PLAINTIFF'S EXHIBIT

API-92

API SUBCOMMITTEE ON CARCINOGENICITY
MEETINGS AND MINUTES 1956-1959

CONDENSED SUMMARY OF THE OBJECTIVES AND FINDINGS OF AN EXPERIMENTAL PROGRAM FOR THE APPRAISAL OF THE POTENTIAL CARCINOGENIC CHARACTERISTICS OF CERTAIN PETROLEUM PRODUCTS

I. INTRODUCTION

Experiments were initiated in 1947 in order to develop more information concerning the carcinogenic characteristics of certain petroleum oils, some of which had been found by other investigators to be surprisingly active in this respect, when applied upon the skin of experimental animals. The initial work was exploratory in type, but it succeeded in heightening the interest of representatives of both the laboratory and the sponsors in an investigation of broader scope. Accordingly, in 1948, a program was designed and embarked upon which had as its ultimate purpose the determination of the degree of the potential hazard of cutaneous cancer which might be associated with contact of the human skin with a wide variety of petroleum oils. In the course of the investigation some attention was given to an examination of the potential usefulness of certain preventative procedures.

II. OBJECTIVES

The attack upon the primary problem was directed toward three primary objectives:-

1. That of testing representative samples of intermediate and finished petroleum products for their ability to induce cancer of the skin of mice, by methods which would demonstrate their relative activities in this regard in as nearly quantitative and reproducible terms as might

be possible.

2. That of comparing the "carcinogenic potencies" of the various test materials with the chemical or physical characteristics of their components, so as to develop, if possible, out of consistent correlationships, technical means for detecting the carcinogenic properties of petroleum products and determining their relative potencies.

3. That of surveying as large and as representative a segment of the population of the American petroleum industry as might be relevant and available in temporal, special, and occupational terms, in an effort to establish, by appropriate epidemiological and biostatistical methods, the existence or non-existence of the occupational hazard of cancer, generally, in the recent past or at the present time.

III. RESULTS

1. Biological Estimation of Carcinogenic Properties

More than one hundred representative samples of intermediates or products of refining operations were collected, and their relative carcinogenic potency for the skin of inbred mice were determined and so expressed as to denote both the rate of development of tumors and the proportion of experimental mice affected thereby.

(a) Tumors of the skin of mice, at the site of multiple applications, were induced most rapidly by the residual products of catalytic cracking or reforming, and by the cycle gas oils from delayed coking. They developed somewhat less rapidly at the site of contact with the residual products of thermal cracking or reforming. Almost all of the cracked residual oils selected for examination produced a

high frequency of occurrence of tumors of the skin of the mice, when applied thereon three times each week.

(b) The results of tests on unrefined oils covered a very broad spectrum of potency, from the high level of certain "lube" distillates and solvent extracts (which produced tumors about as rapidly as the catalytically cracked residue), to the completely negative behavior of certain other highly refined oils.

(c) Limited numbers of data indicate that extraction with phenol, as commonly applied to lubricating distillates, removes almost all of the polycyclic aromatic carcinogens. Similarly, treatment with fuming sulfuric acid, commonly employed in the manufacture of white oil, appears to render the raffinate free of carcinogenic compounds.

2. Chemical Characteristics of Carcinogenic Oils

Relationships were established between the chemical components of certain oils and the carcinogenic potency of the latter when applied upon the skin of mice:-

(a) Benzo(a)pyrene and its alkyl derivatives were found to be important contributors to the potency of cracked residue, and a fairly rapid method for their determination in the oils was developed.

(b) There being no benzopyrenes in the catalytically cracked fractions in the 700° to 780° range, the development and application of a method of liquid partition chromatography revealed the presence of alkyl derivatives of benzo(c)phenanthrene as important contributors to the carcinogenic potency of these fractions.

(c) There is no general physico-chemical method, as yet, whereby the carcinogenic potency of refinery streams generally can be estimated. However, a fairly satisfactory classification of residua (fractionator bottoms) of catalytically cracked oils can be made through chemical measurements of their polycyclic aromatic components by means of the combined techniques of chromatography and spectrometry (mass and ultraviolet), in correlation with their potency for the skin of mice.

