of results will be deemed desirable in the near future. The Committee recognizes the right of the Laboratory to publish, and urges that the mechanism be established so that these publications can be reviewed in a finite period of time. As a suggestion, it is proposed that this mechanism be so established that review by API management and suggestions and criticisms for the laboratory from API management be made available within sixty (60) days. If no criticisms or suggestions are obtained by the laboratory at the expiration of this time, the laboratory can assume that none are forthcoming and proceed with publication. It should be recognized that [illegible] is for the purpose of helpful criticisms and suggestions [illegible] determination of whether or not there will be publication, since [illegible] the laboratory clearly states that the laboratory [illegible] publication occurs.

[illegible] that a given [illegible]

[illegible] or [illegible]

[illegible] exposure, [illegible]

SUMMARY OF RECENT PROGRESS IN THE INVESTIGATION OF THE CARCINOGENICITY OF PETROLEUM INTERMEDIATES AND PRODUCTS

September 29, 1953

In the course of the biological program to assay the relative carcinogenic potencies of refinery streams, it has become apparent that some of the materials have a practically constant potency, P_{MC}, over a wide range of conditions of exposure. With these oils, the time required for the induction of tumors is essentially the same whether a small dosage, e.g., 5 mg. per application, or a very large dosage, 100 mg., is employed, so long as the same number of exposures per week is involved. When the frequency of application of such samples is varied, the mean time of appearance of tumors changes in just the manner expected for a solution of the synthetic carcinogen, methylcholanthrene, in a "non-accelerating" solvent such as benzene; hence the constancy of the values of P_{MC}, since these are based upon experiments with such solutions as external standards of reference.

Other materials from refining operations have exhibited potencies, P_{MC}, which increase as much as five-fold with increasing severity of exposure. While a number of the catalytically cracked oils have fallen into this category, others do not. Hence it has become apparent that a given refinery stream cannot be classified as variable or constant in its potency, P_{MC}, with variations in conditions of exposure, simply on the basis of the unit from which it was collected. Rather it is necessary to gain an understanding of the relationships between the chemical composition of the oil and its effect on animals under various conditions of exposure.

Although some concern was expressed, when this problem was first discussed about a year ago, that its complexity was such as to render it insoluble, the experience of the succeeding months has already shown that such is not the case. There is a mounting record of evidence that the variability of the potency, P_{MC}, where it occurs, is related to the extent of the contribution of non-carcinogenic but accelerating constituents of the oils. Biological tests on fractions of oils such as the T.C.C. cracked residuum, API-71, and the Technical White Oil, API-80, have demonstrated further that the major part of the accelerators are found in the range, 450-650°F., and are mainly saturated hydrocarbons, some contribution also being made by alkyl (or alicyclic) derivatives of benzene and naphthalene of a restricted range of molecular lengths. Experiments with pure hydrocarbons furnished by other API Research Projects are being carried out to define the limits of this range more sharply.

Chemical research on the carcinogenic constituents of the oils has led to the development of a method of analysis for benzo(a)pyrene, outlined briefly in Appendix I. The analyses for a number of typical refinery streams (Appendix II) show that this compound contributes importantly to the potencies of cracked residua, but to a much lesser extent to those of distillate gas oils. Current efforts are, therefore, being directed towards the characterizations of the carcinogens which are more volatile than benzo(a)pyrene, particularly those which are derivatives of the 4-ringed polycyclic aromatic hydrocarbons.

The compounds which were extracted from the catalytically cracked residuum, API-8, by repeated reaction with maleic anhydride have been tested on mice (as solutions in benzene). The potencies so determined indicate that approximately one-third of the carcinogens of the oil were removed by this method. By chromatographic fractionation, a concentrate (API-8-23d) of these "Diels-Alder" carcinogens was prepared, the potency of which indicates that it contains an equivalent of 18 percent benzpyrene. Further experiments are in progress to identify the potent constituents of this fraction and to develop a method of analysis for them.

