PLAINTIFF'S EXHIBIT
API-131

# INTERIM REPORT

## API RESEARCH PROJECT MC-1

## OCTOBER 1, 1955

THE KETTERING LABORATORY
in the
Department of Preventive Medicine and Industrial Health
College of Medicine
UNIVERSITY OF CINCINNATI, CINCINNATI, OHIO

For Information Only - Not for Publication

API Research Project MC-1

# TABULAR SUMMARY

# OF

# CURRENT AND COMPLETED

# BIOLOGICAL EXPERIMENTS

October 1, 1955

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

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TABLE I

CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | GRAVITY °API | FRACTION DISTILLING < 750°F. (%) | BENZOPYRENE (%) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (% - week) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|---|---|
| **Non-catalytic cracking of virgin gas oil** | | | | | | | |
| 2 | Cracked Side-stream | 21.2 | | 0.0002 | 1 - 100 | 0-75 | - |
| 6 | Cracked residuum | 5.2 | 33 | 0.013 | 3 - 100 | 72-30 | $\sim$ 0.08 |
| 59 | Cracked residuum | 8.5 | | 0.005 | 3 - 100 | 82-69 | 0.02X |
| 65 | Cracked residuum | 6.6 | 43.8 | 0.04 | 3 - 100 | 89-29 | 0.11X |
| 72 | Cracked residuum | 9.6 | 35 | 0.06 | 3 - 100 | 73-18 | 0.21X |
| 94 | Cracked residuum | 10.4 | 35 | 0.02 | 3 - 100 | 80-39 | 0.09X |
| 108 | Cracked residuum | 2.3 | 32 | 0.12 | 3 - 100 | 71-28 | 0.12X |
| 108 | | | | | 3 - 5 | 100-52 | $0.05 \pm .01$ |
| **Non-catalytic cracking of catalytic gas oil** | | | | | | | |
| 20 | Cracked residuum | 4.7 | 51 | 0.24 | 3 - 100 | 100-22 | $\sim$ 0.18 |
| 20 | | | | | 3 - 100 | 90-21 | 0.17X |
| 20-1 | 50% oil No. 20, 50% dodecylbenzene | | | | 3 - 100 | 100-25 | $\sim$ 0.18 |
| 23 | FCC gas oil feed | 26.7 | 78.5 | 0.043 | 3 - 100 | 100-19 | $\sim$ 0.24 |
| 23 | | | | | 2 - 100 | 94-28 | $0.22^{+.04}_{-.03}$ |
| 24 | Cracked residuum from No. 23 | 5.9 | 32.3 | 0.24 | 3 - 100 | 100-15 | $\sim$ 0.4 |
| 29 | TCC gas oil feed | 15.7 | 73 | 0.10 | 1 - 100 | 84-30 | $0.31 \pm .04$ |
| 30 | Cracked residuum from No. 29 | 8.5 | 36 | 0.23 | 1 - 100 | 100-33 | $0.26^{+.04}_{-.02}$ |
| 34 | Houdry gas oil feed | 28.0 | | 0.014 | 3 - 100 | 84-32 | $\sim$ 0.1 |
| 35 | Cracked residuum from No. 34 | 2.7 | 35 | 0.18 | 3 - 100 | 100-20 | $\sim$ 0.15 |

TABLE I (page 2)

CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | GRAVITY °API | FRACTION DISTILLING <750°F. (%) | BENZOPYRENE (%) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (% - weeks | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|---|---|
| 38 | Total cracking charge; combination unit | 16.1 | 32.2 | ≦0.005 | 3 - 100 | 62-58 | ~ 0.06 |
| 39 | Cracked residuum from No. 38 | 7.8 | 31.0 | 0.03 | 3 - 100 | 56-24 | ~ 0.15 |
| 44 | FCC decanted oil feed | 15.2 | 31.1 | 0.15 | 1 - 100 | 94-40 | 0.22X |
| 45 | Cracked residuum from No. 44 | -1.7 | 26.4 | 0.38 | 1 - 100 | 88-41 | 0.18X |
| 46 | FCC gas oil feed | 23.6 | 87.9 | 0.03 | 3 - 100 | 100-24 | ~ 0.15 |
| 47 | Cracked residuum from No. 46 | 9.6 | 76 | 0.21 | 3 - 100 | 93-17 | ~ 0.22 |
| 54 | Total cracking charge | 33.0 | 93.9 | 0.041 | 3 - 100 | 100-36 | ~ 0.09 |
| 55 | Cracked residuum from No. 54 | 4.2 | 55.9 | 0.23 | 3 - 100 | 89-19 | ~ 0.21 |
| 61 | Cracked residuum | 6.3 | 66.8 | 0.05 | 3 - 100 | 88-26 | ~ 0.20 |
| 63 | Houdry gas oil feed | 25.6 | 48.5 | 0.05 | 3 - 100 | 89-26 | $0.12^{+.02}_{-.01}$ |
| 63 | | | | | 3 - 100 | 100-19 | $0.18 \pm .03$ |
| 63 | | | | | 3 - 100 | 89-28 | 0.21X |
| 63 | | | | | 2 - 100 | 100-33 | $0.15^{+.03}_{-.02}$ |
| 63 | | | | | 3 - 20 | 100-45 | $0.11 \pm .03$ |
| 63 | | | | | 3 - 5 | 88-37 | $0.09^{+.01}_{-.02}$ |
| 64 | Cracked residuum from No. 63 | 19.9 | 52.5 | 0.11 | 3 - 100 | 100-23 | $0.17 \pm .02$ |
| 91 | FCC gas oil feed | 20.4 | 80.1 | 0.037 | 2 - 100 | 95-23 | $0.26^{+.06}_{-.04}$ |
| 92 | Cracked residuum from No. 91 | 6.1 | 70.5 | 0.072 | 2 - 100 | 91-23 | $0.31^{+.04}_{-.03}$ |
| 93 | Cracked residuum | 7.9 | 87 | 0.03 | 3 - 100 | 94-40 | $0.07 \pm .01$ |

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CINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | GRAVITY °API | FRACTION DISTILLING <750°F. (%) | BENZOPYRENE (%) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|---|---|
| Steam Cracking | | | | | | | |
| 86 | Cracked residuum | 3.5 | 51.9 | 0.02 | 1 - 100 | 100-36 | $0.17^{+.01}_{-.03}$ |
| Viscosity Breaking | | | | | | | |
| 18 | Cracked residuum from No. 17 | 3.1 | 23.7 | 0.018 | 3 - 100 | 56-30 | ~0.1 |
| 66[1] | Cracked residuum | 6.5 | 22.1 | 0.055 | 2 - 100 | 100-37 | $0.10^{\pm}.01$ |
| 67[1] | Cracked sidestream from fractionator producing No. 66 | 15.6 | 84.6 | 0.060 | 2 - 100 | 89-17 | $0.40^{+.06}_{-.09}$ |
| Dubbs coking | | | | | | | |
| 52[1] | Cracked sidestream | 21.0 | 95.2 | 0.005 | 3 - 100 | 100-36 | ~0.1 |
| 53[1] | Blowdown oil | 10.5 | 61.3 | 0.15 | 3 - 100 | 100-15 | ~0.4 |
| Batch coking | | | | | | | |
| 87 | Cracked sidestream | 14.9 | | 0.21 | 2 - 20 | 91-30 | $0.19^{+.01}_{-.09}$ |
| Delayed coking | | | | | | | |
| 28 | Cracked sidestream | 15.3 | | 0.03 | 3 - 100 | 100-15 | ~0.3 |
| 28 | | | | | 1 - 100 | 85-33 | $0.26^{+.06}_{-.05}$ |
| 74 | Total furnace | 12.5 | 22.3 | 0.03 | 2 - 100 | 100-47 | $0.10^{+.01}_{-.04}$ |
| 33 | Cracked sidestream from No. 74 | 16.8 | 60 | 0.008 | 3 - 100 | 95-15 | ~0.33 |
| 33 | | | | | 1 - 100 | 95-30 | $0.39^{+.09}_{-.07}$ |
| 84 | Cracked sidestream | 30.2 | 79 | 0.006 | 3 - 100 | 95-24 | $0.17^{+.02}_{-.03}$ |
| 90 | Cracked sidestream | 30.5 | 90.2 | 0.003 | 3 - 100 | 100-38 | $0.10^{\pm}.02$ |
| 96 | Cracked sidestream | 33.2 | 77.7 | 0.004 | 3 - 100 | 93-27 | $0.17^{+.02}_{-.04}$ |

[1] Feed to unit included catalytically cracked components.

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CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | GRAVITY (°API) | FRACTION DISTILLING <750°F. (%) | BENZOPYRENE (%) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|---|---|
| Delayed coking | | | | | | | |
| 97 | Total furnace charge (including recycle) | 16.6 | 57.8 | 0.11 | 3 - 100 | 87-22 | 0.16X |
| 98 | Cracked sidestream from No. 97 | 31.0 | 100 | >0.001 | 3 - 100 | 73-39 | 0.15X |
| 103 | Cracked sidestream | 25.2 | 43.9 | 0.02 | 3 - 100 | 94-23 | $0.19^{+.02}_{-.03}$ |
| 41 | Wax tailings, 50% benzene | 1.2 | 9.6 | 1.03 | 2 - 100 | 85-25 | 0.15X |
| Naphtha Reforming | | | | | | | |
| 19 | Cracked residuum | 17.0 | 91 | 0.00 | 3 - 100 | 86-37 | 0.08X |
| 58 | Cracked residuum from kerosene feed | 6.3 | 85 | 0.06 | 3 - 100 | 89-30 | ~ 0.12 |
| 76<br>76 | Cracked residuum | 30.6 | ~ 91 | 0.001 | 3 - 100<br>3 - 50 | 100-30<br>83-50 | ~ 0.08<br>inc. |
| Polyforming | | | | | | | |
| 13 | Cracked residuum | 10.1 | 63 | 0.006 | 2 - 100 | 89-61 | $0.12^{+.02}_{-.05}$ |
| 37 | Cracked residuum | 11.2 | 66 | 0.005 | 3 - 100 | 94-46 | ~0.1 |
| 69 | Cracked residuum | 15.9 | 75.1 | ≦0.005 | 3 - 100 | 80-29 | ~0.10 |
| Hydroforming | | | | | | | |
| 49 | Cracked residuum | 10.1 | ~ 95 | 0.13 | 1 - 100 | 84-41 | $0.15^{\pm}.01$ |
| 77 | Cracked residuum | 22.8 | 100 | 0.018 | 3 - 100 | 100-38 | ~0.07 |

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CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | GRAVITY (°API) | FRACTION DISTILLING 750°F. (%) | BENZOPYRENE (%) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|---|---|
| Thermofor Catalytic Cracking | | | | | | | |
| 7 | Cracked residuum | 20.2 | ~100 | 0.019 | 1 - 100 | 11-56 | - |
| 9 | Cracked residuum | 18.4 | 97 | 0.07 | 3 - 100 | 100-47 | $0.05^{\pm}.01$ |
| 9 | | | | | 3 - 100 | 100-41 | ~ 0.06 |
| 10 | Cracked residuum | 11.6 | 56.7 | 0.23 | 1 - 100 | 94-39 | 0.3X |
| 10 | | | | | 1 - 100 | 90-31 | ~0.5 |
| 31 | Cracked residuum | 16.0 | 63 | 0.65 | 1 - 100 | 100-32 | $0.37^{+.03}_{-.09}$ |
| 36 | Cracked residuum | 21.9 | ~50 | 0.18 | 1 - 100 | 94-44 | $0.19^{+.01}_{-.05}$ |
| 40 | Cracked residuum | 19.8 | 77.2 | 0.09 | 1 - 100 | 100-42 | 0.16X |
| 71 | Cracked residuum | 22.8 | 77 | 0.10 | 1 - 100 | 90-22 | $0.52^{\pm}.05$ |
| 71 | | | | | 1 - 20 | 90-37 | $0.36^{\pm}.02$ |
| 71 | | | | | 2 - 20[1] | 100-27 | $0.21^{\pm}.02$ |
| 71A | | | | | 2 - 20[1] | 100-25 | $0.21^{+.03}_{-.02}$ |
| 71 | | | | | 2 - 5 | 94-36 | $0.19^{+.05}_{-.03}$ |
| 71 | | | | | 1 - 5 | 85-70 | $0.10^{\pm}.03$ |
| 78 | Cracked residuum | 16.1 | 45.7 | 0.41 | 1 - 100 | 88-20 | $0.60^{+.06}_{-.11}$ |
| 82 | Cracked residuum | 13.6 | 25.7 | 0.53 | 1 - 100 | 95-34 | $0.30^{+.02}_{-.08}$ |
| 82 | | | | | 1 - 10 | 100-50 | $0.20^{+.01}_{-.04}$ |
| 60 | Sidestream | 24.9 | 100 | <.0004 | 3 - 100 | 57-48 | ~0.03X |
| 109 | Sidestream | 24.1 | | 0.35 | 3 - 100 | 93-25 | $0.14^{\pm}.03$ |

[1] API-71 involved repeated application until death. API-71A involved repeated application only until appearance of papilloma in each mouse. No significant difference in the average time to the appearance of gross carcinoma was noted.

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CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | GRAVITY °API | FRACTION DISTILLING <750°F. (%) | BENZOPYRENE (%) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|---|---|
| Fluid Catalytic Cracking | | | | | | | |
| 8 | Cracked residuum | 11.1 | 75 | 0.42 | 3 - 100 | 89-7 | $1.18^{+.45}_{-.26}$ |
| 8 | | | | | 2 - 100 | 94-14 | $0.95^{+.33}_{-.43}$ |
| 8 | | | | | 2 - 100 | 100-14 | > 0.6 |
| 8 | | | | | 2 - 20 | 92-20 | 0.26X |
| 8 | | | | | 1 - 100 | 100-32 | $0.43^{+.04}_{-.11}$ |
| 8 | | | | | 1 - 100 | 100-31 | $0.40^{+.03}_{-.12}$ |
| 8 | | | | | 1 - 100 | 94-24 | $0.57^{+.13}_{-.10}$ |
| 8 | | | | | 1 - 20 | 100-50 | $0.14^{+.03}_{-.02}$ |
| 8 | | | | | 1 - 20 | 97-42 | $0.21^{+.01}_{-.02}$ |
| 8 | | | | | 1 - 50 | 91-40 | $0.23^{\pm.05}$ |
| 8 | | | | | 1 - 50 | 100-32 | $0.37^{+.07}_{-.05}$ |
| 8 | | | | | 1 - 5 | 88-48 | $0.20^{+.01}_{-.04}$ |
| 8 | | | | | 3 - 15 | 100-18 | $0.25^{+.04}_{-.03}$ |
| 8-4 | 50% API-8, 50% (white oil + W. Texas residuum) | | | | 3 - 100 | 90-23 | 0.14X |
| 8-16 | 50% API-8, 50% sec.-amylbenzene | | | | 1 - 100 | 100-52 | $0.18^{+.01}_{-.05}$ |
| 8-21 | 50% API-8, 50% API-8-24 | | | | 1 - 100 | 87-43 | 0.32X |
| | Chromatography of API-8: | | | | | | |
| 8-5 | Aromatics | | | | 1 - 100 | 79-28 | ~ 0.3 |
| 8-5 | | | | | 1 - 100 | 92-22 | 0.42X |
| 8-24 | Colorless fraction | | | | 3 - 50 | 0-86 | - |
| 257 | Solution of 0.239% BP in API-8-24 | | | | 1 - 50 | 100-43 | $0.15^{\pm.02}$ |
| 8-17 | Reblend of all fractions | | | | 1 - 100 | 94-30 | $0.56^{+.14}_{-.13}$ |