(d) The potency of an oil containing a minute proportion of aromatic components in the molecular range of 325 to 350, depends greatly upon the extent to which other constituents of the oil exert an indirect influence upon the carcinogenic process (see below in (d1) a brief account of "acceleration"). The available data are insufficient for the estimation of such activity by physico-chemical methods. Therefore, while a limited number of unprocessed oils and cracked distillates may be classified as carcinogenic on the sole basis of their content of polycyclic aromatic hydrocarbons, the majority of such oils can now be so classified only in terms of the responses elicited by their application upon the skin of suitable test animals.

(d1) The carcinogenic potency of certain oils for the skin of mice was found to vary with the nature of their non-carcinogenic components. Some completely saturated fractions containing no polycyclic aromatic compounds were found to be capable of accelerating, three- or four-fold, the rate at which a given carcinogenic agent, introduced therein in a known concentration, induced tumors of the skin of mice. The investigation of the "accelerating activity" of various pure compounds indicated that this property was shared by a wide variety of

hydrocarbons containing 10 to 30 carbon atoms, including such examples as n-dodecane, dodecylbenzene, methylnaphthalene, and triisopropylbenzene. Experiments with various distilled fractions of petroleum oils indicated that the accelerating compounds occurred mainly in the fraction distilling between 650 and 700°F., whereas the compounds that were truly carcinogenic for the skin of mice occurred predominately in the higher boiling fractions.

(d2) A limited group of results indicated that certain sulfur compounds in catalytic cycle gas oils were also contributing to the carcinogenic potency of these oils. Further experiments with a pure sulfur compound, benzyldisulfide, indicated that this contribution was probably that of a special type of accelerator rather than that of a carcinogenic agent. The nature of this activity is being investigated further.

(d3) White oils employed as diluents have been found to be disproportionately effective in reducing the accelerating activity of n-dodecane and dodecylbenzene, as compared with the similar effect (apparently simple dilution) of more common solvents such as benzene and decahydronaphthalene.

B. Experimental Reduction of Carcinogenic Action by Washing Skin.

Washing of an oil from the skin of mice shortly after its application, by washing with a typical aqueous detergent, lengthened the time required for the production of cutaneous tumors. Such washing also reduced the frequency of the occurrence of tumors on the skin of the mice within groups subjected to multiple applications of the oils (with the exception of the more potent of those produced by catalytic cracking).

4. Epidemiological Information

The results of the epidemiological survey have been reported in detail and are not dealt with in this summary, except to indicate that, while they were unsatisfactory in several respects and therefore, inconclusive, they yielded no evidence of the occurrence of occupational cancer within the population surveyed. This summary has dealt with the potential hazard of occupational cancer, therefore, in relation to the products investigated, as revealed by the responses of mice to carcinogenic stimuli, rather than to a present and demonstrable danger within the industry. To the extent that this dubiously negative evidence is reassuring, it may well be accepted as a favorable condition for the further development and maintenance of a technologic surveillance of petroleum products, and an hygienic and medical supervision of occupational conditions and personnel.

IV. PUBLICATIONS

In addition to the regular interim reports to the Subcommittee on Carcinogenicity of the Medical Advisory Committee of the American Petroleum Institute, certain of the results of these investigations have been published in scientific journals as follows:

1. Tye, R., Grad, B.J., and Horton, A.W.: Determination of Benzo(a)pyrene in complex mixtures; use of catalytic isomerization on activated alumina. Anal. Chem. 27, 345-53 (1955).

2. Horton, A.W. and Benson, E.T.: Carcinogenesis of the skin. A re-examination of methods for the quantitative measurement of the potencies of complex materials. Cancer Research 16, 701-5 (1956)

3. Horton, A.W., Benson, E.T. and Prescott, E.F.: Carcinogenesis of the skin. II. The accelerating properties of aliphatic and related hydrocarbons. Cancer Research 17, 752-60 (1957).