The picture which has been developed of the interrelationships between the five variables, 1. the sum of the effective concentrations of the carcinogens (three important classes), 2. the effective concentration of the accelerators, 3. the severity of exposure (dosage per application and frequency of application), 4. the relative potency, P_{MC}, and 5. the relative area of the skin covered by a standard weight of the oil in question (as compared to the coverage by the same weight of the standard of reference, methylcholanthrene in benzene), may be expressed algebraically by an equation of the following type:

$$P_{MC} = f(c_a d)\ [\text{Area}^\circ]\ [K_{BP}C_{BP} + K_{DA}C_{DA} + K_4C_4]\ .$$

The function, $f(c_a d)$, has been found to be of sigmoid form, approaching the value, 1, as c_a, the concentration of accelerators, becomes small. Thus, when accelerators do not make a significant contribution, the potency, P_{MC}, is independent of the severity

of exposure and depends only upon the dosage of carcinogens (the summation in brackets of the effective concentrations of benzpyrene, "Diels-Alder" carcinogens, and the third class, as yet undefined) per unit area of the skin.

The relationships between concentration of carcinogen (in g./100 ml.) and average latent period for induction of tumors by the standards of reference (methylcholanthrene in benzene), have previously been plotted as three parallel curves, one for each frequency of application. It has been found that, if the dosage, . of methylcholanthrene is expressed in the units, weight per unit area per week, the data from all of the experiments are related by the following hyperbolic functions (see Figure I):

For the average rate of induction of papillomas,

$$(\bar{x}_{pap} - 2.8)(d + 0.09) = 8.5 \qquad (1)$$

For the average rate of induction of grossly malignant tumors,

$$(\bar{x}_{ca} - 15.5)(d + 0.07) = 6.3 \qquad (2)$$

$$P_{MC} = \frac{d}{f}, \qquad (3)$$

where f = number of applications per week.

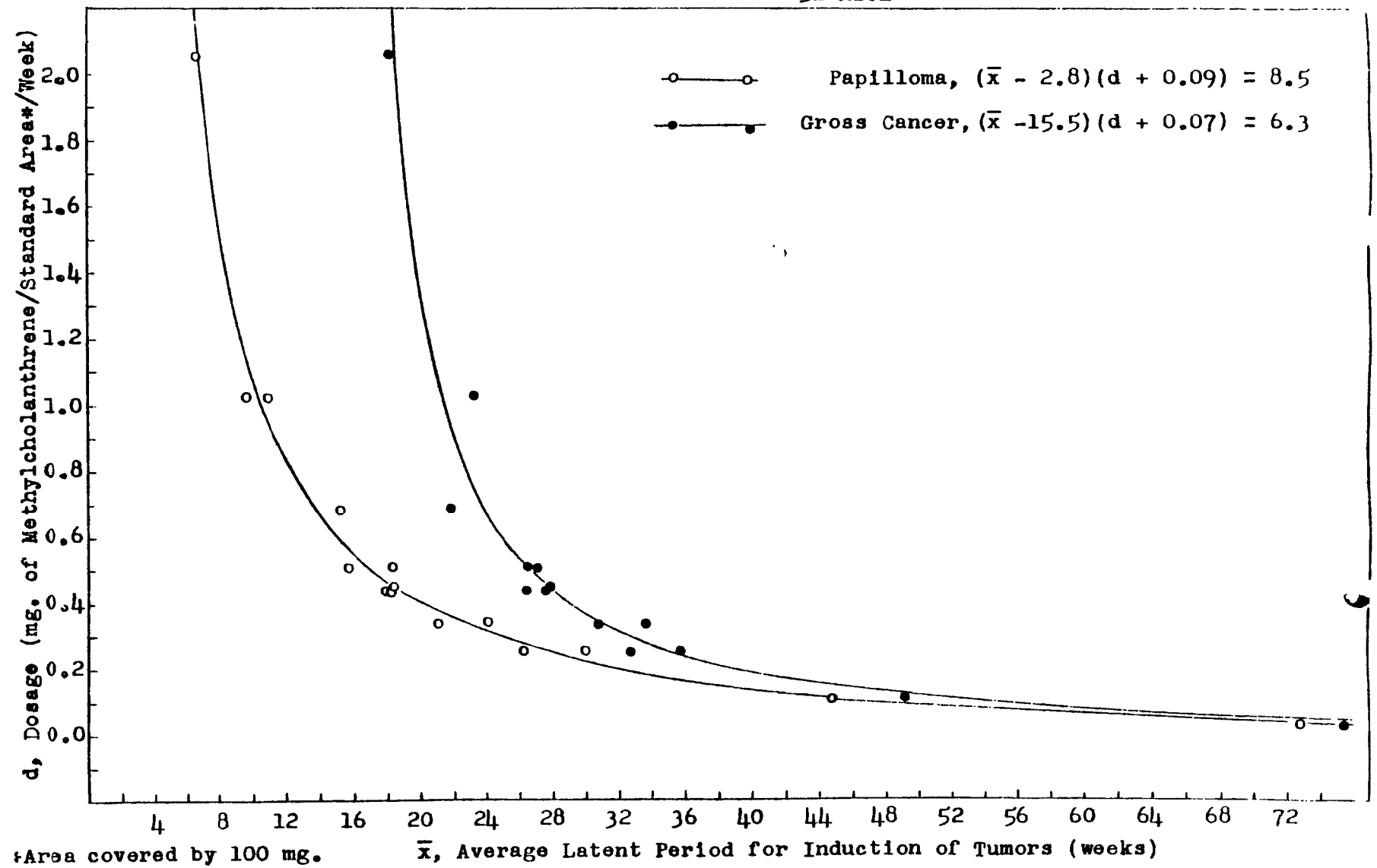
The relative areas of the skin covered by solutions of methylcholanthrene in other solvents have been measured. The average latent period for induction of tumors by such solutions may be calculated from the above equations, making the proper correction of the dosage factor, d, for the solution in question, so long as the solvent is a non-accelerator, i.e., sec.-amylbenzene