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CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | GRAVITY (°API) | FRACTION DISTILLING <750°F. (%) | BENZOPYRENE (%) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $F_{MC}$ |
|---|---|---|---|---|---|---|---|
| 12 | Cracked residuum | 18.1 | | 0.42 | 1 - 100 | 88-34 | ~0.4 |
| 12 | | | | | 3 - 100 | 100-14 | ~0.4 |
| 12-2 | Colorless fraction from chromatography | | | | 3 - 100[2] | 0-93 | - |
| 25 | 700°+ bottoms from cracked residuum | 24.3 | 49 | 0.09 | 3 - 100 | 95-19 | $0.24 \pm .03$ |
| 25-1 | 50% API-25, 50% (White oil + West Texas residuum | 21.1 | | | 3 - 100 | 92-40 | $0.09^{+.01}_{-.02}$ |
| 26 | Cracked residuum | 7.3 | 61.3 | 0.63 | 1 - 100 | 100-20 | 0.6X |
| 42 | Cracked residuum | 14.2 | 28.6 | 0.36 | 1 - 100 | 94-34 | $0.34^{+.03}_{-.06}$ |
| 43 | Cracked residuum | 24.2 | 24.5 | 0.27 | 1 - 100 | 100-37 | $0.18^{+.01}_{-.02}$ |
| 43-1 | Dewaxed API-43 | 12.9 | 29.5 | 0.47 | 1 - 100 | 95-25 | $0.37 \pm .04$ |
| 43-1 | | | | | 2 - 20[1] | 94-17 | $0.36^{+.07}_{-.05}$ |
| 43-1A | | | | | 2 - 20[1] | 100-19 | $0.32^{+.05}_{-.04}$ |
| (44) | Cracked residuum | 15.2 | 31.1 | 0.15 | 1 - 100 | 94-40 | 0.22X |
| 48 | Cracked residuum | 6.0 | 47.1 | 0.32 | 1 - 100 | 100-36 | 0.19X |
| 68 | Cracked residuum | 9.8 | 43.3 | 0.52 | 1 - 100 | 100-17 | $0.59^{+.05}_{-.06}$ |
| 73 | Cracked residuum | 17.5 | 21 | 0.35 | 1 - 100 | 83-22 | 0.41X |
| 73 | | | | | 1 - 100 | 100-31 | $0.27^{+.05}_{-.03}$ |
| 85 | Cracked residuum | 8.1 | 42.6 | 0.42 | 1 - 100 | 100-25 | $0.44^{+.06}_{-.05}$ |
| 23 | Sidestream | 26.7 | 78.5 | 0.027 | 3 - 100 | 100-19 | ~0.24 |
| 23 | | | | | 2 - 100 | 94-28 | $0.22^{+.04}_{-.03}$ |
| 46 | Sidestream | 23.6 | 87.9 | 0.033 | 3 - 100 | 100-24 | ~0.15 |
| 88 | Sidestream | 22.5 | 69.3 | 0.029 | 2 - 100 | 94-26 | $0.25^{+.03}_{-.05}$ |
| 89 | Sidestream | 27.0 | 100 | 0.001 | 3 - 100 | 89-21 | $0.26^{+.04}_{-.05}$ |
| 89-3 | 3+-ringed aromatics of API-89, 40% solution in benzene | | | | 3 - 20 | 0-1 | - |

[1] API-43-1 involved repeated application until death. API-43-1A involved repeated application only until appearance of papilloma in each mouse. No significant difference in the average time to the appearance of gross carcinoma was noted.

[2] Painting discontinued after 41 weeks.

TABLE I (page 8)

CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | GRAVITY °API | FRACTION DISTILLING <750°F. (%) | BENZOPYRENE (%) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|---|---|
| 91 | Sidestream | 20.4 | 80.1 | 0.037 | 2 - 100 | 95-23 | $0.26^{+.06}_{-.04}$ |
| 101 | Sidestream | 24.8 | 89.7 | 0.007 | 3 - 100 | 100-12[1] | 0.33X |
| 102 | Sidestream | 23.5 | 99 | 0.015 | 2 - 20 | 69-43[1] | 0.16X |
| 102 | | | | | 2 - 100 | 93-32[1] | 0.16X |
| 104 | Sidestream | 25.8 | | 0.011 | 2 - 20 | 75-53[1] | 0.08X |
| 104 | | | | | 2 - 100 | 89-26[1] | $0.16^{\pm}.01$ |
| Houdry | | | | | | | |
| 11 | Cracked residuum | 4.3 | 84 | 0.21 | 3 - 100 | 94-19 | 0.19X |
| 34 | Cracked residuum | 28.0 | ~90 | 0.014 | 3 - 100 | 84-32 | ~0.1 |
| 50 | Cracked residuum | 21.3 | 85 | 0.07 | 3 - 100 | 100-21 | ~0.2 |
| 51 | Cracked residuum | 25.7 | 83 | 0.06 | 3 - 100 | 83-19 | ~0.2 |
| 63 | Cracked residuum | 25.6 | 48.5 | 0.05 | 3 - 100 | 89-26 | $0.12^{+.02}_{-.01}$ |
| 63 | | | | | 3 - 100 | 100-19 | $0.18^{\pm}.03$ |
| 63 | | | | | 3 - 100 | 90-28 | 0.21X |
| 63 | | | | | 2 - 100 | 100-33 | $0.15^{+.03}_{-.02}$ |
| 63 | | | | | 3 - 20 | 100-45 | $0.11^{\pm}.03$ |
| 63 | | | | | 3 - 5 | 88-37 | $0.09^{+.01}_{-.02}$ |
| 81 | Cracked residuum | 22.7 | 40.8 | 0.20 | 1 - 100 | 100-36 | $0.20^{+.04}_{-.03}$ |
| 81 | | | | | 1 - 100 | 91-41 | 0.21X |
| 81 | | | | | 1 - 20 | 97-52 | 0.14X |
| Cycloversion | | | | | | | |
| 22 | Cracked residuum | 25.6 | 49.5 | 0.091 | 3 - 100 | 100-17 | ~0.3X |

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

TABLE I (page 9)

CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | GRAVITY (°API) | FRACTION DISTILLING <750°F. (%) | BENZOPYRENE (%) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|---|---|
| Solvent extraction | | | | | | | |
| 16 | Phenol extract from Coastal 900-X | 9.7 | | ≦.003 | 3 - 100 | 67-73 | ~0.01 |
| 16 | | | | | 3 - 100 | 43-70 | ~0.01 |
| 17 | Duosol extract from California waxy residuum, 50% in sec.-amylbenzene | 7.1 | 3 | ≈.006 | 3 - 100 | 87-62 | ~0.1X |
| 27 | Phenol extract from San Joaquin naphthenic distillate | 11.0 | 80 | ≦.002 | 3 - 100 | 89-17 | ~0.3 |
| 70 | Nitro-benzene extract from Barbers Hill 60/80 | 15.7 | .5 | 0.007 | 3 - 100 | 93-44 | $0.06^{\pm}.01$ |
| 75 | $SO_2$ extract from TCC gas oil | 14.4 | 100 | ≈.001 | 3 - 100 | 77-51 | ~0.05 |
| Straight run distillation | | | | | | | |
| 56 | Waxy Midcontinent distillate | 29.9 | 52.4 | 0.003 | 3 - 100 | 88-22 | ~0.16 |
| 56 | | | | | 3 - 100 | 65-42 | 0.09X |
| 56 | | | | | 3 - 20 | 84-54 | 0.06X |
| 79 | San Joaquin naphthenic lube distillate, narrow cut | 16.6 | ~13 | ≦.005 | 2 - 100 | 86-57 | 0.10X |
| 120 | Ditto, wider cut | 19.5 | ~52[1] | ≦.003 | 3 - 50 | 65-60 | $0.07^{+.01}_{-.02}$ |
| 105 | West Texas paraffin distillate | 28.9 | 72.9 | 0.0003 | 3 - 100 | 88-33[2] | $0.11^{+.01}_{-.03}$ |
| 114 | Gulf Coastal distillate | 24.6 | ~50[1] | ≦.002 | 3 - 20 | 54-83 | $0.01^{\pm}.01$ |
| 114 | | | | | 3 - 100 | 55-71 | 0.02X |

[1] A.S.T.M. distillation.
[2] The pattern of response to the irritational effects of this oil was similar to that observed with dodecylbenzene.

TABLE I (page 10)

TOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | GRAVITY °API | FRACTION DISTILLING <750°F. (%) | BENZOPYRENE (%) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (% -weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|---|---|
| 115 | Blend of Gulf Coastal distillates | 23.2 | ~ 50[1] | ≦.002 | 3 - 20 | 77-80 | 0.02X |
| 115 | | | | | 3 - 50 | 63-66 | - |
| 117 | Gulf Coastal distillate | 30.8 | ~ 90[1] | 0.000 | 3 - 50 | 75-64 | - |
| Fractional distillation (British Medical Research Council) | | | | | | | |
| 110-1 | Kuwait Naphtha | 61.0 | 100 | | 3 - 20 | 0-55 | - |
| 111-4 | Lagunillas distillate | 23.0 | | | 3 - 20 | 88-22 | $0.14^{+.02}_{-.01}$ |
| 111-4 | | | | | 3 - 5 | 64-75 | $0.04^{+.01}_{-.02}$ |
| 111-4a | 75% API-111-4, 25% benzene | 22.7 | | | 3 - 5 | 51-82 | $0.02^{+.02}_{-.01}$ |
| 111-4b | Lagunillas distillate b. 650-690° | | | | 2 - 15 | 0-47 | - |
| 616 | Solution of .16% BP in API-111-4b | | | | 3 - 50 | 100-16 | $0.35^{+.10}_{-.07}$ |
| 111-5a | 75% Lagunillas residuum, 25% benzene | 15.4 | | | 3 - 5 | 56-74 | $0.02 \pm .01$ |
| 111-6 | 50% API-110-1, 50% API-111-4 | | | | 3 - 20 | 77-31 | $0.09 \pm .01$ |
| 111-7 | 50% API-111-4 50% API-112-1 | | | | 3 - 20 | 76-44 | $0.09^{+.01}_{-.02}$ |
| 112-1 | Oklahoma naphtha | 65.9 | 100 | | 3 - 20 | 0-58 | - |
| 112-3 | Oklahoma distillate | 39.7 | | | 3 - 20 | 0-58[2] | -[3] |

[1] A.S.T.M. distillation.
[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 (page 11)

CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | GRAVITY (°API) | FRACTION DISTILLING <750°F. (%) | BENZOPYRENE (%) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (% - weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|---|---|
| Lubricating oil | | | | | | | |
| 99 | Naphthenic distillate containing antioxidant | 20.0 | ~38 | <.001 | 3 - 100 | 94-47 | $0.06 \pm .01$ |
| 100 | Solvent extracted, no additives | 29.5 | ~0 | <.001 | 3 - 100 | 0-80 | - |
| 100-1 | 0.2% Antioxidant[1] in API-100 | | | | 3 - 100 | 0-78 | - |
| 100-2 | 0.5% Antioxidant, 2,6-ditert.-butyl-4-methylphenol in API-100 | | | | 3 - 100 | 0-88 | - |
| Wax pressing | | | | | | | |
| 32 | Dewaxed paraffin distillate fraction from Lima crude | | | 0.000 | (3-6)[a]-100 | 50-32<br>100-40 | - |
| 56 | Feed to presses | 29.9 | 52.4 | 0.003 | 6 - 100 | 50-15<br>87-22 | - |
| 57 | Dewaxed oil from API-56 | 28.7 | 80 | ≈.002 | 6 - 100 | 50-17<br>100-25 | - |
| Filtration dewaxing of API-8 | | | | | | | |
| 8-3 | Filtrate oil, 85% of original (.94% S) | 11.3 | 65 | | 3 - 100 | 90-17 | $0.30^{+.06}_{-.04}$ |
| Desulfurization of 8-3 by catalytic hydrogenation | | | | | | | |
| 21 | Hydrogenated heavy gas oil (.15% S) | 18.1 | 74 | 0.23 | 3 - 100 | 100-13 | $0.36^{+.07}_{-.04}$ |

[1] Same type additive as that contained in API-99.
[a] Three applications per week for 14 weeks, six applications per week thereafter.

meeting 3-23-56

# ERRATA

for

Interim Report
API Research Project MC-1
October 1, 1955

| Page Number | Line Number | Suggested Change |
|---|---|---|
| 1 | 4 | Insert "scrotal and other" between "of" and "cutaneous" |
| 1 | 5 | Delete "especially scrotal" |
| 3 | 3 | Replace "satisfactory" with "one-to-one" |
| 3 | 20 | Add "in benzene." after "carcinogen" |
| 6 | 19 | Replace "II" with "VII" |
| 7 | 18 | Insert "(the contribution to potency due to accelerators)" between "$M_a$" and "may" |
| 10 | 1 | Delete "," after "far" |
| 10 | 15 | Replace "after each application failed to prevent the" with "accomplished a" |
| 10 | 16 | Delete "development of tumors. A" |
| 10 | 17 | Delete "could be accomplished" |
| 11 | 21 | Insert "(See Table X for experimental details)" after "applied" |
| 11 | 24 | Replace "III" with "IX" |
| 12 | 2 | Replace "indicated" with "suggested" |

ERRATA AND ADDITIONS TO

THE TABULAR SUMMARY OF CURRENT AND COMPLETED

BIOLOGICAL EXPERIMENTS

October 1, 1955

| TABLE | API EXPERIMENT NUMBER | COLUMN HEADING | SUGGESTED CHANGE |
|---|---|---|---|
| I(page 2) | 39 | $P_{MC}$ | 0.15X |
| (page 3) | 74 | Description | Total furnace charge |
| (page 4) | 76 (2nd exp.) | | 89%-56 weeks, $P_{MC}$= 0.04±.01 |
| (page 5) | 109 | % BP | 0.035 |
| (page 10) | 117 | $P_{MC}$ | X |
| | 111-4b | | 0% - 60 weeks (painting discontinued after 48 weeks, animals killed after 60 weeks.) |
| | 112-3 | $P_{MC}$ | X |
| (page 13) | 8-26a - 8-26d | | 0% - 80 weeks |
| (page 14) | 8-26e | | 0% - 80 weeks |
| | 8-26g | | 28% - 77 weeks |
| | 8-26l | | 90% - 51 weeks, $P_{MC} = 0.05^{+.02}_{-.01}$ |
| (page 16) | 23-1 | Description | ...from Diels-Alder non-adduct from API-23,... |
| | 23-2 | " | ...from Diels-Alder non-adduct from API-23,... |
| | | sub-heading | Fractionation of Catalytically Cracked Residuum, API-12 |
| II | 639 | | 0% - 30 weeks |
| VII (page1) | 602 | $P_{MC}$ of BP | 38 |
| | 269 | solvent | n-hexadecane |
| | 298 | " | hexadecene-1 |

| TABLE | API EXPERIMENT NUMBER | COLUMN HEADING | SUGGESTED CHANGE |
|---|---|---|---|
| VII (page 4) | 633 | | 100% - 42 weeks, $P_{MC}$ = 0.05±.01, $P_{MC}^{o}$ = 63 |
| (page 5) | 635 | | 94% - 44 weeks, $P_{MC}$ = 0.04±.01, $P_{MC}^{o}$ = 50 |
| | 644 | | 0.09% Methylcholanthrene, 100% - 20 weeks, $P_{MC} = 0.28^{+.07}_{-.04}$, $P_{MC}^{o}$ = 311 |
| | 643 | | 100% - 22 weeks, $P_{MC} = 0.12^{+.04}_{-.03}$, $P_{MC}^{o}$ = 71 |
| (page 6) | 619 | $P_{MC}$ | 0.20X |
| | 632a | | 100% - 21 wks., $P_{MC}$ = 0.16±.01, $P_{MC}^{o}$ = 94 |
| | 640 | | 100%-22 wks., $P_{MC} = 0.19^{+.04}_{-.03}$, $P_{MC}^{o}$ = 112 |
| | 641 | | 100%-21 wks., $P_{MC}$ = 0.17±.02, $P_{MC}^{o}$ = 100 |
| | 642 | | 100%-20 wks., $P_{MC} = 0.18^{+.03}_{-.02}$, $P_{MC}^{o}$ = 106 |
| VIII | 76 | | 89% - 56 weeks, 40.3±4.5 |
| | 620 | | 92%- 51 weeks, 35.8±4.0 |
| | 621 | | 79% - 57 weeks, 40.9±4.1 |
| | 622 | | 93% - 50 weeks, 39.6±3.9 |
| IX | 230 | Average latent period[1] | 10.8 |
| | 287 | " | 16.5 |
| | 292 (3x/week) | " | 16.4 |
| | 292 (2x/week) | " | 24.4 |
| | 292 (1x/week) | " | 43.2 |
| XI | 627 | | 88% - 59 weeks |
| XII (page 3) | add 321 between 317 & 320 | | API-8, 105 min., none, detergent solution, 3x/week - 100 mg., 100% - 22 weeks, 16.5±1.3 |

1. Calculated on basis of linear relationship between log time and response.

For Information Only - Not for Publication

INTERIM REPORT

API RESEARCH PROJECT MC-1

OCTOBER 1, 1955

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

ERRATA

for

Interim Report
API Research Project MC-1
October 1, 1955

| Page Number | Line Number | Suggested Change |
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| 1 | 4 | Insert "scrotal and other" between "of" and "cutaneous" |
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API RESEARCH PROJECT MC-1

October 1, 1955

The potential hazards deriving from carcinogenic materials in the intermediates and products of the refining of petroleum are being subjected to systematic investigation. The initiation of this work by the sponsors was stimulated in part by historical and recurrent instances of cutaneous, especially scrotal, cancer among wax pressmen. The immediate impetus came, however, with the recognition of the highly increased aromaticity of certain high boiling fractions produced in the newer catalytic processes. Further, pointed evidence from several centers of investigation showed that certain of these fractions possessed the capacity for the induction of cancers in the skin of experimental animals at a considerably higher level than that of the uncracked distillates associated with the problem among the pressmen.