An oral presentation of additional data was made as part of the Symposium on Polycyclic Aromatic Hydrocarbons at the meeting of the American Chemical Society, September 1958, under the title "Relationships Between the Composition and Carcinogenic Properties of Various Refinery Streams."

Other publications will follow in due course.

From The Kettering Laboratory, Department of Preventive Medicine and Industrial Health, College of Medicine University of Cincinnati, Cincinnati, Ohio.

Report by:

A. Wesley Morton, Ph.D.
Robert A. Kehoe, M.D.

Approved: Robert A. Kehoe
Robert A. Kehoe, M. D.
Director

Date: November 4, 1959

ESSO RESEARCH AND ENGINEERING COMPANY

(FORMERLY STANDARD OIL DEVELOPMENT COMPANY)

P.O. BOX 45, LINDEN, N.J.

MEDICAL RESEARCH DIVISION

TELEPHONE: WABASH 5-1600

October 5, 1960

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

Dear Dr. Kehoe:

The next meeting of the Subcommittee on Carcinogenicity of the API will be held in Chicago on Saturday, November 12, 1960 in association with the Annual Meeting of the American Petroleum Institute.

You will remember that at our last meeting in Rochester in April, the Committee made a series of suggestions to you concerning the report from Dr. Horton which he said you would take under advisement and possibly consider issuing a revised final report from Dr. Horton. This letter will serve as a reminder that if you plan to issue such a revised final report, it would be highly helpful to the Subcommittee on Carcinogenicity if this report could be in their hands no later than November 1, 1960. This would give us adequate time to review the report which as you know is quite extensive prior to the time of our meeting on November 12. I do hope that you and Dr. Horton will try to have any revision of the final report which you contemplate in our hands by November 1.

Sincerely yours,

R. E. Eckardt

R. E. ECKARDT, M. D.
Director

REE/bjm

cc: Dr. A. W. Horton
Mr. E. O. Mattocks
S/C on Carcinogenicity

February 5, 1960

R. E. Eckardt, M.D.
Esso Research and
Engineering Company
P.O. Box 45
Linden, New Jersey

Dear Bob:

I have discussed possible dates with Dr. Kehoe for a March meeting at the Laboratory. We should like to suggest the first part of any of the weeks with a preference for the Tuesdays (March 1, 8, 15, or 29).

Sincerely yours,

A. W. Horton

AWH:bk

cc: Dr. R. A. Kehoe

September 8, 1959

Dr. R. E. Eckardt
Esso Research and Engineering Company
P.O. Box 45
Linden, New Jersey

Dear Doctor Eckardt:

Thanks for your letter of August 18th and the information about the meeting of your Subcommittee in connection with the meeting of the A.P.I., in Chicago on November 7th. In view of the importance of this meeting in relation to our report, I think I should attend this meeting of the Subcommittee, as well as Dr. Horton.

We shall make every effort to have the report in the hands of the Subcommittee well in advance of this meeting. I just returned from my vacation last Wednesday, or I would have answered your letter sooner. I have not had an opportunity to talk with Dr. Horton since my return, and I cannot tell you the exact status of the report until I see him. However, I can acquaint you now with the general situation, and will advise you in more detail later.

As you might expect, the preparation of the report is a large task. In recognition of this fact, the work of putting it together was begun long ago. The greater part of the work is behind us, of course, but it is my purpose to have the job done so well that we shall all have reason to take some pride in it. Accordingly, I have put a very considerable amount of work and time into it. Dr. Horton, of course, has borne the main burden. We are concerned now only with the finishing touches, but these I consider very important. The report has gone through several drafts and, with but a few exceptions, here and there, it is going through its final draft. We shall wish to have the fullest and frankest comments of the Subcommittee.

Sincerely yours,

Robert A. Kehoe, M. D.