or cottonseed oil. For example, a given weight of a solution of methylcholanthrene in sec.-amylbenzene covers 1.7 times the area covered by the same weight of a solution of methylcholanthrene in benzene; hence the dosage of methylcholanthrene per unit area for the former would be only 0.6 that obtained with the latter, assuming that the concentration of methylcholanthrene in weight percent is the same in both cases. Note in Table II (page 30 of Tabular Summary) that, for experiments involving sec.-amylbenzene as the solvent, P_{MC} is approximately equal to 0.6 of the concentration of methylcholanthrene employed.

When solutions of methylcholanthrene or benzpyrene in accelerating solvents, such as cetane or dodecylbenzene, are applied, an appreciably larger area is covered than is the case with the non-accelerating materials. Hence the relationships between the surface activity of these solutions and their specific irritating properties are being carefully examined to discover, if possible, something about the mechanism by which they accelerate the rate of induction of tumors by polycyclic carcinogens.

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF METHYLCHOLANTHRENE IN BENZENE

UPON THE SKIN OF C3H MICE



*Area covered by 100 mg.

API 05718

APPENDIX I

ANALYSIS FOR BENZO(a)PYRENE IN REFINERY STREAMS

(1) Prepare a chromatography tube by joining a 300 ml. reservoir to one end of a Corning 39570 HEYXY sealing tube containing a 20 mm., coarse, fritted disc. This should provide a smooth-bored tube, 22 mm. in internal diameter and more than 90 mm. long.

(2) On a 7.5 cm. column of alumina (Alcoa, activated alumina, grade F 20) in the above tube, chromatograph a 100 mg. sample of oil to be analyzed (added to column as a solution in 10 ml. of 50:50 benzene-isooctane). Wash first with 100 ml. additional 50:50 benzene-isooctane, yielding fraction No. 1; then wash with 250 ml. of a 70 percent benzene, 30 percent isooctane mixture, yielding fraction No. 2. Fraction No. 1 is discarded. Evaporate the solvent from fraction No. 2 under nitrogen and redissolve in 10 ml. of C.P. benzene. With a pipette, divide this solution into two equal parts (5.00 ml. each), termed A and B throughout the following procedures.

(3) Iodinate A by this method:

(a) To a 2.5 cm. column of alumina in the chromatography tube, add a solution of 0.5 g. of iodine in 5 ml. of benzene.

(b) To A, add a solution of 0.5 g. of iodine in 5 ml. of benzene and pour the mixture on the column.

(c) Elute the column with 90 ml. of benzene, collecting the total eluate.

(d) Remove the free iodine from the eluate by washing with aqueous sodium thiosulfate.

