PLAINTIFF'S EXHIBIT
API-130

INTERIM REPORT TO THE API MEDICAL ADVISORY COMMITTEE

RESEARCH PROJECT MC-1

April 5, 1955

The importance of long-chain compounds as accelerators of the action of polycyclic carcinogens on the skin of mice has been emphasized in previous reports. Recent work on coal tars has provided further data that point to the importance of these compounds in the development of the occupational cancers of the skin which have resulted from exposure to slack wax and certain spindle oils (mule spinners' cancer). The following comparisons of experimental data with human experience may be significant.

Material	Relative Carcinogen Content	Maximum Probable Percentage of Long-chain Accelerators	Mice: Average ~~Latent~~ Period* (weeks)	Human Experience: Average ~~Latent~~ Exposure Period (years)
Paraffin Distillate (Slack Wax)	Low	60	20-35	20 or more
Spindle Oil	Low	40	60	40 (Henry)
Coal Tar	High	Negligible	12-27	23 (Henry)
Pitch	Very High	Negligible	-	
Heavy Catalytic Cycle Oil	Low to Medium	75	10-25	no data
Catalytically Cracked Residua	Medium to High	10-60	6-20	no data

* Three applications per week.

Chemical and biological experiments on coal tars and fractions thereof have indicated that long-chain accelerators are

absent. Although these materials regularly contain higher concentrations of polycyclic carcinogens than do catalytically cracked oils, they are frequently less potent when applied upon the skin of mice. It is also notable that Henry's investigation of the occurrence of cancer of the skin among workmen who handled coal tar or pitch in British industries indicated that the latent period of tumor formation was about the same as that observed among wax pressmen in two petroleum refineries in the United States. Since it may be estimated conservatively that coal tar contains at least ten times as much carcinogen as paraffin distillates, the role of the long-chain accelerators in the latter appears to be a highly important factor in their induction of tumors.

Experimental data indicate that there is a considerable variation from one straight run distillate to another in the accelerating activity of the fraction which distills over between 480 and 660°F. Fortunately, useful quantitative correlations between the physical properties of these fractions and this activity are being found. These variations may help to explain partially, at least, the differences in the incidence of scrotal cancer among wax pressmen in different refineries.

Further experimental work aimed at learning more about the role which may be played by personal hygiene in bringing about these apparent differences, has been carried out. It was found that the average period of exposure to the wax distillate, API-56, required to induce tumors in control C3H mice (32 weeks) was about doubled (63 weeks), when the skin of the animals was washed with detergent solution 7 hours after each application.

In 1951, similar observations on the effect of washing suggested that the use of medium distillates to rinse off most of the carcinogenic oil, before using the detergent, actually decreased the latent period of cancer induction, as compared with that associated with washing with detergent solution alone. The influence of accelerators, as demonstrated subsequently, furnished a possible explanation of this surprising result. It seemed questionable, therefore, that any petroleum distillate should be used for this purpose. The results of tests which were started last fall to answer this question are summarized in the attached Table.

Two conclusions from these data seem warranted. The use of distillates in the 500-700° range as rinses tends to accelerate the experimental induction of epithelial cancers. Kerosene or oils containing less than 10 percent of hydrocarbons which boil below 700°F. do not seem to exert this effect to a demonstrable degree, but they do not contribute to the capacity, possessed by the detergent alone, of diminishing the rate of cancer induction. Waterless cleansers should be examined by similar means for their content of accelerators in the 500-700° range.

API EXPERIMENT NUMBER	DESCRIPTION OF EXPERIMENT	DOSAGE PER APPLICATION[1] (mg.)	MAXIMUM INCIDENCE OF TUMORS (T.I./weeks)	AVERAGE LATENT PERIOD OF TUMOR INDUCTION (weeks)	RELATIVE CARCINOGENIC POTENCY, P_{MC}
8	F. C. C. Cracked Residuum (no washing)	100	89/7	5.4	> 0.6
8	F. C. C. Cracked Residuum (no washing)	15	100/18	12.5	0.25
321	API-8, after 1 hour, 45 min. washed with detergent solution	100	100/21	16.4	0.17
319	API-8, after 1 hour, 25 min. rinsed with refined kerosene, washed with detergent solution	100	89/18	16	0.17
320	API-8, after 1 hour, 35 min. rinsed with API-80, technical white oil (95 SSU at 100°F.) washed with detergent solution	100	100/16	11	0.30
318	API-8, after 1 hour, 15 min. rinsed with medicinal white oil (340 SSU at 100°F.) washed with detergent solution	100	95/21	17	0.16

[1] Three applications per week on the skin of C3H mice.