RAK:ss

cc: Dr. A. W. Horton

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R. E. ECKARDT, PH.D., M.D.
DIRECTOR

B. E. BENNINSON, M. D.
ASSISTANT DIRECTOR

N. V. HENDRICKS, CH. E.
SR. ENG. ASSOC.

H. W. GERARDE, PH.D., M.D.
RES. ASSOC.

August 18, 1959

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

Dear Dr. Kehoe:

At the present time the Subcommittee on Carcinogenicity is planning a meeting in association with the coming American Petroleum Institute meeting in Chicago on Saturday, November 7, at 2:00 p.m. Undoubtedly this meeting will be held some place in the Hilton Hotel in Chicago, although the exact meeting room has not yet been decided upon. I am writing to you at this time in the hopes that Dr. Horton's report of his work on carcinogenicity will be prepared and in the hands of the Subcommittee well in advance of this meeting so that the Subcommittee members could go over it in detail and be prepared to make comments and suggestions by the time of the meeting of the Subcommittee. It would also be appreciated if Dr. Horton could be in attendance at this Subcommittee meeting so that he might receive the comments and suggestions of the members of the Subcommittee.

Sincerely yours,

H. E. GERARDE, M. D.

HEG:ch

cc: Dr. A. W. Horton

THE DESIGN OF EXPERIMENTS AND THE USE OF COMPUTERS IN MEDICAL RESEARCH

A One Day Seminar Sponsored by The Committee on Chronic Disease Epidemiology

September 12, 1959

PROGRAM

8:30 Introduction

8:40 Fundamental Necessity of Design; Alan E. Treloar, Director of Research, American Hospital Association.

9:30 Panel Discussion; Moderator - Eugene L. Saenger, Department of Radiology, University of Cincinnati.

10:00 Coffee

10:20 Simple and Complex Analyses With Help of Computers; Frank J. Massey, Department of Biostatistics, School of Public Health, UCLA.

11:10 Panel Discussion; Moderator - Robert A. Kehoe, Director, Institute of Industrial Health, University of Cincinnati.

11:40 Discussion of the Afternoon Demonstrations; Staff, Biometric Section.

12:20 Lunch

1:30 Computers; Paul Herget, Department of Astronomy, University of Cincinnati.

2:30 Demonstrations

GROUP A

2:30 Demonstrations in the Computing Center on Campus (Bus transportation will be provided).

3:45 Mechanics of Getting Data on the Computer; Theodor D. Sterling, Department of Preventive Medicine.

4:30 Demonstration in the Computing Center in the College of Medicine; Staff, Biometric Section.

GROUP B

2:30 Mechanics of Getting Data on the Computer.

3:15 Demonstration in the Computing Center in the College of Medicine.

3:45 Demonstrations in the Computing Center on Campus.

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

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

CABLE ADDRESS: KETLAB, CINCINNATI
TELEPHONE: AVON 1-2568

October 20, 1959

TO: Members and Associates of the A.P.I. - Medical Advisory Committee

W. O. Armstrong, M.D.	T. M. Frank, M.D.	T. H. Mitchell, M.D.
V. C. Baird, M.D.	F. D. Gassaway, M.D.	M. N. Newquist, M.D.
Lamson Blaney, M.D.	J. H. Hege, M.D.	J. W. Osborn, M.D.
F. F. Boys, M.D.	C. H. Hine, M.D.	R. C. Page, M.D.
Richard Call, M.D.	W. F. Kahle, M.D.	R. J. Potts, M.D.
J. W. Crookshank, M.D.	T. J. Kelly, M.D.	B. B. Reeve, M.D.
L. E. Curtis, M.D.	E. K. Linder, M.D.	J. C. Ruddock, M.D.
Kieffer Davis, M.D.	E. P. Luongo, M.D.	G. M. Saunders, M.D.
R. E. Eckardt, M.D.	B. S. Miller, M.D.	Ralph Schneider, M.D.
K. R. Fourcher, M.D.	C. R. Miller, M.D.	Leo J. Wade, M.D.
		E. R. Ware, M.D.
Mr. Paul Halley	Dr. R. C. Mithoff	Mr. A. C. Pabst

Gentlemen:

Enclosed is the Introduction and Summary of the Final Report on A.P.I. Research Project MC-1. The completed report which will include twelve chapters describing the materials, methods, and results in detail should be ready by the time of the Chicago meeting.