Attention was directed in 1949 to products of the following processes, in which polycyclic aromatics might be synthesized and/or concentrated:

STRAIGHT THERMAL CRACKING PROCESSES

Non-catalytic cracking of virgin gas oil
Non-catalytic cracking of catalytic gas oil
Viscosity breaking
Naphtha reforming
Coking
Polyforming
Steam cracking

CATALYTIC CRACKING PROCESSES

Houdry
Thermofor catalytic cracking
Fluid catalytic cracking
Cycloversion
Catalytic reforming

SPECIFIC PRODUCTS

Slack waxes and press oils
Raw lube stocks from straight run distillation
Solvent extracts
Acid oils from acid sludge

With the full cooperation of the research and refining departments of the companies represented on the Medical Advisory Committee, detailed tables of information were assembled in the Laboratory, showing the variations in operating conditions and feed stocks of some 200 different units involved in the above processes. From this comparison of available materials, it was possible to select a series of about 600 samples to cover the extremes of the ranges of each important variable. Each company then obtained certain analytical data on a selected group of its samples and made this additional information available to responsible personnel in the Laboratory.

One item among these data was the absorption spectrum of a fraction representative of the heart-cut of the polycyclic hydrocarbons regarded as potentially carcinogenic. Estimates of the relative potency of each sample were based upon certain characteristics of these spectra. Although this empirical technique proved subsequently to be applicable mainly to residual fractions from catalytic cracking, the approach served a useful purpose. It pointed up one salient characteristic of the group of materials which, when tested biologically, were found to have potencies much higher than those predicted. Almost invariably, these samples contained high percentages of components boiling below 700°F. This observation, coupled with the results of parallel experiments on solutions of 3-methylcholanthrene in certain non-volatile solvents, led to the recognition of the contribution made to the potency of many petroleum products by a group of non-carcinogenic hydrocarbons, with boiling points in the range, 500-750°F. These materials, termed "accelerators" for reasons of convenience, will be referred to in some detail later.

From the series of samples which had been collected and analyzed in this manner, approximately 120 were subjected to tests of their relative carcinogenic potency when applied upon the skin of C3H mice. This inbred

strain has proved particularly useful, in that the results of tests made to differentiate non-carcinogenic from carcinogenic materials by means of application of these materials upon the skin, have shown a satisfactory correlation thus far with the results of prolonged contact of human skin in those instances (admittedly limited in number) in which occupational exposure has been documented properly. Since the 120 samples represented a wide range of potencies for the skin, certain modifications of the time-honored experimental procedure (for the application of such materials on the skin of animals) were developed in the course of the research. As described in an article which has been circulated and will appear soon in Cancer Research, these improvements have made this experimental method more flexible and more readily subject to quantitative interpretation.

The relative potencies of these samples are shown in Table I. The scale on which they are expressed is based upon a series of parallel tests on solutions of 3-methylcholanthrene in benzene. The conventionalized expression ($P_{MC}$) for the capacity of a material to induce cancer in the skin of the mouse, simply indicates that the oil in question induces tumors in the skin of mice at the same rate, under comparable experimental conditions, as a solution of that level of concentration, in percent by weight, of the synthetic carcinogen.

It may be pertinent at this point to glance at the relative potencies of certain products of another industry which has experienced an increased incidence of skin cancer among specific groups of its employees. Crude coal tars from by-product coke ovens have shown potencies in the $P_{MC}$ range, 0.08 to 0.4, there being some evidence that the majority of these would be included in the 0.10 to 0.15 part of this range. Thus, it will be noted that some uncracked distillates from petroleum (e.g., API-79 and 105) have approxiamtely the same potency for mice as these coal tars. The average

duration of the exposure of workmen who developed cancer of the skin in association with contact with tar was comparable to that of wax pressmen, about 15 to 20 years.

It is apparent from the data in Table I that thermal cracking of catalytic gas oils, as it is usually practiced, does not reduce their carcinogenic potency. Indeed, when one notes the relative increase in the content of benzo[a]pyrene (BP) which often results from this process, it might be expected that potency would increase significantly, were it not for the fact that the probable accompanying destruction of long-chain accelerators operates in the opposite direction.

Such correlations between the relative potencies of different oils and their chemical composition have been among the major aims of this investigation. It was recognized from the outset that the needs of such a dynamic industry would not be met by determining and listing the potencies of samples selected more or less arbitrarily at any particular time. The changes in refining methods which have accompanied the competitive technological developments of the past decade have had a profound effect upon the composition of many fuels and other petroleum products. Since continued biological testing is time-consuming and costly, the need for chemical-analytical methods for the estimation of carcinogenic potency of complex mixtures has been evident.

To these ends an intensive program of fractionation and analysis of selected carcinogenic oils was initiated in 1949. In its early stages this work yielded suggestive evidence of a relationship between the carcinogenic potency of cracked residua for mice and the intensity of a band in the absorption spectra of certain distillates prepared from these oils in the laboratory. The most intensive work has been carried out with a sample of slurry from Fluid Catalytic Cracking, API-8. Spectrographic evidence of

the presence in this oil of the well known carcinogenic hydrocarbon, benzo[a]-pyrene, led eventually to its isolation and its identification with a synthetic sample of the pure compound. Further evidence that the concentration of this particular family of carcinogens in many residual oils was of such a level as to contribute to their carcinogenic potency to a major extent furnished the stimulus for the development of a generally applicable method of analysis for this family of compounds. The method has been published in Analytical Chemistry, 27, 248 (1955).

The content of benzo[a]pyrene has been determined in each of the oils which have been tested by application on the skin of mice. The results are shown on Table I. With certain striking exceptions, it will be noted that there is a rough correlation between the content of BP and the relative potency of the residual products from any given process. One of the exceptions is sample API-71 from Thermofor Catalytic Cracking. A detailed examination of this oil, and of certain of the distillates (sidestreams) which have been tested, has been made in order to learn more about other classes of compounds which contribute significantly to the carcinogenic potency of these oils

In parallel with the program of fractionation of samples obtained from refining operations, solutions of synthetic carcinogens in various solvents and in mixtures of known composition have been investigated. Generally, it has been found that the replacement of benzene by progressively less volatile solvents has resulted in progressive retardation of the rate at which a given concentration of carcinogen would induce tumors. Comparison of the relative areas of skin wetted by given quantities of the solution in benzene with those involved in contact with the less volatile solvents has suggested a very plausible explanation for the slower induction of tumors by the latter. It could be shown that, so long as the dosage in milligrams of the carcinogenic solute per unit area of skin was kept constant,

the rate of induction of tumors was unchanged. For example, since solutions of methylcholanthrene (MC) in amylbenzene spread about twice as far over the skin as solutions in benzene, it is necessary to use almost 0.2 percent MC in the alkylbenzene to obtain the same dose per unit area and rate of carcinogenesis as were obtained with 0.1 percent MC in benzene.

Extension of this work to include solutions of MC in the detergent intermediate, dodecylbenzene, yielded results which were surprising at first, but subsequently rewarding in that they provided the explanation for the potency of oils such as API-71. Solutions of MC in this 18-carbon solvent spread more widely upon the skin then did those in amylbenzene, and yet induced tumors much more rapidly than did the corresponding solutions in benzene. The presence of fractions with comparable "accelerating"properties in a number of petroleum oils was demonstrated subsequently. It soon became apparent that these materials are derived from the crude petroleum, that they may increase in concentration to some extent under the conditions of catalytic cracking, and that they may eventually be reduced significantly by very drastic cracking.

Further investigation of solutions of BP in various pure solvents (Table II) has shown that this property of acceleration is shared by at least some members of almost all classes of hydrocarbons containing 10 to 20 carbon atoms per molecule. The shape of the molecule, as well as its overall length, seems to be an important characteristic, since 7-cyclohexyltridecane (Experiment API-279) proved to be rather weak as an accelerator. The finding that normal paraffins, such as cetane, may contribute significantly to the carcinogenic potency of a mixture, although they themselves are non-carcinogenic, has thrown some light, it seems, upon the apparent paradox involved in the occurrence of scrotal cancer, under certain circumstances, among men engaged in wax-pressing operations, despite the low aromaticity of the distillates which enter into these operations.

The current systematic study of the properties of distillates from a variety of cracked and straight run oils represents an effort to quantitate the knowledge which has been accumulated on accelerators. The goal is an analytical method by which the factor introduced into the potency equation by these fractions in any given oil may be determined.

The knowledge accumulated thus far from numerous experiments on solutions of certain polycyclic hydrocarbons in solvents of well defined composition suggests that a realistic technique for estimating the potency of any given oil on the basis of its physical and chemical characteristics may involve a summation of four separate analyses. In algebraic terms

$$P_{MC} = M_a (C_1 + C_2 + C_3) .$$

The summation of $C_1$, $C_2$, and $C_3$ represents the effective potency contributed by three major categories of polycyclic carcinogens, expressed in methylcholanthrene equivalents. Included in these three classes are (1) the benzopyrenes previously discussed, (2) carcinogenic substances extractable by maleic anhydride (probably derivatives of benzanthracene), and (3) carcinogenic substances insoluble in concentrated sulfuric acid (sometimes referred to as low-boiling carcinogenic compounds). The factor $M_a$ may vary, apparently, from 1 to 8, and thus in certain instances, such as catalytic cycle gas oils and light lube distillates, may provide the major contribution to potency. Hence, the quantitation of the effects of accelerators becomes a matter of considerable practical importance.

The available evidence indicates that a significant fraction of the carcinogens may be extracted from catalytically cracked oils by maleic anhydride. In the case of API-8, approximately 40 percent of the carcinogenic material (in terms of methylcholanthrene equivalents) may be separated from the oil by this technique. Experiments 8-25a and 8-25b have shown that there

is no significant difference in potency between the fractions obtained by successive extractions of API-8 with maleic anhydride, even though the mass spectra of the different fractions indicate that there are gross differences in their chemical composition.

Similarly, when such an extraction is applied to a cracked sidestream, such as API-89, a small amount of carcinogenic material may be extracted. Because of the uncertainty about the multiplication factor due to accelerators in API-89, it cannot be said yet what portion of the carcinogen were removed by maleic anhydride. However, separation of the extract from API-89 by chromatography yielded valuable information to the effect that the large proportion of the fraction which was desorbed more easily than benzanthracenes, approximately 90 percent of the total Diels-Alder adduct, contained practically none of the carcinogenic materials. Further, to resolve some of these questions a series of chromatographic fractionations are being applied to a series of straight-run and cracked distillates, similar in boiling range to API-89 (600 to 750°F.), to produce accelerator-free concentrates of carcinogens, which may then be tested directly for their relative potency. This should then provide values for the summation ($C_1 + C_2 + C_3$) in the potency equation. A parallel series of extractions of the oils by maleic anhydride will furnish quantitative information regarding the relative contribution of this class of carcinogens to the effective sum. Some evidence has been collected which indicates that these compounds extracted by maleic anhydride contribute relatively less to the potency of sidestreams than to that of residual oils.

From the practical standpoint of the occupational hazard of skin cancer, perhaps the most important oils are the distillates obtained in the range 550 to 800°F. Such materials as wax distillates, diesel fuels, and base stocks for cutting oils are found within this range. It is probable

that the first two major classes of carcinogenic substances, $C_1$ and $C_2$ in the potency equation, may contribute relatively little to these distillates. Both of these classes would be extracted in fairly large part by concentrated sulfuric acid. It has been noted previously that the raffinate, API-8-20, from such an extraction of the lower boiling carcinogenic distillates of API-8 contains most of the carcinogens of these fractions. A large batch of polycyclic aromatics concentrated from API-8 by chromatography has been subjected to careful distillation through a column having a theoretical efficiency of 80 plates. Selected fractions are being tested under the code number 8-26.

The fractions which were distilled below 720°F. showed at most a very low order of carcinogenic potency. The behavior of the fractions between 675 and 710°F. suggested the presence of a trace of carcinogen in an active accelerating medium. This was confirmed by experiment 8-26-2, which demonstrated that the accelerators in these fractions had a multiplication factor, with respect to potency, of about two. The alkylanthracenes removed during the same chromatography were tested for potential acceleration in experiment 8-26-3. Their lack of significant activity in this respect is compatible with the general idea that more alkylation of such a nucleus would be required then would be found in a cut of this boiling range.

The major components of the carcinogenic fractions boiling between 720 and 760°F. are derivatives of pyrene, benzfluorene, and fluoranthene, together with a substantial amount of non-hydrocarbons, particularly derivatives of carbazole. A separation of these classes is being carried out in order to determine their relative contribution to the potency of straight-run and cracked distillates.

This report thus far, has concerned itself with the problem of the relationships between chemical composition and carcinogenic potency. Considerations of industrial hygiene involved in the general problem have also been investigated in a number of ways. Experimental work on the possibility of reducing the hazard by washing the materials from the skin, and by the application of so-called barrier creams, has been carried out. Generally speaking, it has been found that the development of tumors could be retarded significantly by washing the skin with soap and water at an appropriate interval after the application of a carcinogenic material, so long as the frequency of application did not exceed once per week. For example, in an experiment in which the oil API-8 was removed by washing within 10 minutes after its application, no tumors developed during the entire life span of the mice. However, in most of the experiments involving three applications of a material per week, the washing of the skin with an apparently effective detergent after each application failed to prevent the development of tumors. A significant retardation of the rate at which the tumors developed could be accomplished, but, as a general rule, half or more of the animals developed neoplastic growths. The use of barrier creams prior to the application of a carcinogenic oil had no significant effect upon the outcome of the experiment.

The use of various hydrocarbon solvents to rinse off the excess of oil prior to washing the skin with a detergent has been referred to in some detail in a previous report and in verbal discussions. Briefly to summarize these observations, these procedures in some instances, have augmented the carcinogenic effect instead of contributing to the efficiency of the cleansing of the skin by the detergent and water. Solvents containing accelerators have proved to be particularly disadvantageous in this respect. In short, it appears that such rinsing with solvents does not improve the efficiency

of the washing, and may accelerate the induction of experimental cancers. As a measure of occupational hygiene, such a procedure does not appear to be desirable.

In the course of the general experimental program, a number of other questions raised withing the Laboratory and by representatives of the Medical Advisory Committee have been answered. For example, numerous experiments have shown that if the applications of a carcinogenic oil from catalytic cracking be discontinued at the time the first evidence of neoplastic growth of the skin of the mouse appears, the likelihood of the further development of the lesion into a malignant tumor is the same as it would be if the applications had been continued. On the other hand, if the applications upon the skin of all of the numbers of a group of mice terminated at the time of the earliest appearance of a papilloma on the skin of the first member of its group, widely variant results are obtained in different experiments. In the case of a test with API-71, the majority of the animals subjected to no further applications went on to develop tumors at almost the same rate as that which characterized a parallel group which was the subject of uninterrupted applications. On the other hand, in an experiment with API-43-1, very few additional animals developed tumors after the interruption of the applications until at a much later time, after a second period during which the carcinogenic oil was applied.

The action of accelerators upon skin previously subjected to contact with carcinogenic materials, has also been investigated. A number of experiments referred to in Table III have demonstrated that accelerators such as dodecylbenzene and dodecane are capable of eliciting tumors in skin previously subjected to single applications of catalytically cracked oil.