APPENDIX I (Continued)

(4) Chromatograph B similarly, without the use of iodine.

(5) Equalize the weights of A and B (to W grams) and determine the spectrum (365-415 mμ) of the iodinated A, using B as the blank. At wavelengths where B has the higher absorbance, balance the spectrophotometer on A and plot the absorbance readings as negative values.

(6) Draw a straight line intersecting the absorbance curve at 405 mμ and 380 mμ. Let the difference in absorbance between the straight line and the curve at 389 mμ be $\triangle D_{BP}$. Then,

$$\% \text{ BP} = \frac{\triangle D_{BP}}{35} \times \frac{W}{.87} = \frac{\triangle D_{BP} \cdot W}{30.5}$$

While it is obviously not necessary to determine the entire spectrum (difference in absorption between the iodinated A and the non-iodinated B) over the range, 365-415 mμ, to calculate $\triangle D_{BP}$, it is desirable in order to confirm qualitatively the presence of benzpyrene by the negative peaks at about 370 and 390 mμ and the positive peak of 6-iodobenzo(a)pyrene at 405 mμ.

APPENDIX II

TYPE OF REFINERY STREAM	API SAMPLE NUMBER	PERCENT BENZPYRENE (BP)	P_{MC} (100 mg.)	$\frac{\% BP}{P_{MC}}$
Catalytically Cracked Residuum	8	0.34	0.5 - 0.8	0.5
	9	0.07 - 0.09	0.06	1.33
	12	0.42	0.42-0.46	0.95
	20	0.12	0.16	0.75
	26	0.63	0.65	0.98
	43-1	0.47	0.43	1.09
	48	0.32 - 0.36	0.22	1.55
	50	0.07 - 0.08	0.15	0.50
	63	0.05	0.14-0.19	0.30
	71	0.10	0.55	0.18
	82	0.53	0.33	1.61
Thermally Cracked Residuum	6	0.02	0.08	0.25
	65	0.06	0.12	0.50
	113	0.09 - 0.10	0.18	0.53
Medium Distillate	23	0.02 - 0.03	0.25	0.10
	28	0.02	0.31	0.06
	33	0.01	0.51	0.02
	79	< 0.01	0.14	< 0.07
	91	0.03 - 0.04	0.28	0.13
	102	0.01	0.19	0.05
	105	< 0.01	0.11	< 0.09
Heavy Cracked Distillate	41	1.03	0.34	3.03

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Robert A. Kehoe, M.D.
Director

Date: September 29, 1953

Copy from D. V. Stroop for Information of All Members and Associates of the Medical Advisory Committee October 13, 1953

ESSO LABORATORIES
Standard Oil Development Company
P. O. Box 51, Linden, N.J.

Medical Research Division Industrial Hygiene Section

October 8, 1953

Mr. D. V. Stroop
American Petroleum Institute
50 West 50th Street
New York 20, New York

Dear Mr. Stroop:

I am enclosing a revised copy of the report of the RP (MC-1) Advisory Committee submitted on September 29, 1953 to the Subcommittee on Carcinogenicity of the API Medical Advisory Committee. By verbal arrangement with Dr. Davis it is my suggestion that you have this report duplicated and distributed to all members and associates of the Medical Advisory Committee.

Sincerely yours,

/s/ R. E. Eckardt

R. E. ECKARDT, M. D.

REE:ilk
Enclosure

REPORT OF RP (MC-1) ADVISORY COMMITTEE SUBMITTED ON SEPTEMBER 29, 1953,

TO SUBCOMMITTEE ON CARCINOGENICITY, API MEDICAL ADVISORY COMMITTEE

SUMMARY OF THE API PROJECT ON CARCINOGENICITY AT KETTERING LABORATORY

The original program of carcinogenic work at Kettering Laboratory grew out of the results obtained from testing a series of 8 oils. The conclusion of this work, reported on November 5, 1948, was that all 8 oils affected the skin. Two of them produced mild irritation, two produced a few verrucous papillomata, one produced papillomas and two questionable cancers, two produced a definite cancer each, and one was highly carcinogenic.