Sincerely yours,

Robert A. Kehoe

Robert A. Kehoe, M.D.

RAK:bk

October 21, 1959

R. E. Eckardt, M.D.
Medical Research Division
Esso Research and Engineering
P.O. Box 121
Linden, New Jersey

Dear Doctor Eckardt:

Enclosed please find three additional copies of the Introduction and Summary of the Final Report of A.P.I. Research Project MC-1.

Since we have not received a recent copy of the addresses of those who are on the present Medical Advisory Committee, we have not been able to send copies to the following members:

Richard Call, M.D.
B. S. Miller, M.D.
T. H. Mitchell, M.D.

We would greatly appreciate any efforts on your part in forwarding these copies to the above mentioned members. Also, if possible, could you send a present list of the members with attached addresses to us.

Thank you for your consideration.

Sincerely,

Brenda Kirkham, Secretary
to Dr. A. W. Horton

March 19, 1958

R. E. Eckardt, M.D.
Esso Research and Engineering Company
P.O. Box 45
Linden, New Jersey

Dear Doctor Eckardt:

Attached is a copy of our Interim Report on API Research Project MC-1. I must apologize for our oversight in not getting this to you sooner. Apparently we got it to everyone in the list at the top of your letter, but pulled the prize boner of missing the chairman, whose name came at the end.

I should be looking forward to seeing you next Monday.

Sincerely yours,

A. Wesley Horton

AWH:tb

March 4, 1958

R. E. Eckardt, M.D.
Esso Research and Engineering Company
P.O. Box 45
Linden, New Jersey

Dear Doctor Eckardt:

Doctor Kehoe, Doctor Phair and I have discussed the proposed dates for the next meeting of the subcommittee to be held here in Cincinnati. Apparently, the only two that are compatible with local schedules are March 24 or April 11. If the April date is suitable for the members of the subcommittee, it might be the preferable one in that it may be possible to have the report on the epidemiologic phase completed by that time.

As you have suggested, we shall plan to have a copy of the report on the experimental phase out at least a week ahead of whichever meeting date is selected.

Sincerely yours,

A. Wesley Horton

AWH:tb

cc: Dr. R. A. Kehoe
Dr. J. J. Phair

ESSO RESEARCH AND ENGINEERING COMPANY

(FORMERLY STANDARD OIL DEVELOPMENT COMPANY)

P.O. BOX 45, LINDEN, N.J.

MEDICAL RESEARCH DIVISION

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N. V. HENDRICKS, CH. E.
HEAD INDUSTRIAL HYGIENIST

HORACE W. GERARDE, PH. D., M.D.
HEAD TOXICOLOGIST

February 17, 1953

Messrs E. W. Adams - Standard Oil Co of Indiana, Research Dept, Whiting, I
C. H. Hine - Shell Development Co. Emeryville, Calif
E. K. Linder - Atlantic Refining Co. 260 Broad St. Phila. Pa.
R. C. Mithoff - Calif. Res. Corp. Richmond, Calif.
M. N. Newquist Sepia Co. Chrysler Bldg. 42nd & Lexington NYC.
A. C. Pabst - Socony Mobile Oil Co. 42nd & Lexington NYC

Gentlemen:

I suddenly realize that today is February 17 and that the next meeting of the Subcommittee on Carcinogenicity should be scheduled for roughly one month from today in order that we might have our report available for the Medical Advisory Committee for its April meeting. It seems that we all thought in terms of the last weekend of March or the first week of April for a meeting of our Subcommittee. It has been proposed that this meeting be held in Cincinnati for two reasons. One reason is the convenience of the Kettering group, and the other is so that we might have another look at the facilities and work which is going on. In view of this, therefore, I am asking each of you to let me have your thoughts about a date for the next meeting of our Subcommittee. JP

I would propose the dates of March 24, 28, 31 and April 11. I leave out April 4 since this is Good Friday and I leave out April 7 because April 6 is Easter. Holding our meeting on either a Monday or Friday will permit our West Coast friends to travel one day at least over the weekend. My preference would be that our meeting be held in Cincinnati on March 28, but I am willing to hold this meeting in accordance with the wishes of the majority. Please let me have your thoughts on this at your earliest convience.