Other experiments have shown that contact with the accelerating alkylbenzenes may so alter the skin as to augment the effects of its subsequent contact with carcinogenic oils. The nature of this alteration is speculative,

but the phenomenon, of itself, suggests certain approaches in investigating the mechanisms of acceleration. That these are multiple is indicated by the indication (Experiments 600 and 620) that dodecane seems to lack the capacity to condition the skin in this manner.

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# Appraisal of the Potential Carcinogenic Properties of American Petroleum Products

Report of the Progress
in the
Epidemiological Studies
October 1955

The Kettering Laboratory
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## Introduction

The planning for the epidemiological aspects of this project was begun in 1949. The objectives as finally defined by the Medical Advisory Committee are as follows:

1. To ascertain the incidence and prevalence of neoplastic disease among employees of the interested petroleum companies.

2. To compare these rates with those of the general population and other industrial groups.

3. To evaluate, employing epidemiological methods, housekeeping and hygienic arrangements directed toward eliminating or controlling exposure to possible irritants.

4. To advise, utilizing the results of these studies, possible improvements or modifications of present hygienic measures.

Among the various approaches to these goals are:

1. Historical Survey. Assembling and reviewing of the records of known cases in the files of the interested companies.

2. Current Case Registry. Establishing by mutual agreement a central file for receiving and tabulating reports of new cases as they occur among their employees.

3. Insurance Record Surveys. Employing the records of various health benefit plans to determine the incidence of neoplastic disease, not only in the refineries, but also in other industries located in the same general area and using the same labor pool.

4. Studies of Skin Changes. Comparing the incidence and prevalence of keratoses and/or similar hypertrophic lesions in groups of petroleum workers exposed.

5. Slack Wax Studies. Repeating the observations on employees exposed to possible unusual hazards due to their work in wax extraction processes.

6. Advisory Service. Furnishing epidemiological consultant service to aid in planning investigation and control programs for individual companies.

7. Literature Review Service. A literature review service was considered but later rejected. Critical abstracts of pertinent medical literature were to be prepared and circulated periodically to the members of the Medical Advisory Committee.

Only the first two have been implemented to date. The study of health insurance records has been held up until satisfactory relationships can be established. Field surveys were abandoned early because it was quite apparent that such studies must be carried out by the individual company. While the advice and help in the collection of records continues to be given on request, the literature review was never attempted.

Present Status of the Central Registry

Since late in 1950 until September 15, 1955, 1,877 reports have been received from sixteen companies. Twenty-nine have not been included in the various tabulations because the amount of information submitted is inadequate. The acceptable cases have been listed by year of onset and the reporting company number in Table 1a. (See last year's communication for company identification.)

Geographical coverage of the industry is now almost complete. An additional company has decided to participate and is planning to report current cases. Efforts are continuing to improve the accuracy of the reports; to include a larger number of employees in the reporting base (ten of the sixteen participating companies reported that they were recording cancer cases in approximately 120,000 employees); and to obtain the participation of all the major companies represented on the Medical Advisory Committee. Completeness of reporting is likewise a serious problem. From the 120,000 employees, only 185 cases were reported during the year 1954, a rate of approximately 150 per 100,000, or about 1/3 of the value found for the age group 50-54 in the Public Health Service Study. While the age distribution may account for some of this difference, it is obvious that a deficit is present.

At the start of this phase of the project, the information from the clinical and occupational record forms was coded and transferred to key sort cards sorted manually. Late in 1954 when it became evident that participation by a large segment of the industry was assured and the number of reports reached a point where the necessary manipulations became cumbersome, this method of tabulation was abandoned. Electronic methods utilizing IBM equipment were substituted. This change insures greater flexibility and permits the study of more variables in finer detail.

Throughout the first nine months of 1955, the work centered on the preparation of a new code; transferring the information to master tables; and finally punching the cards. Unfortunately, difficulties were encountered, some of which are still unresolved. Additional clerical assistance was assigned, but the task was not completed until September 1, 1955. As a consequence, no tabulations were prepared for the Buffalo Meeting, and only a few very basic summary tables are ready at this time although more complex analyses will be undertaken in the near future.

Table 1a - NUMBER OF INDIVIDUALS WITH SINGLE NEOPLASMS ACCORDING TO YEAR OF ONSET AS REPORTED BY 16 COMPANIES

| Company | Prior to 1950 | 1950 | 1951 | 1952 | 1953 | 1954 | 1955* | Total** |
|---|---|---|---|---|---|---|---|---|
| 01 | | | | | | | | |
| 02 | 3 | 2 | | | | | | 5 |
| 03 | | | | | | | | |
| 04 | | | | | | | | |
| 05 | | | | | | | | |
| 06 | 121 | 78 | 66 | 1 | | | | 266 |
| 07 | 53 | 9 | 8 | 9 | 11 | 13 | | 103 |
| 08 | 79 | 6 | 8 | | | | | 93 |
| 09 | 27 | 7 | 10 | 6 | 9 | 1 | | 60 |
| 10 | | 3 | | 1 | 3 | 5 | 1 | 13 |
| 11 | 19 | 3 | 2 | 2 | | | | 26 |
| 12 | 3 | 4 | 4 | 16 | 14 | 14 | 2 | 57 |
| 13 | | | | | | | | |
| 14 | | 7 | 11 | 11 | 18 | 20 | 10 | 77 |
| 15 | 2 | 2 | 2 | 5 | 4 | 12 | 1 | 28 |
| 16 | | | | | | | | |
| 17 | 70 | 14 | 13 | 14 | 32 | 38 | 25 | 206 |
| 18 | 32 | 31 | 32 | 32 | 63 | 33 | 6 | 229 |
| 19 | 13 | 14 | 19 | 17 | 15 | 10 | 4 | 92 |
| 20 | | | | | | | | |
| 21 | | | | | | | | |
| 22 | | | | | | | | |
| 23 | 231 | 39 | 24 | 8 | 12 | 9 | 4 | 327 |
| 24 | 26 | 9 | 9 | 17 | 11 | 25 | 1 | 98 |
| 25 | 76 | 26 | 14 | 13 | 19 | 17 | 3 | 168 |
| Total | 755 | 254 | 222 | 152 | 211 | 197 | 57 | 1,848* |

*To September 15, 1955

**Twenty-nine reports are not included because:

(a) four onsets were prior to employment in the petroleum industry;
(b) eleven were totally inadequate and no more information was obtained;
(c) three did not give a diagnosis;
(d) eleven were not neoplasms as defined in this study.

Forty-two of the individual cases had multiple tumors.

Table 1b gives the number of individuals according to sex, race, and date of onset. It will be noted that 1,093, or 59% of the 1,848 acceptable reports, concern cases with onsets subsequent to January 1, 1950, the date arbitrarily chosen to separate historical from current records. This means that a reasonable number of new cases are at hand for further study.

It is noteworthy that 42 individuals were reported with two or three neoplasms. These cases are presented in Table 1c. In subsequent tabulations, the totals will include this group, counting each tumor as a separate occurrence. Some better method of including this group in the summaries will be sought during the coming year. In Table 2, therefore, the 1935 neoplasms are listed according to sex, race, and date of onset. Since the known colored group is such a small segment of the total, racial separation is also neglected in the following summary tables.

The first two of the simple summaries compares by sex and date of onset the relative frequency of different forms of cancer, both as to primary site and type, with the results of the 1947 Public Health Service Survey. It must be emphasized that these values are not incidence rates but represent the measurement of the frequency of one form of cancer by comparing the number of that form of cancer with the total number of all cases.

The distribution of tumors reported by the participating companies, both prior and subsequent to 1950 and both as to primary site and type of tumor, follow very closely the pattern found in the PHS Survey. A slight excess, 31.4% as compared to 28.7% of digestive system neoplasms, is noted among males with onsets prior to 1950. This difference is erased, and a smaller proportion is found in this category among the current cases. However, skin and soft tissue lesions are more frequent, 25.9% as to 19.3%, in the group with onsets subsequent to January 1, 1950. A higher proportion of non-glandular epithelial tumors were reported from both groups.

The question of age adjustment always enters the picture. In these particular comparisons, no effort has been made to take this into account. The error introduced by failure to consider this aspect is probably small, but it should be considered in the future.

Summary Tables 3 and 4 represent an attempt to relate the occupation of the patient in the petroleum industry with the primary site of the tumor. Summary Tables 5 and 6 are a similar attempt to ascertain the relationship of occupation to type. Unfortunately, for many of the occupational categories, the number of cases reported is too small to permit adequate analyses, and no reliance can be placed in the differences found. It is noteworthy, however, that these comparisons again show a relative

TABLE 1b - NUMBER OF INDIVIDUALS WITH SINGLE NEOPLASMS ACCORDING TO SEX, RACE, DATE OF ONSET, AND MALIGNANCY AS REPORTED FROM 16 COMPANIES

| Sex | Race | Onset Prior to 1950 | | | Onset Subsequent to 1950 | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Malignant | Benign | Total | Malignant | Benign | Total | Malignant | Benign | Total |
| MALE | White | 578 | 21 | 599 | 927 | 34 | 961 | 1,505 | 55 | 1,560 |
| | Colored | 17 | 1 | 18 | 17 | | 17 | 34 | 1 | 35 |
| | Not Given | 80 | 23 | 103 | 51 | 5 | 56 | 131 | 28 | 159 |
| | TOTAL | 675 | 45 | 720 | 995 | 39 | 1,034 | 1,670 | 84 | 1,754 |
| FEMALE | White | 23 | | 23 | 56 | | 56 | 79 | | 79 |
| | Not Given | 6 | 3 | 9 | 2 | 1 | 3 | 8 | 4 | 12 |
| | TOTAL | 29 | 3 | 32 | 58 | 1 | 59 | 87 | 4 | 91 |
| Not Given | | 3 | | 3 | | | | 3 | | 3* |
| Total Both Sexes | | 707 | 48 | 755 | 1,053 | 40 | 1,093 | 1,760 | 88 | 1,848 |

*These cases are not in subsequent tabulations.

Table 1c - NUMBER OF INDIVIDUALS WITH MULTIPLE NEOPLASMS ACCORDING TO SEX, RACE, DATE OF ONSET, AND MALIGNANCY AS REPORTED FROM 16 COMPANIES

| Sex | Race | Onset Prior to 1950 | | | | | Onset Subsequent to 1950 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Three Malign | Two Malign | One Benign One Malign | Two Benign | Total | Three Malign | Two Malign | One Benign One Malign | Two Benign | Total |
| MALE | White | 2 | 14 | 1 | | 17 | 1 | 14 | 2 | 1 | 18 |
| | Colored | | 1 | | | 1 | | | | | |
| | Not Given | | 1 | 2 | 2 | 5 | | | | | |
| | Total | 2 | 16 | 3 | 2 | 23 | 1 | 14 | 2 | 1 | 18 |
| FEMALE | White | | | | | | | 1 | | | 1 |
| Total Both Sexes | | 2 | 16 | 3 | 2 | 23 | 1 | 15 | 2 | 1 | 19 |

Table 2 - NUMBER OF NEOPLASMS ACCORDING TO SEX, RACE, DATE OF ONSET, AND MALIGNANCY AS REPORTED FROM 16 COMPANIES

| Sex | Race | Onset Prior to 1950 | | | Onset Subsequent to 1950 | | | Total Neoplasms Reported* | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Malignant | Benign | Total | Malignant | Benign | Total | Malignant | Benign | Total |
| MALE | White | 613 | 22 | 635 | 960 | 38 | 998 | 1,573 | 60 | 1,633 |
| | Colored | 19 | 1 | 20 | 17 | | 17 | 36 | 1 | 37 |
| | Not Given | 84 | 29 | 113 | 51 | 5 | 56 | 135 | 34 | 169 |
| | TOTAL | 716 | 52 | 768 | 1,028 | 43 | 1,071 | 1,744 | 95 | 1,839 |
| FEMALE | White | 23 | | 23 | 58 | | 58 | 81 | | 81 |
| | Not Given | 6 | 3 | 9 | 2 | 1 | 3 | 8 | 4 | 12 |
| | TOTAL | 29 | 3 | 32 | 60 | 1 | 61 | 89 | 4 | 93 |
| Not Given | | 3 | | 3 | | | | 3 | | 3** |
| Total Both Sexes | | 748 | 55 | 803 | 1,088 | 44 | 1,132 | 1,836 | 99 | 1,935 |

*In 1,919 individuals reported to September 15, 1955.
**These cases are not included in subsequent tabulations.

increase in frequency of neoplasms of the skin and soft tissues and of a non-glandular epithelial type.

Summation

It is planned to continue these studies following essentially the original plan. Now that the information can be tabulated readily by electronic devices, many further analyses are possible and will be undertaken.

The epidemiological investigations developed slowly for several good and sufficient reasons. The first was that certain of the companies have no centralized medical department to collect the necessary data, past or future. Even with medical departments, some found it difficult to participate because (a) the department is new and has no past records; or (b) the record system in use does not permit easy location of the clinical records of the case. Another is that this was a precedent-breaking departure from usual relationships. Companies and physicians are reporting voluntarily to an unofficial central agency. Physicians have always rebelled against even the official requirement of reporting of communicable disease cases. This makes it more difficult to secure cooperation on a voluntary basis. An occasional management is still wary and is waiting to see what happens.

The cooperation obtained and the progress made in view of these many difficulties is significant although, as yet, little reliance can be placed on the results. As the project grows and matures and more of the current cases are found and reported, worthwhile comparisons will be forthcoming. Further, as the recognition of the need of such studies crystallizes, other and different approaches may become feasible.

Summary Table 1 - MALIGNANT NEOPLASMS
ACCORDING TO SEX, DATE OF ONSET, AND SITE OF TUMOR

| Site | Male | | | | | Female | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | USA* 1947 | Prior to 1950 | | Subsequent to 1950 | | USA* 1947 | Prior to 1950 | | Subsequent to 1950 | |
| | | No. | % | No. | % | | No. | % | No. | % |
| Buccal Cavity 00-0X | 6.9 | 55 | 7.7 | 77 | 7.5 | 2.2 | 0 | 0.0 | 0 | 0.0 |
| Digest. Sys. and Perit. 10-1X | 28.7 | 225 | 31.4 | 273 | 26.6 | 19.8 | 7 | 24.1 | 7 | 11.7 |
| Respiratory System 20-2X | 12.6 | 87 | 12.2 | 153 | 14.9 | 2.3 | 3 | 10.3 | 0 | 0.0 |
| Breast 30 | 0.2 | 0 | 0.0 | 2 | 0.2 | 22.0 | 8 | 27.6 | 22 | 36.7 |
| Genital Organs 40-4X | 10.4 | 58 | 8.1 | 76 | 7.4 | 25.5 | 2 | 6.9 | 19 | 31.7 |
| Urinary System 50-55 | 6.9 | 40 | 5.6 | 60 | 5.8 | 3.1 | 0 | 0.0 | 2 | 3.3 |
| Skin and Soft Tissue 60-6X | 19.3 | 139 | 19.4 | 266 | 25.9 | 13.1 | 4 | 13.8 | 6 | 10.0 |
| Bones 70-75 | 0.8 | 16 | 2.2 | 7 | 0.7 | 0.5 | 3 | 10.3 | 0 | 0.0 |
| Brain 76-78 | 2.7 | 17 | 2.4 | 18 | 1.8 | 1.9 | 0 | 0.0 | 1 | 1.7 |
| Lymph. and Hem. System 80-8Y | 6.7 | 36 | 5.0 | 52 | 5.1 | 4.2 | 0 | 0.0 | 1 | 1.7 |
| Other Sites 90-9X | 4.8 | 43 | 6.0 | 44 | 4.3 | 5.4 | 2 | 6.9 | 2 | 3.3 |
| Total | 100.0 | 716 | 100.0 | 1,028 | 100.0 | 100.0 | 29 | 100.0 | 60 | 100.0 |

*From "Morbidity from Cancer in the United States," Public Health Monograph No. 29, U.S.P.H.S.