As a result of these preliminary studies, the Kettering Laboratory undertook a more extensive research program under the auspices of the API Medical Asvisory Committee designed to 1) survey refining processes and materials which might represent potential hazards from the cancer standpoint, 2)biological testing of indicated oils and tars, 3) chemical research to determine the nature of the carcinogenic components and to develop analytical techniques for their determination, and 4) an epidemiological program to develop sound information regarding the actual incidence of cancer among employees of the petroleum industry and to determine the efficacy over a period of years of the various safety programs which have been or are being set up by individual oil companies.

To implement this program, it was suggested that materials from a number of process be studied, in accordance with the outline on pages 2 and 3 of the Kettering report dated October 27, 1950.

Non-Accelerating Solvents

In order to have a reference standard to which the results of tests of these oils could be referred, the laboratory undertook a study of the carcinogenicity of solutions of methylcholanthrene in benzene. For reasons related to well known dose-response phenomena it was decided to use the average latent period for tumor production as a measure of carcinogenicity, the average latent period being defined as the length of time required to reach 50% tumor indices.

In the course of this work with reference standards, it soon became apparent that C3H mice gave fairly reproducible results, whereas CFW mice gave less reproducible results. It was therefore decided to standardize the mouse strain and to use only C3H mice in subsequent tests, even though a considerable number of tests on oils with CFW mice had already been started or completed.

In additon, it became apparent that if too strong a solution of methylcholanthrene is painted on the C3H mice too frequently, the health of the mice, as determined by non-tumor mortality and weight curves, is impaired, and, apparently, their ability to produce tumors is impaired at the same time. In addition, other factors which influence the health of the mice, such as infections, infestations with lice, etc., also reflected in non-tumor mortality and growth rates, and will seriously affect tumor production. Thus, unhealthy animals frequently do not produce tumors as readily as healthy animals, and the

average latent period is prolonged in the unhealthy animals. Since the average latent period is taken as a measure of carcinogenicity, it is obvious that the apparent carcinogenicity of a meterial could be profoundly influenced by the health of the animals, and misleading results thereby obtained.

The above observations led to the necessity of painting mice once, twice or three times per week, depending on the strength of solution being used, and to the establishment of three or more separate standard curves, depending on the frequency of painting. The most recent report from the Kettering Laboratory, however, has shown that these three curves can be united into a single curve when they are expressed in terms of the dose of carcinogen applied per unit area of skin per week. This has necessitated measuring the area of skin covered by a solution of methylcholanthrene in a solvent. Within limits this has been found to be constant for each solvent tested. The solvents thus far tested have been benzene, hydro-peroxide-free amyl benzene, cotton seed oil, technical white oil and fractions of refinery streams. The effect of these solvents is their effect on the spreading of the solution. Thus, if the same amount of the same concentration of methylcholanthrene in two different solvents were to be painted on the skin 3 times a week, the dose per unit area need not be the same. If one solvent caused the solution to spread over twice the area of the other solvent, the dose per unit area in the first case would be half that in the second case, and the average latent period for the two solutions would be different, leading to different P_{MC} values for the two solutions. The P_{MC} value refers only to concentration of methylcholanthrene in benzene, and serves only as a reference standard. What this work implies is that it will be necessary in carcinogenic work to determine not only the frequency of application and the amount applied per application, but also the area covered by this amount.

Accelerating Solvents

What has been said above applies only to solutions of pure carcinogens in non-accelerating solvents. In the course of the work at the Kettering Laboratory it was observed that certain solvents, in addition to having an effect on the area of spread of the solution, also have a specific effect on the carcinogenicity of the solution. Thus it was found that different concentrations of methylcholanthrene in some solvents, even though they spread over the same area, have essentially the same average latent period. According to the above, this should not be the case since the dose per unit area should be different. In this case the area remains constant, the amount applied per application remains constant; but the concentration varies, and hence dose per unit area varies. Theoretically, therefore, the average latent period should vary, but actually this was not found to be the case. The explanation for this effect is that the solvent exerts some specific accelerating action on carcinogenesis. To summarize these two concepts, it may be well to give some equations. Thus, dose per unit area per week may be defined as follows:

$$d = \frac{mgm \times c \times f}{a}$$

where mgm = mgm of solution applied per application
c = concentration
f = number of applications per week
a = area covered

In the first case of 2 non-accelerating solvents with different spreading, mgm, c, and f were constant, but a varied, thereby influencing d. In the second case, mgm, f, and a were constant, but c varied, and hence d also was variable; but this did not influence average latent period. Hence two situations exist, one in which the rate of tumor formation is related directly to d, the other in which it is not. To date, dodecyl benzene, normal hexadecane, methyl naphthalene, cyclohexyl decane, phenyl dodecane, cetane and phenyl decane have been found to be accelerating solvents, although gasoline is not.