In addition, it would be extremely helpful if Dr. Horton could have in the hands of each of the Subcommittee members by Monday, March 17 at the latest, a copy of anything which he plans to prepare for the Subcommittee for its meeting in order that we each might have an opportunity to review this prior to the meeting. The same is true of anything which Dr. Phair plans to make up for the Subcommittee.

Again, I ask each of you to let me know your preferences on dates so that we can get this meeting setup and still have adequate time to prepare our meeting for the MAC

Sincerely yours,

R. E. Eckardt.

R. E. ECKARDT, M. D.

REE/cjh
cc: Dr. A. W. Horton ✓
Mr. E. O. Mattocks
Dr. R. A. Kehoe
Dr. J. J. Phair

* - In Duplicate

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HEAD INDUSTRIAL HYGIENIST

HORACE W. GERARDE, PH. D., M.D.
HEAD TOXICOLOGIST

September 9, 1957

Messrs. E. W. Adams R. C. Mithoff
C. H. Kline* M. M. Newquist
E. K. Linder A. C. Pabst

Gentlemen:

To date I have not heard from all of you regarding a meeting of the Subcommittee on Carcinogenicity with the Kettering Laboratory. Three of you have answered and indicated roughly that you are available anytime, with minor exceptions, between September 15 and October 18, 1957. In view of this, I shall exercise the Chairman's prerogative of setting a date for this meeting.

I propose that we meet with the Kettering Group in Chicago on Friday, September 27, beginning at 9:30 a.m. I would propose that we meet at the Blackstone Hotel, where I shall attempt to obtain a suite for the meeting. I would also propose that the Subcommittee gather at 9:30 and that we ask the Kettering Group to join us at 11:00. This should permit the Kettering Group to leave Cincinnati Friday morning thus being out of the office only one day. Unless I hear to the contrary, I shall plan to see each of you at that time.

I strongly believe that each member of the Subcommittee should be present, with no attempt to provide alternates for this particular meeting. So, if you cannot make it, please suggest another date early enough that our plans can be made.

Mr. Mattocks has requested that we let him know if we wish to hold a Subcommittee meeting in Chicago in November. The Subcommittee meetings are scheduled for Tuesday, November 12. If you wish such a meeting, please let me know at the time you let me know of the meeting with the Kettering Group on September 27.

Sincerely,

Mtg for JP on Oct 4 or 11

R. E. ECKARDT, M. D.

REE:ejh
cc: Drs. J. J. Fhair, A. W. Horton, R. A. Kehoe

* - In Duplicate

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HORACE W. GERARDE, PH. D., M.D.
HEAD TOXICOLOGIST

February 28, 1958

Messrs. E. W. Adams R. C. Mithoff
C. H. Hines* M. N. Newquist
E. K. Linder A. C. Pabst

Gentlemen:

The vote for our next meeting shows the following at the present time: one individual could only make the 24th; another prefers the 24th because it would tie in with another trip he has to make; one prefers the 31st, but could make the 24th; another could make the 24th; one member could not make any of the dates proposed; and two members have not been heard from.

In view of this, the majority rule would suggest March 24 as the next meeting of our Subcommittee. The meeting would be scheduled in Cincinnati at the Kettering Laboratory beginning at 9 a.m. Unless I hear violent objections to the contrary, this will be the date of our next Subcommittee meeting.