Summary Table 2 - MALIGNANT NEOPLASMS
ACCORDING TO SEX, DATE OF ONSET, AND TYPE OF TUMOR

| Type of Tumor | | Male | | | | | Female | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | USA* 1947 | Prior to 1950 | | Subsequent to 1950 | | USA* 1947 | Prior to 1950 | | Subsequent to 1950 | |
| | | | No. | % | No. | % | | No. | % | No. | % |
| Gland. Epith. | 00-09 | 22.4 | 114 | 15.9 | 161 | 15.7 | 31.1 | 7 | 24.1 | 22 | 36.7 |
| Non-Gland. Epith. | 11-19 | 60.1 | 484 | 67.6 | 703 | 68.4 | 54.7 | 17 | 58.6 | 31 | 51.7 |
| Leukemia | 20-29 | 2.9 | 12 | 1.7 | 13 | 1.3 | 1.7 | 1 | 3.4 | 0 | 0.0 |
| Lymphoma | 30-39 | 3.8 | 29 | 4.1 | 41 | 4.0 | 2.4 | 0 | 0.0 | 1 | 1.7 |
| Nervous Tissues | 40-49 | 2.0 | 5 | 0.7 | 14 | 1.4 | 1.4 | 0 | 0.0 | 1 | 1.7 |
| Vascular Tissues | 50-59 | 0.2 | 1 | 0.1 | 2 | 0.2 | 0.2 | 0 | 0.0 | 0 | 0.0 |
| Muscle | 66-69 | 0.2 | 0 | 0.0 | 1 | 0.1 | 0.4 | 0 | 0.0 | 0 | 0.0 |
| Non-Epith. Tissues | 70-79 | 2.0 | 18 | 2.5 | 20 | 1.9 | 1.6 | 1 | 3.4 | 1 | 1.7 |
| Embry. and Mixed Tissues | 80-89 | 1.5 | 14 | 2.0 | 16 | 1.6 | 1.3 | 0 | 0.0 | 0 | 0.0 |
| Not Classified | 97-99 | 4.8 | 39 | 5.4 | 57 | 5.5 | 5.0 | 3 | 10.3 | 4 | 6.7 |
| Total | | 100.0 | 716 | 100.0 | 1,028 | 100.0 | 100.0 | 29 | 100.0 | 60 | 100.0 |

*From "Morbidity from Cancer in the United States," Public Health Monograph No. 29, U.S.P.H.S.

Summary Table 3 - PERCENTILE DISTRIBUTION OF MALIGNANT NEOPLASMS IN MALES WITH ONSETS PRIOR TO JANUARY 1, 1950, ACCORDING TO SITE OF TUMOR AND PETROLEUM OCCUPATION AS COMPARED TO THE UNITED STATES' EXPERIENCE

| Principal Pet. Occupation | USA* | Production | Refining | | | | | | | Transport | Market and Exec. | Others |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Site | 1947 | 01-09 | Cracking 20-29 | Lub. and Grease 30-35 | Paraffin 36-39 | Str. Run 40-49 | Spec. Prod. 50-59 | Maintenance 60-69 | Others 70-79 | 80-89 | 90-98 | 99 |
| Buccal Cavity 00-0X | 6.9 | 5.2 | 12.5 | 12.5 | 0.0 | 15.4 | 23.1 | 7.7 | 6.9 | 12.3 | 6.8 | 0.0 |
| Digest. Sys. and Perit. 10-1X | 28.7 | 28.6 | 37.5 | 37.5 | 33.3 | 23.1 | 15.4 | 31.6 | 34.6 | 31.6 | 30.8 | 20.0 |
| Respiratory System 20-2X | 12.6 | 18.2 | 18.8 | 12.5 | 4.8 | 7.7 | 38.5 | 8.6 | 13.2 | 10.5 | 12.0 | 10.0 |
| Breast 30 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Genital Organs 40-4X | 10.4 | 2.6 | 0.0 | 12.5 | 38.1 | 15.4 | 0.0 | 8.6 | 5.7 | 14.0 | 6.0 | 20.0 |
| Urinary System 50-55 | 6.9 | 3.9 | 6.3 | 12.5 | 0.0 | 7.7 | 7.7 | 4.8 | 3.1 | 5.3 | 10.5 | 10.0 |
| Skin and Soft Tissue 60-6X | 19.3 | 23.4 | 25.0 | 12.5 | 14.3 | 30.8 | 15.4 | 22.5 | 20.1 | 12.3 | 13.5 | 30.0 |
| Bones 70-75 | 0.8 | 3.9 | 0.0 | 0.0 | 4.8 | 0.0 | 0.0 | 2.9 | 1.9 | 0.0 | 2.3 | 0.0 |
| Brain 76-78 | 2.7 | 1.3 | 0.0 | 0.0 | 4.8 | 0.0 | 0.0 | 1.9 | 2.5 | 3.5 | 3.8 | 0.0 |
| Lymph. and Hem. System 80-8Y | 6.7 | 2.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 7.2 | 5.7 | 5.3 | 5.3 | 0.0 |
| Other Sites 90-9X | 4.8 | 10.4 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 4.3 | 6.3 | 5.3 | 9.0 | 10.0 |
| Total | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |

*From "Morbidity from Cancer in the United States," Public Health Monograph No. 29, U.S.P.H.S.

Summary Table 4 - PERCENTILE DISTRIBUTION OF MALIGNANT NEOPLASMS IN MALES WITH ONSETS SUBSEQUENT TO JANUARY 1, 1950, ACCORDING TO SITE OF TUMOR AND PETROLEUM OCCUPATION AS COMPARED TO THE UNITED STATES' EXPERIENCE

| Principal Pet. Occupation / Site | USA* 1947 | Production 01-09 | Refining | | | | | | | Trans-port 80-89 | Market and Exec. 90-98 | Others 99 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Cracking 20-29 | Lub. and Grease 30-35 | Paraffin 36-39 | Str. Run 40-49 | Spec. Prod. 50-59 | Maintenance 60-69 | Others 70-79 | | | |
| Buccal Cavity 00-0X | 6.9 | 6.3 | 2.7 | 15.0 | 5.6 | 10.5 | 12.5 | 7.4 | 9.8 | 6.8 | 7.1 | 0.0 |
| Digest. Sys. and Perit. 10-1X | 28.7 | 15.1 | 35.1 | 5.0 | 22.2 | 31.6 | 25.0 | 29.6 | 29.4 | 24.8 | 29.0 | 24.0 |
| Respiratory System 20-2X | 12.6 | 16.7 | 8.1 | 25.0 | 11.1 | 10.5 | 37.5 | 14.8 | 9.8 | 19.7 | 15.2 | 24.0 |
| Breast 30 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.9 | 0.0 | 0.0 | 0.0 | 0.0 |
| Genital Organs 40-4X | 10.4 | 7.1 | 5.4 | 0.0 | 27.8 | 0.0 | 0.0 | 7.4 | 5.4 | 14.5 | 6.2 | 4.0 |
| Urinary System 50-55 | 6.9 | 6.3 | 5.4 | 15.0 | 11.1 | 10.5 | 0.0 | 6.5 | 3.9 | 3.4 | 5.4 | 16.0 |
| Skin and Soft Tissue 60-6X | 19.3 | 36.5 | 29.7 | 40.0 | 22.2 | 31.6 | 25.0 | 24.3 | 28.4 | 21.4 | 19.6 | 24.0 |
| Bones 70-75 | 0.8 | 0.8 | 2.7 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.5 | 1.7 | 0.9 | 0.0 |
| Brain 76-78 | 2.7 | 0.8 | 2.7 | 0.0 | 0.0 | 0.0 | 0.0 | 1.3 | 2.5 | 1.7 | 2.7 | 0.0 |
| Lymph. and Hem. System 80-8Y | 6.7 | 6.3 | 2.7 | 0.0 | 0.0 | 0.0 | 0.0 | 5.2 | 7.4 | 3.4 | 4.9 | 4.0 |
| Other Sites 90-9X | 4.8 | 4.0 | 5.4 | 0.0 | 0.0 | 5.3 | 0.0 | 2.6 | 2.9 | 2.6 | 8.9 | 4.0 |
| Total | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |

*From "Morbidity from Cancer in the United States," Public Health Monograph No. 29, U.S.P.H.S.

Summary Table 5 - PERCENTILE DISTRIBUTION OF MALIGNANT NEOPLASMS IN MALES WITH ONSETS PRIOR TO JANUARY 1, 1950, ACCORDING TO TYPE OF NEOPLASM AND PETROLEUM OCCUPATION AS COMPARED TO THE UNITED STATES' EXPERIENCE

| Principal Pet. Occupation / Type of Neoplasm | USA* 1947 | Production 01-09 | Refining | | | | | | | Transport 80-89 | Market and Exec. 90-98 | Others 99 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Cracking 20-29 | Lub. and Grease 30-35 | Paraffin 36-39 | Str. Run 40-49 | Spec. Prod. 50-59 | Maintenance 60-69 | Others 70-79 | | | |
| Gland. Epith. 00-09 | 22.4 | 5.2 | 6.3 | 12.5 | 23.8 | 23.1 | 30.8 | 18.7 | 15.7 | 17.5 | 13.5 | 40.0 |
| Non-Gland. Epith 11-19 | 60.1 | 83.1 | 87.5 | 75.0 | 66.7 | 61.5 | 69.2 | 59.8 | 64.8 | 64.9 | 73.7 | 60.0 |
| Leukemia 20-29 | 2.9 | 1.3 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.4 | 3.1 | 1.8 | 1.5 | 0.0 |
| Lymphoma 30-39 | 3.8 | 2.6 | 0.0 | 0.0 | 0.0 | 7.7 | 0.0 | 6.2 | 4.4 | 3.5 | 3.0 | 0.0 |
| Nervous Tissues 40-49 | 2.0 | 0.0 | 0.0 | 0.0 | 4.8 | 0.0 | 0.0 | 0.5 | 0.0 | 1.8 | 1.5 | 0.0 |
| Vascular Tissues 50-59 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.6 | 0.0 | 0.0 | 0.0 |
| Muscle 66-69 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Non-Epith. Tissues 70-79 | 2.0 | 1.3 | 0.0 | 12.5 | 0.0 | 0.0 | 0.0 | 1.9 | 4.4 | 3.5 | 2.3 | 0.0 |
| Embry. and Mixed Tissues 80-89 | 1.5 | 2.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.9 | 0.6 | 5.3 | 3.0 | 0.0 |
| Not Class. 97-99 | 4.8 | 3.9 | 6.3 | 0.0 | 4.8 | 7.7 | 0.0 | 9.6 | 6.3 | 1.8 | 1.5 | 0.0 |
| Total | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |

*From "Morbidity from Cancer in the United States," Public Health Monograph No. 29, U.S.P.H.S.

Summary Table 6 - PERCENTILE DISTRIBUTION OF MALIGNANT NEOPLASMS IN MALES WITH ONSETS SUBSEQUENT TO JANUARY 1, 1950, ACCORDING TO TYPE OF NEOPLASM AND PETROLEUM OCCUPATION AS COMPARED TO THE UNITED STATES' EXPERIENCE

| Principal Pet. Occupation / Type of Neoplasm | USA* 1947 | Production 01-09 | Refining | | | | | | | Transport 80-89 | Market and Exec. 90-98 | Others 99 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Cracking 20-29 | Lub. and Grease 30-35 | Paraffin 36-39 | Str. Run 40-49 | Spec. Prod. 50-59 | Maintenance 60-69 | Others 70-79 | | | |
| Gland Epith. 00-09 | 22.4 | 7.9 | 27.0 | 10.0 | 22.2 | 21.1 | 25.0 | 14.3 | 12.3 | 25.6 | 15.2 | 28.0 |
| Non-Gland Epith. 11-19 | 60.1 | 75.4 | 56.8 | 85.0 | 72.2 | 63.2 | 75.0 | 65.2 | 71.6 | 64.1 | 68.3 | 60.0 |
| Leukemia 20-29 | 2.9 | 1.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.7 | 1.5 | 0.0 | 1.3 | 4.0 |
| Lymphoma 30-39 | 3.8 | 6.3 | 2.7 | 0.0 | 0.0 | 0.0 | 0.0 | 3.5 | 5.9 | 3.4 | 3.6 | 0.0 |
| Nervous Tissues 40-49 | 2.0 | 0.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.9 | 2.0 | 0.9 | 2.2 | 4.0 |
| Vascular Tissues 50-59 | 0.2 | 0.8 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.4 | 0.0 | 0.0 | 0.0 | 0.0 |
| Muscle 66-69 | 0.2 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 0.4 | 0.0 |
| Non-Epith. Tissues 70-79 | 2.0 | 0.8 | 5.4 | 0.0 | 5.6 | 5.3 | 0.0 | 3.9 | 1.0 | 1.7 | 0.9 | 0.0 |
| Embry. and Mixed Tissues 80-89 | 1.5 | 1.6 | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 | 1.3 | 1.5 | 1.7 | 2.7 | 0.0 |
| Not Class. 97-99 | 4.8 | 4.8 | 8.1 | 5.0 | 0.0 | 10.5 | 0.0 | 8.7 | 4.4 | 2.6 | 5.4 | 4.0 |
| Total | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |

*From "Morbidity from Cancer in the United States," Public Health Monograph No. 29, U.S.P.H.S.

TABLE I (page 12)

TOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | GRAVITY °API | FRACTION DISTILLING <750°F. (%) | BENZOPYRENE (%) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|---|---|
| Acid treating | | | | | | | |
| 62 | Hydrolyzed acid sludge | 14.2 | | ≦.002 | 3 - 100 | 25-79 | - |
| Effect of viscosity on tumor induction | | | | | | | |
| 114 | Gulf Coastal distillate, 235 SSU/100° | 24.6 | ~ 50 | ≦.002 | 3 - 20 | 67-83 | $0.01^{\pm}.01$ |
| 114 | | | | | 3 - 100 | 80-71 | 0.02X |
| 114-1 | 95% API-114, 5% alkylpolystyrene, 1756 SSU/100° | 25.4 | | | 3 - 20 | 86-74 | $0.03^{\pm}.01$ |
| 114-1 | | | | | 3 - 100 | 75-74 | $0.04^{+.01}_{-.02}$ |
| Fuel oil Blending | | | | | | | |
| 113 | Industrial fuel oil | 8.3 | 43 | 0.10 | 3 - 20[1] | 77-27 | 0.11X |
| 113 | | | | | 3 - 20[2] | 88-28 | $0.14^{+.02}_{-.01}$ |
| 113 | | | | | 3 - 20[3] | 100-25 | $0.14^{+.02}_{-.01}$ |
| 113 | | | | | 2 - 20[3] | 91-40 | $0.14^{\pm}.02$ |
| 113 | | | | | 1 - 20[3] | 95-45 | $0.17^{+.01}_{-.02}$ |
| 113 | | | | | 3 - 100[3] | 100-25 | $0.15^{+.02}_{-.01}$ |
| 113 | | | | | 3 - 5[3] | 92-34 | $0.15^{+.02}_{-.01}$ |
| 113 | | | | | 3 - 20[3] | 100-27 | 0.13X |
| 113 | | | | | 3 - 20[4] | 100-26 | $0.14^{+.03}_{-.02}$ |
| 118 | Catalytically cracked residuum component of API-119 | | 35.2 | 1.1 | 2/month-100 | 100-50 | $0.32^{+.05}_{-.06}$ |
| 119 | 10% API-118, 90% light catalytic cycle oil b. 450-600° | 23.3 | | | 2/month-100 | 81-85 | $0.12^{+.04}_{-.03}$ |
| 119 | | | | | 2 - 100 | 96-30 | $0.16^{+.02}_{-.01}$ |

[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 (page 13)

CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | FRACTION | ESTIMATED CORRECTED BOILING RANGE (in °F. at 760mm.) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|
| Fractional distillation (30 plate column) | | | | | |
| | Fraction from API-8 | | | | |
| 8-6 | 0-9.3% [1] | 435-560 | 2 - 100 | 0-66 | - |
| 8-7 | 9.3-19.4% [1] | 560-630 | 2 - 100 | 0-74 | - |
| 8-8 | 19.4-30.3% [1] | 630-695 | 2 - 100 | 0-74 | - |
| 8-9 | 30.3-39.8% [1] | 695-710 | 2 - 100 | 56-62 | ~0.03 |
| 8-10 | 39.8-49.6% [1] | 710-765 | 2 - 100 | 94-44 | $0.10^{+.01}_{-.02}$ |
| 8-11 | 49.6-59.2% [1] | 765-800 | 2 - 100 | 90-33 | $0.14^{+.01}_{-.02}$ |
| 8-12 | 59.2-69.1% [1] | 800-830 | 2 - 100 | 93-28 | $0.21 \pm .03$ |
| Diels-Alder Reaction | | | | | |
| 8-12a | Non-adduct from reaction (95.4% of API-8-12) [1] | | 2 - 100 | 100-26 | $0.23 \pm .04$ |
| Fractional distillation (30 plate column) | | | | | |
| | Fraction from API-8 | | | | |
| 8-13 | 69.1-78.5% [2] | 830-850 | 2 - 100 | 79-25 | $0.17 \pm .02$ |
| 8-14 | 78.5-80.8% [2] | 850-875 | 2 - 100 | | X |
| 8-15 | Residue; 80.8-100% [3] | >875 | 2 - 100 | 92-35 | $0.11^{+.02}_{-.01}$ |
| 8-18 | Proportionate reblend of distillation fractions, 8-6 through 8-15 | | 1 - 100 | 87-39 | $0.48^{+.29}_{-.15}$ |
| | Aromatics from API-8 | | | | |
| 8-26a | 28.5-30.8% [1] | 641-646 | 3 - 10 | 0-76 | - |
| 8-26b | 30.8-32.0% [1] | 646-651 | 3 - 10 | 0-76 | - |
| 8-26c | 32.0-34.1% [1] | 651-656 | 3 - 10 | 0-76 | - |
| 8-26d | 34.1-36.0% [1] | 656-662 | 3 - 10 | 0-76 | - |

[1] 50% solution in benzene.
[2] 33.3% solution in benzene. Analysis indicated a content of .85% BP.
[3] 50% solution in benzene. Analysis indicated a content of 2.0% BP.