An interesting observation recently made is that if dodecyl benzene is applied once to the skin, and then serial biopsies taken, holes in the epithelium can be observed microscopically but not grossly. It has been postulated by the Kettering Laboratory that these holes provide foci of rapidly regenerating epithelium which may be responsible for the accelerating action observed.

Refinery Streams

As a result of the above information of a fundamental nature developed over the past several years, the Kettering Laboratory now believes that carcinogenic refinery streams may be divided into two main classes:

1). Those streams or materials in which P_{MC} is related to d.

2). Those streams or materials in which P_{MC} is not related to d.

In the first group fall those materials such as catalytically cracked residua in which carcinogen concentration is so high or accelerators relatively so low that the carcinogen concentration becomes of first importance as a measure of tumor activity in mice. In the second group, characterized by medium distillates, the carcinogen concentration is so low and the accelerator concentration relatively so high that the accelerators are more important in the rate of tumor production of the mouse skin than the carcinogens.

The laboratory has developed information which indicates that the accelerators are present in those refinery streams boiling from 450-650°F., while carcinogens are present in those streams boiling above 650-700°F. Thus in mixtures which have a wide boiling range, say from 450-1000°F., the carcinogenicity of the mixture may not be dependent alone on the amount of 700°F.+ material present, but also on the amount and nature of the 450-650°F. fraction.

In partial support of this concept, the laboratory has analyzed a series of refinery streams for their benzpyrene content, in accordance with a method developed by the laboratory, and have related the determined benzpyrene content to the P_{MC} (appendix II of January-September, 1953 Progress Report). These determinations indicate that the % BP/P_{MC} ratio essentially divides into two groups, those that run from 0.30 and higher, and those that run from 0.10 and lower. The first group of materials falls in the first class of refinery materials, and the second group into the second class.

Tables of P_{MC}

In the newly distributed tables of P_{MC} values distributed on September 1, 1953, essentially three types of results are given:

1). Those in which both the average latent period and the P_{MC} values are given in parentheses. It is the feeling of the laboratory that these results are open to serious errors in their accuracy due to uncontrollable variables in the biological experiments such as poor health, toxicity of applied materials, etc.

2). Those in which the average latent period is enclosed in parentheses but the P_{MC} value is not. These are pretty good experiments from a biological standpoint, but the laboratory still has some reservations about the accuracy.

3). Those in which neither the average latent period nor the P_{MC} values are enclosed in parentheses. These experiments are believed to be as good a biological experiment as it is possible to obtain.

Of the samples in these tables for which a P_{MC} value is given, 57 fall into the first group, 93 fall into the second group, and 27 fall into the third group. It is the feeling that the 57 samples which fall into type 1 results should be examined critically and some of them repeated and brought into a type 2 or 3 experiment. Since much of the validation of the theories of the laboratory is dependent upon accurate P_{MC} values, it is highly desirable that these P_{MC} values be made as accurate as biological experimentation will permit.

Another serious defect of these tables is that in some experiments, animals have been eliminated from the experiment because the laboratory believed that biologically it was unsound to include them. In several cases the results are based on as few as 6 animals. It is to be desired that no results will be finally reported unless a minumum number of 20 animals are included in the experiment. The Committee recognizes the validity of throwing out some animals, but feels that where this has been done, the experiment should be repeated to include at least 20 animals.

Other Observations

The laboratory has determined that washing is an effective way of reducing the carcinogenicity of an oil to the skin of the mouse. In general, the sooner the oil is washed off, the better. Limited experiments with barrier creams are difficult to interpret but the laboratory feels the use of barrier creams in accordance with recognized practice followed by washing may offer advantages greater than washing alone.

Epidemiology

The epidemiological data is accumulating in the laboratory, with some 1200 cases now having been reported. No definite trends are as yet