Sincerely yours,

R. E. Eckardt

R. E. ECKARDT, M. D.

REE:cjh
cc: Mr. E. O. Mattocks
Dr. A. W. Horton
Dr. R. A. Kehoe
Dr. J. J. Phair

* - In Duplicate

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

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

CABLE ADDRESS: KETLAB, CINCINNATI
TELEPHONE: CAnyon 1414

April 16, 1957

Dr. Robert E. Eckardt
Medical Research Division
Esso Research and Engineering Company
P. O. Box 121
Linden, New Jersey

Dear Doctor Eckardt:

The completed Interim Report should be in your office either before this letter reaches you or shortly thereafter. Figure 1 in this final edition (extra copy attached) includes, in addition to the dose-response curves for methylcholanthrene and benzopyrene in non-accelerating solvents, that for a reference carcinogen having a curve intermediate between the first two. This curve (actually its asymptotes) is believed to be close to that for the typical carcinogens of petroleum oils, since its use has given close agreement between the total potency (non-accelerated) of mixtures of different classes of such carcinogens and the sum of the contributions of the parts of these mixtures (separated by distillation or chromatography or liquid-liquid partition). (If the dose-response curve for methylcholanthrene is used for this purpose, the non-accelerated potency of the whole mixture tends to run slightly smaller than the sum of the parts).

Any curve which meets the preceding practical specification that its use permits the proper relation of the whole to its parts may be used for the conversion of $\underline{e}_b$ to $\underline{e}_c$ (where $\underline{e}_b$ is the average duration of tumor-free life for the blend of the polycyclic carcinogens in benzene and $\underline{e}_c$ is as defined in Appendix 1). In general, any hyperbola having the general equation,

$$(\underline{e} - 13)(\underline{d} + B) = 59B \ ,$$

meets this requirement satisfactorily. The specific one in which B equals 0.17 is preferred on the grounds that it seems most representative of typical active carcinogens.

It is important to keep in mind that it is the relative, not the absolute values of the dosage, $\underline{d}$ ($\underline{d}_b$ and $\underline{d}_o$ corresponding to $\underline{e}_b$ and $\underline{e}_c$) that are important in the estimation of $\underline{e}_c$. For this application $\underline{d}_b$ and $\underline{d}_o$ are simply intermediate parameters which are related by certain ratios depending on the conditions of the biological tests. In the example in Appendix 1, $\underline{d}_o/\underline{d}_b$ equals 1/3.2 .

You suggest in your letter that the value of 26 weeks for $\underline{e}_b$ might correspond to any value of $\underline{d}_b$ from 0.1 to 1.6 mg. per unit area per week. Very well, let us calculate the value of $\underline{e}_c$ resulting from the use of these extreme values of $\underline{d}_b$.

If $\underline{d}_b = 0.1$ when $\underline{e}_b = 26$, the dose-response curve which would meet the requirement stated in the first paragraph (the potency of a mixture equals the sum of the potencies of its parts) would have the following equation

$$(\underline{e} - 13)(\underline{d} + 0.028) = 1.67 \ .$$

Since $$\underline{d}_o = \frac{\underline{d}_b}{3.2} = \frac{0.1}{3.2} = .031 \ ,$$

$$(\underline{e}_c - 13)(.031 + .028) = 1.67$$

or $$\underline{e}_c = 40 \text{ weeks} \ .$$

If $\underline{d}_b = 1.6$ when $\underline{e}_b = 26$, the reference carcinogen must have a curve with the following equation:

$$(\underline{e} - 13)(\underline{d} + 0.45) = 26.6 \ .$$

Since in this case $$\underline{d}_o = \frac{1.6}{3.2} = 0.5 \ ,$$

$$(\underline{e}_c - 13)(0.5 + 0.45) = 26.6$$

or $$\underline{e}_c = 41 \text{ weeks} \ .$$

Thus the value of $\underline{e}_c$ is independent of the absolute value of the intermediate parameter $\underline{d}_b$.

All current tests on polycyclic fractions are being carried out in such a way as to obtain additional direct information on the shape of the dose-response curve for the carcinogens in these fractions. It is expected that this information will provide a more exact definition of the horizontal asymptote of the hyperbola, which may modify the absolute values of $\underline{e}_c$ and A slightly. Any change in the current values should not exceed 10% and, furthermore, all such changes would be in the same direction.