TABLE I (page 14)

CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF EXPERIMENT | ESTIMATED CORRECTED BOILING RANGE (in °F. at 760 mm.) | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|
| 8-26e | 36.0-38.0%[1] | 662-668 | 3 - 10 | 0-76 | - |
| 8-26f | 38.0-40.0%[1] | 668-674 | 3 - 10 | 7-42 | - |
| 8-26g | 40.0-43.9%[1] | 674-686 | 3 - 10 | 20-72 | - |
| 8-26h | 43.9-46.0%[1] | 686-693 | 3 - 10 | 12-25 | - |
| 8-26i | 46.0-50.3%[1] | 693-709 | 3 - 10 | 36-61 | - |
| 8-26j | 50.3-52.5%[1] | 709-717 | 3 - 10 | 25-41 | - |
| 8-26k | 52.5-54.8%[2] | 717-727 | 3 - 40 | 83-19 | 0.21X |
| 8-26l | 54.8-57.3%[1] | 727-736 | 3 - 10 | 55-38 | - |
| 8-26m | 57.3-60.4%[2] | 736-747 | 3 - 40[3] | 93-35 | $0.24^{+.16}_{-.07}$ |
| 8-26n | 60.4-62.4%[1] | 747-759 | 3 - 10 | 100-39 | $0.17^{+.02}_{-.07}$ |
| | Contribution of accelerators to above fractions | | | | |
| 8-26-2 | 0.17% BP in 80% saturates through alkylnaphthalenes fraction of 8-26g, h, and i, and 20% benzene | | 3 - 50 | 100-19 | $0.19^{+.01}_{-.02}$ |
| 8-26-3 | 0.17% BP in 80% 3-ringed aromatic fraction of 8-26g, h, and i, and 20% benzene | | 3 - 50 | 100-26 | $0.14^{+.02}_{-.03}$ |
| Air Oxidation (cobalt naphthenate catalyst) | | | | | |
| 8 | FCC cracked residuum (prior to oxidation | | 2 - 100 | 94-14 | $0.95^{+.33}_{-.43}$ |
| 83 | Product of 2 hour oxidation of API-8 | | 2 - 100 | 100-17 | 0.39X |
| 83-1 | Product of 4 hour oxidation of API-8 | | 2 - 100 | 94-17 | 0.45X |
| 8-22 | 69% aromatics of API-8, 31% sec.-amylbenzene | | 1 - 100[4] | 63-39 | 0.20X |
| 83-2 | 69% aromatics of API-83, 31% sec.-amylbenzene | | 1 - 100[4] | 79-45 | $0.23^{+.02}_{-.07}$ |

[1] 50% solution in benzene.
[2] 50% solution in dodecylbenzene.
[3] Painting discontinued after 10 weeks; [4] 20 weeks.

TABLE I (page 15)

CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF FRACTION | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|
| Materials regenerated from Diels-Alder reactions (Maleic anhydride extraction) | | | | |
| 8-25a | Material from 1st adduct formed (2.7% of API-8), 1% in benzene | 3 - 15 | 100-62 | 0.03±.01 |
| 8-25b | Material from 2nd adduct formed (1.8% of API-8), 1% in benzene | 3 - 15 | 100-58 | 0.03±.01 |
| 8-23g | Material from total Class B[1] adduct (1.6% of API-8), 1.5% in benzene | 3 - 15 | 92-50 | 0.03±.01 |
| 8-23h | Material from total Class A[1] adduct (3.5% of API-8), 2.2% in benzene | 3 - 15 | 100-43 | 0.05±.01 |
| | Chromatographic fractionation of extract similar to 8-23h | | | |
| 8-23a | Crystalline material from 1st fraction (.15% of API-8), .34% in benzene | 3 - 15[a] | 0-68 | - |
| 8-23c | Crystalline material from 2nd fraction (.17% of API-8), .34% in benzene | 3 - 12[a] | 0-68 | - |
| 8-23b | Material in mother liquor from 8-23a and 8-23c (1.5% of API-8), 1.5% in benzene | 3 - 15 | 100-51 | 0.04±.01 |
| 8-23d | Third fraction (.4% of API-8), .8% in benzene | 3 - 15 | 100-38 | 0.07±.01 |
| 8-23e | Fourth fraction (.33% of API-8), .57% in benzene | 3 - 15[a] | 13-46 | - |
| 8-23f | Fifth fraction (.37% of API-8), .57% in benzene | 3 - 15[a] | 0-68 | - |
| 8-26n-1 | Total material from 8-26n, 2% in 50% benzene, 50% dodecylbenzene | 3 - 50 | 0-8 | - |

[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.

[a] Painting discontinued after 30 weeks; [3] 37 weeks; [4] 32 weeks.

TABLE I (page 16)

CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF FRACTION | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|
| 89-1 | Anthracenic chromatographic fraction (1.6% of API-89) of material from total adduct, 2% in benzene | 3 - 15 | 0-74[1] | <0.02 |
| 89-2 | Remainder of chromatographic fractions (mixed anthracenes, benzanthracenes, etc., 0.2% of API-89), .5% in benzene | 3 - 10 | 100-68 | $0.03^{\pm}.01$ |
| 120-1 | Material from naphthenic distillate, API-120, corresponding to API-89-2, 2% in benzene | 3 - 20 | 0-4 | - |
| Solvent extraction with conc. $H_2SO_4$ | | | | |
| 8-19 | 50% extract[2] from API-8-10 and 8-11, 50% benzene | 2 - 100[3] | 22-32 | <0.09 |
| 8-20 | 50% raffinate[2] from API-8-10 and 8-11, 50% benzene | 2 - 100[3] | 83-25 | ~0.16 |
| 23-1 | 80% extract[2] from API-23, 20% benzene | 2 - 100[3] | 90-26 | $0.24^{+.05}_{-.04}$ |
| 23-2 | 80% raffinate[2] from API-23, 20% benzene | 2 - 100[3] | 100-44 | $0.13^{\pm}.02$ |
| Fractionation of API-12 | | | | |
| 12-7 | 30% non-adduct of Diels-Alder reaction on raffinate from sulfuric extraction of aromatic fraction b. ~680-780°, 70% benzene | 2 - 20[4] | 77-65 | $0.04^{+.01}_{-.02}$ |
| 12-8 | Ditto from fraction b.~780-950°, 70% benzene | 2 - 15 | 90-58 | 0.07X |

[1] Two papillomas appeared at 48 weeks but regressed.
[2] Accelerators removed prior to extraction and reblended proportionately in extract and raffinate.
[3] Painting discontinued after 24 weeks; [4] 43 weeks.

TABLE I (page 17)

CARCINOGENIC POTENCY OF VARIOUS FRACTIONS FROM THE REFINING OF PETROLEUM

| API SAMPLE NUMBER | DESCRIPTION OF FRACTION | SCHEDULE OF APPLICATIONS (no./week - mg.) | INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|
| Chromatography | | | | |
| 8-13a | First aromatic fraction,[1] 2%[2] of API-8-13 | 3 - 20[3] | 9-36 | <0.05 |
| 8-13b | Second aromatic fraction, 2.4%[2] of API-8-13 | 3 - 20[4] | 14-58 | <0.03 |
| 8-13c | Third aromatic fraction, 8.7%[2] of API-8-13 | 3 - 20 | 100-42 | 0.07X |
| 8-13d | Fourth aromatic fraction, 5.6%[2] of API-8-13 | 3 - 20 | 100-29 | $0.10 \pm .02$ |
| 8-13e | Fifth aromatic fraction, 5.6%[2] of API-8-13 | 3 - 20 | 86-40 | 0.07X |
| 8-13f | Sixth aromatic fraction, 2%[2] of API-8-13 | 3 - 20[4] | 83-45 | $0.07^{+.01}_{-.03}$ |
| 8-13g | Seventh aromatic fraction, 16.9%[2] of API-8-13 | 3 - 20 | 100-27 | 0.11X |
| 8-13h | Eighth aromatic fraction, 2.4%[2] of API-8-13 | 3 - 20 | 100-37 | $0.09^{+.01}_{-.02}$ |
| 8-13i | Ninth aromatic fraction, 6.9%[2] of API-8-13 | 3 - 20 | 73-36 | 0.09X |
| 71-2 | Proportionate reblend of all fractions from API-71 | 1 - 20 | 93-59 | $0.23^{+.02}_{-.06}$ |
| 71-1 | Reblend of all fractions except dark resin preceeding aromatics | 1 - 20 | 83-64 | $0.16^{+.01}_{-.04}$ |
| 71-1 | | 1 - 100 | 100-15 | 0.90X |

[1] Preceeding 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 3 of Table VII.

[2] Tested at this percentage in benzene.

[3] Painting discontinued after 35 weeks; [4] 41 weeks.

TABLE II

CONTROL EXPERIMENTS WITH VARIOUS SOLVENTS

| API EXPERIMENT NUMBER | SOLVENT | SCHEDULE OF APPLICATIONS (no./week - mg.) | STRAIN OF MICE | MAXIMUM INCIDENCE OF TUMORS (% - weeks) | INCIDENCE OF GROSS CARCINOMA (% - weeks) |
|---|---|---|---|---|---|
| 80 | White oil (95SSU) | 3 - 100[1] | C3H | 0-80 | 0-80 |
| 95 | White oil (95SSU) | 3 - 100[1] | CFW | 0-80 | 0-80 |
| 221 | Dodecylbenzene | 3 - 100 | C3H | 33-37 | 0-52 |
| 221a | 8-84% fraction b. 548-572° from distillation of API-221 | 3 - 50[2] | C3H | 0-52 | 0-52 |
| 224 | Sec.-amylbenzene | 3 - 100 | CFW | 18-59[3] | 0-82 |
| 228 | Benzene | 3 - 100 | C3H | 0-100 | 0-100 |
| 228 | Benzene | 3 - 100 | CFW | 0-62 | 0-62 |
| 241 | Distilled water | 3 - 100[4] | C3H | 7-78 | 7-78 |
| 294 | Dodecane | 3 - 50 | C3H | 0-80 | 0-80[5] |
| 294a | Dodecane for 12 weeks followed by 70% dodecane, 30% 340SSU white oil | 3 - 50 | C3H | 0-82 | 0-82 |
| 639 | 75% dodecylbenzene 25% benzene | 3 - 50 | C3H | 4-15 | 0-19 |

[1] [3] Painting discontinued after 60 weeks; [2] 31 weeks; [4] 61 weeks.
[5] Histopathological examination confirmed only one of the four gross lesions as a papilloma; the others were termed hyperkeratosis. Histopathological examination showed one fibrosarcoma in 70 weeks.

TABLE III

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF METHYLCHOLANTHRENE IN VARIOUS SOLVENTS UPON THE SKIN OF C3H MICE

| API EXPERIMENT NUMBER | SOLVENT | CONCENTRATION ( % by weight) | SCHEDULE OF APPLICATIONS (no./week - mg.) | MAXIMUM INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ | |
|---|---|---|---|---|---|---|
| 218 | Crude residuum, API-5 | 0.31 | 3 - 100 | 100-30 | $0.09 \pm .01$ | |
| 625 | API-80, 95 SSU white oil | 0.10 | 3 - 10 | 100-32 | $0.10 \pm .01$ | |
| 624 | API-80 | 0.20 | 2 - 10 | 95-32 | $0.15^{+.01}_{-.02}$ | |
| 293 | 340 SSU white oil | 0.50 | 3 - 20 | 100-20 | 0.16X | |
| 607 | 50% benzene, 50% 340 SSU white oil | 0.10 | 3 - 10 | 93-38 | $0.09^{+.01}_{-.02}$ | |
| 281 | Cottonseed oil | 0.04 | 3 - 100 | 89-69 | $0.03 \pm .01$ | |
| 291 | Cottonseed oil | 0.50 | 3 - 20 | 95-23 | $0.17^{+.02}_{-.06}$ | |
| 246 | Naphtha, API-112-1 | 0.21 | 3 - 20 | 100-22 | $0.19 \pm .02$ | |
| 246 | | | 3 - 20 | 100-21 | $0.19 \pm .02$ | |
| 248 | Naphtha, API-110-1 | 0.21 | 3 - 20 | 100-22 | $0.16^{+.02}_{-.01}$ | |
| 223 | Sec.-amylbenzene, API-224 | 0.09 | 3 - 100 | 81-46 | $0.04 \pm .01$ | |
| 222 | API-224 | 0.18 | 3 - 100 | 100-44 | $0.09^{+.01}_{-.02}$ | |
| 234 | API-224 | 0.35 | 2 - 100 | 100-27 | $0.27^{+.04}_{-.08}$ | |
| 235 | API-224 | 0.70 | 2 - 100 | 100-19 | $0.28 \pm .03$ | |
| 608 | Decalin | 0.08 | 3 - 50 | 92-45[1] | 0.04X | |
| 609 | Dinonylnaphthalene | 0.08 | 3 - 50 | 88-56 | $0.05 \pm .01$ | |

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

TABLE IV

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF BENZOPYRENE IN NON-ACCELERATING SOLVENTS UPON THE SKIN OF C3H MICE

| API EXPERIMENT NUMBER | SOLVENT | CONCENTRATION (% by weight) | SCHEDULE OF APPLICATIONS (no./week - mg.) | MAXIMUM INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ | |
|---|---|---|---|---|---|---|
| 602 | n-octane | 0.21 | 3 - 100 | 100-36 | $0.08^{+.02}_{-.03}$ | |
| 604 | isooctane | 0.15 | 3 - 100 | 100-31 | $0.10 \pm .01$ | |
| 299 | 340 SSU white oil | 0.08 | 3 - 5 | 96-43 | $0.04 \pm .01$ | |
| 296 | 340 SSU white oil | 0.20 | 3 - 50 | 100-36 | $0.08^{+.01}_{-.02}$ | |
| 282 | Benzene | 0.08 | 3 - 20 | 100-50 | $0.07 \pm .01$ | |
| 244 | Benzene | 0.17 | 3 - 100 | 100-33 | $0.09 \pm .01$ | |
| 244 | | | 3 - 20 | 94-37 | 0.07X | |
| 252 | Benzene | 0.32 | 3 - 100 | 100-26 | $0.13^{+.01}_{-.02}$ | |
| 252 | | 0.32 | 3 - 20 | 100-27 | 0.10X | |
| 252 | | 0.32 | 2 - 20 | 94-54 | 0.10X | |
| 252 | | 0.32 | 1 - 20 | 96-43 | 0.15X | |
| 613 | 85% b-methyl-naphthalene, 15% benzene | 0.20 | 2 - 15 | 100-40 | $0.08 \pm .01$ | |
| 613 | | | 2 - 50 | 100-37 | 0.10X | |
| 285 | Cottonseed oil | 0.50 | 3 - 20 | 100-32 | 0.09X | |
| 286 | Cottonseed oil | 1.0 | 3 - 20 | 95-25 | $0.12 \pm .01$ | |

TABLE V

EXPERIMENTS TO DETERMINE THE POTENCY OF MIXTURES OF POLYCYCLIC HYDROCARBONS IN TECHNICAL WHITE OIL FOR THE SKIN OF MICE

| API EXPERIMENT NUMBER | HYDROCARBON | CONCENTRATION (% by weight) | SCHEDULE OF APPLICATIONS (no./week - mg) | MAXIMUM INCIDENCE OF TUMORS (% - weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ |
|---|---|---|---|---|---|
| 624 | Methylcholanthrene control | 0.20 | 2 - 10 | 95-32 | $0.15^{+.01}_{-.02}$ |
| 623 | Methylcholanthrene<br>Benzopyrene | 0.10<br>0.20 | 2 - 10 | 100-26 | $0.17 \pm .02$ |
| 625 | Methylcholanthrene control | 0.10 | 3 - 10 | 100-32 | $0.10 \pm .01$ |
| 626 | Methylcholanthrene<br>Benzanthracene | 0.10<br>0.20 | 3 - 10 | 100-34 | 0.08X |

TABLE VI

EXPERIMENTS INVOLVING THE APPLICATION OF SOLUTIONS OF METHYLCHOLANTHRENE (MC) IN DODECYLBENZENE[1] UPON THE SKIN OF MICE

| API EXPERIMENT NUMBER | CONCENTRATION (% by weight) | STRAIN OF MICE | SCHEDULE OF APPLICATIONS (no./week - mg) | MAXIMUM INCIDENCE OF TUMORS (% - weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ | $P_{MC}^{o}$ OF MC |
|---|---|---|---|---|---|---|
| 221 | 0 | C3H | 3 - 100 | 33-37 | - | - |
| 221a | 0 | C3H | 3 - 50[2] | 0-52 | - | - |
| 226 | 0.006 | C3H | 3 - 100 | 50-40 | -[3] | - |
| 226 | 0.006 | CFW | 3 - 100 | 41-54 | - | - |
| 225 | 0.012 | C3H | 3 - 100 | 81-43 | 0.05X | 417 |
| 225 | 0.012 | CFW | 3 - 100 | 100-54 | ~0.03 | ~250 |
| 213 | 0.05 | CFW | 3 - 100 | 100-18 | ~0.30 | ~600 |
| 211 | 0.12 | C3H | 3 - 100 | 100-22 | $0.35^{+.06}_{-.12}$ | 292 |
| 211 | 0.12 | CFW | 3 - 100 | 100-17 | ~0.30 | ~250 |
| 208 | 0.15 | C3H | 3 - 100 | 100-15 | $0.33 \pm .03$ | 220 |
| 249 | 0.17 | C3H | 3 - 100 | 100-12 | $0.43^{+.08}_{-.07}$ | 252 |
| 249 | 0.17 | C3H | 3 - 20 | 89-14 | $0.35^{+.06}_{-.04}$ | 206 |
| 212 | 0.35 | C3H | 3 - 100 | 100-18 | $0.35^{+.06}_{-.09}$ | 100 |

[1] Product obtained by alkylation of benzene with the propylene tetramer (aluminum chloride catalyst).
[2] Painting discontinued after 31 weeks.
[3] No gross or microscopic evidence of invasive malignancy.

TABLE VII

ACCELERATING ACTIVITY OF VARIOUS SOLVENTS ON RATE OF INDUCTION OF TUMORS BY DISSOLVED BENZOPYRENE (BP) IN C3H MICE

| API EXPERIMENT NUMBER | SOLVENT | CONCENTRATION (% by weight) | SCHEDULE OF APPLICATIONS (no./week - mg.) | MAXIMUM INCIDENCE OF TUMORS (%- weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ | $P_{MC}^{o}$ OF BP |
|---|---|---|---|---|---|---|
| PARAFFINS | | | | | | |
| 602 | n-octane | 0.21 | 3 - 100 | 100-36 | $0.08^{+.02}_{-.03}$ | 40 |
| 278 | n-decane | 0.21 | 3 - 50 | 100-21 | $0.18^{+.02}_{-.01}$ | 86 |
| 295 | dodecane | 0.20 | 3 - 50 | 100-22 | $0.20 \pm .02$ | 100 |
| 269 | cetane (chromatographed on silica gel) | 0.20 | 3 - 50 | 50-10 | X | |
| 269 | | | 3 - 20 | 100-25 | $0.14^{+.02}_{-.03}$ | 70 |
| OLEFINS | | | | | | |
| 298 | n-hexadecene-1 | 0.19 | 3 - 40 | 100-25 | $0.19^{+.04}_{-.03}$ | 100 |
| CYCLOPARAFFINS | | | | | | |
| 608 | Decalin | 0.08[1] | 3 - 50 | 92-45[2] | 0.04X | 50[1] |
| 263 | Cyclohexyldecane | 0.18 | 3 - 20 | 95-20 | $0.22^{+.06}_{-.04}$ | 122 |
| 279 | 7-cyclohexyltridecane, PSC-504 | 0.18 | 3 - 40 | 100-29 | $0.12^{+.02}_{-.04}$ | 67 |
| WHITE OIL (Mixtures of Paraffins and Cycloparaffins) | | | | | | |
| 258 | API-80, 95 SSU white oil | 0.23 | 1 - 50 | 95-51 | $0.15^{+.02}_{-.01}$ | 65 |
| 264 | API-80 | 0.18 | 3 - 100 | 100-31 | $0.09 \pm .01$ | 50 |
| 264 | | | 3 - 20 | 100-31 | $0.09 \pm .01$ | 50 |
| 264 | | | 3 - 5 | 100-36 | $0.09 \pm .02$ | 50 |
| 270 | API-80 | 0.35 | 3 - 20 | 100-27 | 0.11X | 31 |
| 271 | API-80 | 0.5-0.1[3] | 3 - 20 | 100-27 | $0.11^{+}_{-}.01$ | |

[1] Carcinogen in this case was methylcholanthrene.
[2] The pattern of response to the irritational effects of this solution was similar to that observed with dodecylbenzene.
[3] Solutions applied alternately.

TABLE VII (page 2)

ACCELERATING ACTIVITY OF VARIOUS SOLVENTS ON RATE OF INDUCTION OF TUMORS BY DISSOLVED BENZOPYRENE (BP) IN C3H MICE

| API EXPERIMENT NUMBER | SOLVENT | CONCENTRATION (% by weight) | SCHEDULE OF APPLICATIONS (no./week - mg.) | MAXIMUM INCIDENCE OF TUMORS (% -weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ | $P_{MC}$° OF BP |
|---|---|---|---|---|---|---|
| FRACTIONS FROM 2 DISTILLATIONS OF API-80 | | | | | | |
| | Percent of API-80 / Boiling Range | | | | | |
| 276-1 | 0-3.5 / 505-585° | 0.17 | 3 - 50 | 100-22 | $0.16^{+.07}_{-.04}$ | 94 |
| 276-2 | 3.5-6.4 / 585-615° | 0.17 | 3 - 50 | 100-22 | $0.15^{+.08}_{-.04}$ | 88 |
| 276-3 | 6.4-10.9 / 615-630° | 0.17 | 3 - 50 | 100-22 | $0.15 \pm .03$ | 88 |
| 276-4 | 10.9-15.7 / 630-640° | 0.17 | 3 - 50 | 100-32 | $0.08 \pm .01$ | 47 |
| 276-7 | 8.7-16.7 / 625-645° | 0.17 | 3 - 100 | 94-24 | $0.14 \pm .02$ | 82 |
| 276-8 | 16.7-19.5 / 645-655° | 0.17 | 3 - 100 | 100-28 | 0.11X | 65 |
| 276-5 | 15.7-36.3 / 640-685° | 0.17 | 3 - 100 | 100-30 | $0.10 \pm .01$ | 59 |
| 276-9 | 19.5-30.3 / 655-675° | 0.17 | 3 - 100 | 100-24 | $0.14^{+.01}_{-.03}$ | 82 |
| 276-10 | 30.3-40.5 / 675-700° | 0.17 | 3 - 100 | 100-24 | $0.11^{+.02}_{-.01}$ | 65 |
| 276-6 | 36-100 / >700° | 0.17 | 3 - 100 | 100-29 | $0.10 \pm .01$ | 59 |
| 276-6 | (residue purified by percolation through silica gel) | | 3 - 50 | 92-29 | 0.09X | 53 |
| FRACTIONS FROM DISTILLATION OF SATURATED COMPONENTS OF TCC RESIDUUM, API-71 | | | | | | |
| | Percent / Boiling Range | | | | | |
| 277-1 | 0-2.9 / 430-500° | 0.18 | 3 - 30 | 88-17 | $0.22^{+.06}_{-.04}$ | 122 |
| 277-3 | 6.1-7.4 / 550-565° | 0.18 | 3 - 20 | 83-18 | $0.23^{+.50}_{-.10}$ | 128 |
| 277-4 | 7.4-11.3 / 580-600° | 0.18 | 3 - 40 | 100-25 | $0.17^{+.06}_{-.05}$ | 94 |
| 277-5 | 11.3-15.4 / 600-620° | 0.18 | 3 - 50 | 100-27 | $0.12^{+.02}_{-.03}$ | 67 |

TABLE VII (page 3)

ACCELERATING ACTIVITY OF VARIOUS SOLVENTS ON RATE OF INDUCTION OF TUMORS BY DISSOLVED BENZOPYRENE (BP) IN C3H MICE

| API EXPERIMENT NUMBER | SOLVENT | CONCENTRATION (% by weight) | SCHEDULE OF APPLICATIONS (no/week - mg.) | MAXIMUM INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ | $P_{MC}^{o}$ OF BP |
|---|---|---|---|---|---|---|
| 257 | API-8-24, colorless fraction from chromatography of API-8 | 0.24 | 1 - 50 | 100-43 | $0.15 \pm .02$ | 63 |
| 266 | 50% colorless fraction from chromatography of API-8-13, 50% benzene | 0.15 | 3 - 100 | 100-34 | $0.07 \pm .01$ | 47 |
| ALKYLBENZENES | | | | | | |
| 605 | Diisopropylbenzene | 0.17 | 3 - 50 | 100-47 | $0.05 \pm .01$ | 29 |
| 275 | Triisopropylbenzene | 0.17 | 3 - 50 | 100-18 | $0.22^{+.06}_{-.03}$ | 130 |
| 275 | | 0.17 | 3 - 30 | 100-30 | $0.12 \pm .02$ | 71 |
| 606 | t-octyltoluene | 0.17 | 3 - 50 | 100-21 | 0.17X | 100 |
| 262 | 1-phenyldecane | 0.18 | 3 - 20 | 95-16 | $0.33^{+.05}_{-.04}$ | 183 |
| 629 | Dodecylbenzene (DDB) | 0.08 | 3 - 20 | 75-30 | $0.14^{+.03}_{-.02}$ | 180 |
| 245 | DDB | 0.17 | 3 - 100 | 100-19 | $0.30^{+.08}_{-.06}$ | 176 |
| 245 | | | 3 - 20 | 100-31 | $0.16 \pm .05$ | 94 |
| 245 | | | 3 - 5 | 100-23 | $0.19 \pm .04$ | 112 |
| LAB DISTILLATION OF COMMERCIAL ALKYLATES | | | | | | |
| | Distillation of Alkylbenzene[1] | | | | | |
| 274-8 | Fraction b. 450-500° | 0.17 | 3 - 40 | 100-22 | $0.15^{+.14}_{-.06}$ | 88 |
| 274-13 | Fraction b. 555-560° | 0.17 | 3 - 50 | 100-12 | $0.40^{+.08}_{-.06}$ | 236 |

[1] Product of alkylation of benzene with polypropylene.

TABLE VII (page 4)

ACCELERATING ACTIVITY OF VARIOUS SOLVENTS ON RATE OF INDUCTION OF TUMORS BY DISSOLVED BENZOPYRENE (BP) IN C3H MICE

| API EXPERIMENT NUMBER | SOLVENT | CONCENTRATION (% by weight) | SCHEDULE OF APPLICATIONS (no./week - mg.) | MAXIMUM INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ | $P_{MC}$° OF BP |
|---|---|---|---|---|---|---|
| | Distillation of PDDB[1] | | | | | |
| 267-1 | Fraction b.603-642° | 0.17 | 3 - 20 | 100-31 | $0.10^{+.02}_{-.01}$ | 59 |
| 267-3 | Fraction b.655-683° | 0.17 | 3 - 20 | 100-33 | $0.07 \pm .01$ | 41 |
| 267-5 | Fraction b.664-730° | 0.17 | 3 - 20 | 100-38 | $0.06 \pm .01$ | 35 |
| 267-8 | Fraction b.659-760° | 0.17 | 3 - 20 | 100-36 | $0.07 \pm .01$ | 41 |
| ALKYLNAPHTHALENES | | | | | | |
| 613 | 85% b-methylnaphthalene, 15% benzene | 0.20 | 2 - 50 | 100-37 | 0.10X | 50 |
| 265 | Butyl-dimethylnaphthalene | 0.16 | 3 - 20 | 100-25 | $0.14^{+.05}_{-.02}$ | 88 |
| 272 | Monoamylnaphthalenes, b.570° | 0.16 | 3 - 40 | 100-19 | $0.17 \pm .03$ | 106 |
| 273 | Diamylnaphthalenes b.630-690° | 0.16 | 3 - 50 | 100-19 | $0.28^{+.17}_{-.08}$ | 175 |
| 609 | Dinonylnaphthalene | 0.08[2] | 3 - 50 | 88-56 | $0.05 \pm .01$ | 63[2] |
| MIXTURES OF ACCELERATORS WITH WHITE OILS | | | | | | |
| 260 | 5% DDB, 95% API-80 | 0.17 | 3 - 100 | 100-33 | $0.07 \pm .01$ | 41 |
| 259 | 20% DDB, 80% API-80 | 0.17 | 3 - 100 | 100-32 | $0.08^{+.01}_{-.02}$ | 47 |
| 633 | 50% DDB, 50% API-80 | 0.08 | 3 - 50 | 64-37 | $\sim 0.06$ | $\sim 75$ |
| 637 | 50% DDB, 50% API-80 | 0.17 | 3 - 50 | 100-27 | $0.10 \pm .01$ | 59 |

[1] Alkylbenzene, residual by-product of commercial alkylation of benzene with propylene tetramer.

[2] Carcinogen in this case was methylcholanthrene.

TABLE VII (page 5)

ACCELERATING ACTIVITY OF VARIOUS SOLVENTS ON RATE OF INDUCTION OF TUMORS BY DISSOLVED BENZOPYRENE (BP) IN C3H MICE

| API EXPERIMENT NUMBER | SOLVENT | CONCENTRATION (% by weight) | SCHEDULE OF APPLICATIONS (no./week - mg.) | MAXIMUM INCIDENCE OF TUMORS (%-weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ | $P_{MC}^{o}$ OF BP |
|---|---|---|---|---|---|---|
| 636 | 75% DDB, 25% API-80 | 0.08 | 3 - 50 | 100-27 | $0.13^{+.01}_{-.02}$ | 163 |
| 638 | 75% DDB, 25% API-80 | 0.17 | 3 - 50 | 100-29 | $0.12^{+.02}_{-.01}$ | 71 |
| 635 | 50% DDB, 50% 340 SSU white oil | 0.08 | 3 - 50 | 42-36 | $\sim 0.05$ | $\sim 63$ |
| 297 | 50% dodecane, 50% 340 SSU white oil | 0.20 | 3 - 100 | 100-24 | $0.13 \pm .01$ | 65 |
| 297 | | | 3 - 50 | 100-29 | $0.13^{+.01}_{-.03}$ | 65 |
| 297 | | | 3 - 20 | 100-33 | $0.08 \pm .01$ | 40 |
| 614 | 75% dodecane, 25% 340 SSU white oil | 0.20 | 3 - 50 | 100-28 | $0.12 \pm .01$ | 60 |
| 614 | | | 2 - 50 | 100-26 | $0.15 \pm .01$ | 75 |
| 614 | | | 1 - 50 | 100-34 | $0.20^{+.02}_{-.01}$ | 100 |
| MIXTURES OF DDB WITH AROMATIC HYDROCARBONS | | | | | | |
| 628 | 50% DDB, 50% b-methylnaphthalene | 0.08 | 3 - 40 | 93-32 | $0.11 \pm .02$ | 138 |
| 634 | 50% DDB, 50% benzene | 0.08 | 3 - 50 | 95-23 | $0.14^{+.03}_{-.01}$ | 175 |
| 644 | 50% DDB, 50% benzene | 0.09 | 3 - 50 | 68-13 | - | - |
| 643 | 50% DDB, 50% benzene | 0.17 | 3 - 50 | 30-13 | - | - |

TABLE VII (page 6)

ACCELERATING ACTIVITY OF VARIOUS SOLVENTS ON RATE OF INDUCTION OF TUMORS BY DISSOLVED BENZOPYRENE (BP) IN C3H MICE

| API EXPERIMENT NUMBER | SOLVENT | CONCENTRATION (% by weight) | SCHEDULE OF APPLICATIONS (no./week - mg.) | MAXIMUM INCIDENCE OF TUMORS (% -weeks) | RELATIVE CARCINOGENIC POTENCY, $P_{MC}$ | $P_{MC}$ OF BP |
|---|---|---|---|---|---|---|
| DISTILLATES FROM VARIOUS CARCINOGENIC OILS | | | | | | |
| 603 | Fraction of TCC residuum, API-9, b. 540-600° | 0.16 | 3 - 50 | 100-30 | $0.14^{+.04}_{-.02}$ | 88 |
| 615 | Lagunillas distillate, b.550-650° | 0.16 | 3 - 50 | 100-16 | $0.27^{+.07}_{-.05}$ | 169 |
| 616 | Lagunillas distillate, b. 650-690° | 0.16 | 3 - 50 | 100-16 | $0.35^{+.10}_{-.07}$ | 219 |
| DISTILLATES FROM CRUDE ASSAYS BY BUREAU OF MINES[1] | | | | | | |
| | Boiling Range | Specific Dispersion / Correlation Index | | | | |
| 617 | 480-660° | 141 / 26 | 3 - 50 | 100-24 | 0.14±.01 | 78 |
| 618 | 480-660° | 186 / 49 | 3 - 50 | 100-19 | 0.20±.02 | 118 |
| 619 | 480-660° | 164 / 54 | 3 - 50 | 100-19 | $0.20^{+.03}_{-.02}$ | 118 |
| 630 | 480-660° | 154 / 31 | 3 - 50 | 92-19 | 0.18±.02 | 106 |
| 631 | 480-660° | 190 / 53 | 3 - 50 | 100-18 | 0.23±.04 | 135 |
| 632 | 480-660° | 145 / 37 | 3 - 50 | 95-19 | $0.20^{+.03}_{-.02}$ | 116 |
| 632a | 50% API-632, diluted 50% with benzene | | 3 - 50 | 5-13 | - | - |
| 640 | 480-660° | 141 / 24 Diluted 50% with benzene | 3 - 50 | 26-13 | - | - |
| 641 | 480-570° | 130 / 21 Diluted 50% with benzene | 3 - 50 | 10-10 | - | - |
| 642 | 570-660° | 138 / 23 Diluted 50% with benzene | 3 - 50 | 11-10 | - | - |

[1] Experiments run at a concentration of 0.17% BP.

TABLE VIII

EFFECT OF EARLY EXPOSURE TO ACCELERATING SOLVENTS ON RESULTS OF SUBSEQUENT EXPOSURE TO CARCINOGENS

| API EXPERIMENT NUMBER | DESCRIPTION: MATERIALS APPLIED TO MICE DURING FIRST SIX WEEKS OF EXPERIMENT | DESCRIPTION: MATERIALS APPLIED TO MICE DURING SEVENTH WEEK TO END OF EXPERIMENT | STRAIN OF MICE | SCHEDULE OF APPLICATION OF CARCINOGEN (no./week - mg.) | INCIDENCE[1] OF TUMORS (%-weeks)[2] | AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in weeks) |
|---|---|---|---|---|---|---|
| 221 | DDB[3] | DDB | C3H | 3 - 100 | 33-37 | - |
| 9 | TCC residuum, API-9 | API-9 | C3H | 3 - 100 | 100-47 | $36.2 \pm 3.9$ |
| 221-9 | DDB | API-9 | C3H | 3 - 100 | 100-21 | $14.5 \pm 1.8$ |
| 221-9 | | | C3H | 3 - 100 | 100-22 | $12.8 \pm 2.4$ |
| 253-9 | PDB[3] | API-9 | C3H | 3 - 100 | 94-26 | $13^{+4}_{-1}$ |
| 57 | API-57[4] | API-57 | CFW | 6 - 100 | 50-16<br>100-25 | - |
| 221-57 | DDB | API-57 | CFW | 6 - 100 | 50-13<br>100-16 | - |
| 208 | API-208[5] | API-208 | C3H | 3 - 100 | 100-15 | $10.4 \pm .6$ |
| 221-208 | DDB | API-208 | C3H | 3 - 100 | 100-14 | $8.1 \pm 1.1$ |
| 82 | TCC residuum, API-82 | API-82 | C3H | 1 - 10 | 100-50 | $30^{+7}_{-1}$ |
| 600 | Dodecane | API-82 | C3H | 1 - 10 | 100-42 | $30.7 \pm 4.0$ |
| 601 | 340 SSU white oil | API-82 | C3H | 1 - 10 | 100-41 | $30.2 \pm 5.4$ |
| 76 | Reformer tar, API-76 | API-76 | C3H | 3 - 50 | 83-52 | $\sim 34$ |
| 620 | Dodecane | API-76 | C3H | 3 - 50 | 67-48 | $\sim 33$ |
| 621 | 95 SSU white oil | API-76 | C3H | 3 - 50 | 55-45 | $\sim 43$ |
| 622 | 340 SSU white oil | API-76 | C3H | 3 - 50 | 60-47 | $\sim 35$ |

[1] Schedule of application of accelerator was the same as that of the carcinogen except in experiments 600 and 601 in which case 50 mg. was applied three times each week.

[2] Time measured from date of initial painting with carcinogenic material.

[3] Dodecylbenzenes obtained by alkylation of benzene with 12-carbon olefins; DDB obtained with propylene tetramer; 2-phenyldodecane (PDB) obtained with 1-dodecene.

[4] Filtrate oil from pressing of Midcontinent paraffinic distillate.

[5] Solution of 0.15% methylcholanthrene in dodecylbenzene.

TABLE IX

EXPERIMENTS TO DETERMINE THE CARCINOGENIC PROMOTING ACTIVITY OF VARIOUS MATERIALS FOR THE SKIN OF C3H MICE

| API EXPERIMENT NUMBER | CARCINOGENIC INITIATOR, SINGLE APPLICATION | INCIDENCE OF TUMORS FROM SINGLE APPLICATION (%-weeks) | TIME OF 2nd APPLICATION (if applicable) (wks.-mg.) | PROMOTER USED FROM 3rd WEEK TO END | SCHEDULE OF APPLICATION OF PROMOTER (no./week - mg.) | MAXIMUM INCIDENCE OF TUMORS (%-weeks) | AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in weeks) |
|---|---|---|---|---|---|---|---|
| 229 | 100 mg. API-229 | 13-13 | none | none | - | 13-64 | - |
| 230 | 100 mg. API-229 | | none | Dodecylbenzene, DDB | 3 - 100 | 92-34 | $11.8 \pm 2.8$ |
| 231 | 100 mg. API-8, FCC residuum | 0-63 | none | none | - | 0-63 | - |
| 232 | 100 mg. API-8 | | none | DDB | 3 - 100 | 50-26 | 24X |
| 239 | 100 mg. API-8 | | none | Distilled water | 3 - 100 | 0-76 | - |
| 240 | 100 mg. API-8 | | none | API-80, 95 SSU white oil | 3 - 100 | 0-76 | - |
| 290 | 100 mg. API-290[2] | 4-24 | 28-100 | none | - | 95-59 | $\sim 46$ |
| 287 | 100 mg. API-290 | | none | Alkylbenzene, partly DDB | 3 - 100 | 79-30 | $17^{+2}_{-4}$ |
| 288 | 100 mg. API-290 | 0-28 | 28-100 | API-80 | 3 - 100 | 96-57 | $\sim 48$ |
| 289 | 100 mg. API-290 | 0-28 | 28-100 | 340 SSU white oil | 3 - 100 | 89-72 | $\sim 50$ |
| 292 | 100 mg. API-290 | | none | Dodecane | 3 - 50 | 94-26 | $16^{+3}_{-1}$ |
| 292 | | | | | 2 - 50 | 94-53 | $24^{+6}_{-2}$ |
| 292 | | | | | 1 - 50 | 81-59 | $44.0 \pm 3.9$ |

[1] Solution of 0.5 g. dimethylbenzanthracene in 100 ml. sec.-amylbenzene.
[2] Solution of 0.5 g. dimethylbenzanthracene in 100 ml. 340 SSU white oil.

TABLE X

EFFECT OF TERMINATION OF EXPOSURE OF C3H MICE TO CATALYTICALLY CRACKED OILS AT A CRITICAL PHASE OF THE EXPERIMENT

| API EXPERIMENT NUMBER | DESCRIPTION OF EXPERIMENT | SCHEDULE OF APPLICATIONS | | MAXIMUM INCIDENCE OF TUMORS (%-weeks) | AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in weeks) | AVERAGE TIME FROM PAPILLOMA TO GROSS CARCINOMA (weeks) |
|---|---|---|---|---|---|---|
| | | (no./week - mg.) | TOTAL NUMBER OF WEEKS | | | |
| 43-1 | Dewaxed oil from catalytically cracked residuum | 2-20 | -[1] | 94-17 | 12.7±1.4 | 14 |
| 43-1A | Ditto | 2-20 | 10-19[2] | 100-19 | 13.8±1.2 | 16 |
| 43-1B | Ditto | 2-20 | 9 | 16-12[3] | - | - |
| 71 | TCC residuum | 2-20 | -[1] | 100-27 | 18.5±1.3 | 15 |
| 71A | Ditto | 2 - 20 | 14-25[2] | 100-25 | 18.3±1.5 | 16 |
| 71B | Ditto | 2 - 20 | 12 | 53-18[4] | - | - |

[1] Painting continued in each mouse until gross evidence of malignancy in that mouse.

[2] Painting of each mouse discontinued at time of appearance of papilloma in the individual mouse.

[3] No additional tumors developed up to the 23rd week at which time applications were resumed. They were terminated in the 28th week after the appearance of a papilloma in an additional animal. All survivors had developed tumors by the 56th week.

[4] Procedure similar to API-43-1B. Painting resumed at 30 weeks, discontinued after 32 weeks. By the 64th week all but one of the survivors had developed tumors. Gross malignancy was evident in 58% of the mice.

TABLE XI

EXPERIMENTS TO DETERMINE THE POTENCY
OF CERTAIN POLYCYCLIC HYDROCARBONS FOR THE SKIN OF C3H MICE

| API EXPERIMENT NUMBER | HYDROCARBON | SOLVENT | CONCENTRATION ( % by weight) | SCHEDULE OF APPLICATIONS (no./week - mg.) | MAXIMUM INCIDENCE OF TUMORS (% - weeks) |
|---|---|---|---|---|---|
| 261 | 4,5-dimethyl-phenanthrene | Benzene | 0.86 | 3 - 20 | 0-84 |
| 627 | Benz (a) anthracene | Dodecane | 0.50 | 3 - 50 | 53-45 |

TABLE XII

EXPERIMENTS ON THE RETARDATION OF TUMOR FORMATION BY WASHING CFW MICE

| API EXPERIMENT NUMBER | CARCINOGENIC OIL APPLIED | PERIOD OF EXPOSURE TO OIL BEFORE REMOVAL BY WASHING | MATERIAL USED FOR INITIAL RINSE | AGENT FOR WASHING | SCHEDULE OF APPLICATIONS (no./week - mg.) | MAXIMUM INCIDENCE OF TUMORS (%-weeks) | AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in wks.) |
|---|---|---|---|---|---|---|---|
| 113 | Industrial fuel oil, API-113 | control (no washing) | none | none | 3 - 100 | 94-36 | ~ 16 |
| 113 | | | | | 3 - 100[1] | 97-25 | 17.3±1.2 |
| 309 | API-113 | 1 hour | none | detergent solution | 3 - 100 | 40-67 | X |
| 310 | API-113 | 4 hours | none | detergent solution | 3 - 100 | 54-57 | 56X |
| 311 | API-113 | 4 hours | 95 SSU white oil API-95 | detergent solution | 3 - 100 | 83-52 | 45X |
| 315 | API-113 | 7 hours | none | detergent solution | 3 - 100[1] | 94-46 | ~ 35 |
| 12 | FCC residuum, API-12 | control (no washing) | none | none | 3 - 100 | 100-14 | ~ 10.5 |
| 303 | API-12 | 1 hour | none | soap solution | 3 - 100 | 100-40 | ~ 27 |
| 304 | API-12 | 9 hours | none | soap solution | 3 - 100 | 100-21 | ~ 17 |
| 8 | FCC residuum, API-8 | control (no washing) | none | none | 1-100 | 100-26 | ~ 12X |
| 300 | API-8 | 10 min. | none | soap solution | 1 - 100 | 0-80 | - |
| 301 | API-8 | 1 hour | none | soap solution | 1 - 100 | 20-80 | - |
| 302 | API-8 | 4 hours | none | soap solution | 1 - 100 | 100-70 | ~ 60 |

[1] Strain of mice used for this experiment was C3H.

TABLE XII (page 2)

EXPERIMENTS ON THE RETARDATION OF TUMOR FORMATION

BY WASHING CFW MICE

| API EXPERIMENT NUMBER | CARCINOGENIC OIL APPLIED | PERIOD OF EXPOSURE TO OIL BEFORE REMOVAL BY WASHING | MATERIAL USED FOR INITIAL RINSE | AGENT FOR WASHING | SCHEDULE OF APPLICATIONS (no/week - mg.) | MAXIMUM INCIDENCE OF TUMORS (%-weeks) | AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in weeks |
|---|---|---|---|---|---|---|---|
| 8 | API-8 | control (no washing) | none | none | 3 - 100 | 100-9 | ~8X |
| 305 | API-8 | 20 min. | none | detergent solution | 3 - 100 | 93-51 | ~40 |
| 308 | API-8 | 20 min. | API-95 | none | 3 - 100 | 100-52 | ~32 |
| 306 | API-8 | 1 hour | none | detergent solution | 3 - 100 | 94-44 | ~33 |
| 307 | API-8 | 1 hour | API-95 | detergent solution | 3 - 100 | 85-33 | ~25 |
| 312 | Barrier cream applied 9:00 AM<br>API-8 applied 11:00 AM<br>Removal of oil by washing with detergent solution 12:00 AM | | | | 3 - 100 | 71-45 | ~40X |
| 313 | Barrier cream applied 9:00 AM<br>API-8 applied 11:00 AM<br>API-8 applied 2:00 PM<br>Removal of oil by washing with detergent solution 4:30 PM | | | | 3 - 100 | 100-31 | ~ 25 |

TABLE XII (page 3)

EXPERIMENTS ON THE RETARDATION OF TUMOR FORMATION

BY WASHING C3H MICE

| API EXPERIMENT NUMBER | CARCINOGENIC OIL APPLIED | PERIOD OF EXPOSURE TO OIL BEFORE REMOVAL BY WASHING | MATERIAL USED FOR INITIAL RINSE | AGENT FOR WASHING | SCHEDULE OF APPLICATIONS (no./week - mg.) | MAXIMUM INCIDENCE OF TUMORS (%-weeks) | AVERAGE LATENT PERIOD FOR TUMOR INDUCTION (5% F.L. in weeks) |
|---|---|---|---|---|---|---|---|
| 8 | API-8 | control (no washing) | none | none | 3 - 15 | 100-18 | 12.4±1.2 |
| 8 | | | | | 3 - 100 | 89-9 | 5.2±.6 |
| 316 | none | none | none | detergent solution | 3 - | 0-72 | - |
| 317 | none | none | API-95 | detergent solution | 3 - | 0-72 | - |
| 320 | API-8 | 95 min. | 95 SSU white oil API-80 | detergent solution | 3 - 100 | 95-16 | 10.8±1.2 |
| 318 | API-8 | 75 min. | 340 SSU white oil | detergent solution | 3 - 100 | 100-21 | 16.6±1.4 |
| 319 | API-8 | 85 min. | refined kerosene | detergent solution | 3 - 100 | 94-21 | 16X |
| 56 | Feed to Wax Pressing, API-56 | control (no washing) | none | none | 3 - 20 | 84-54 | 32X |
| 56 | | | | | 3 - 100 | 65-42 | 24X |
| 314 | API-56 | 7 hours | none | detergent solution | 3 - 100 | 67-74 | 55X |