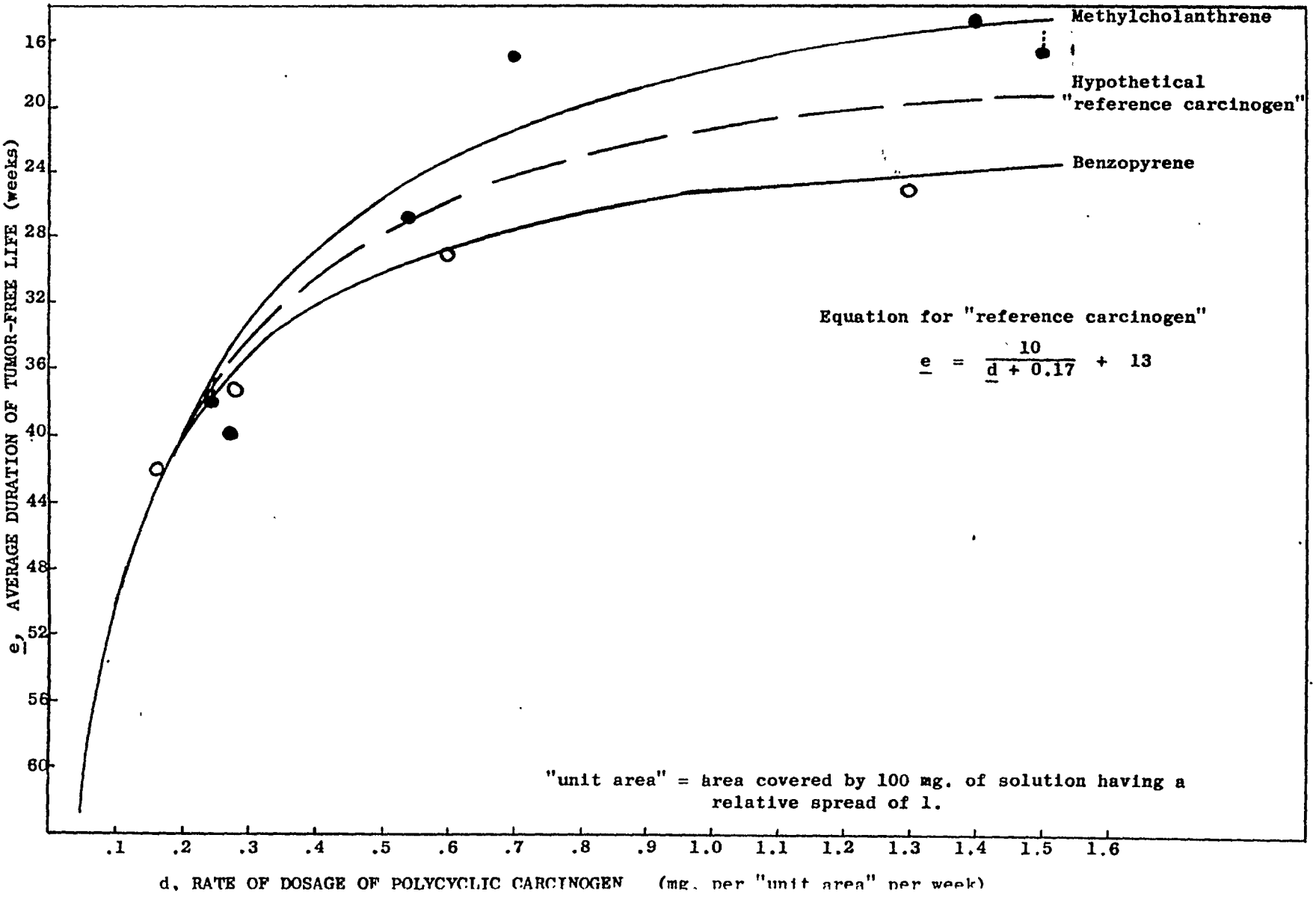
Sincerely yours,

A. Wesley Horton

AWH:mjg
Copy - Subcommittee on Carcinogenicity

FIGURE 1

THE RATE OF INDUCTION OF PAPILLOMAS IN C3H MICE BY THE REPEATED APPLICATION OF 3-METHYLCHOLANTHRENE AND BENZO(a)PYRENE IN NON-ACCELERATING SOLVENTS



ESSO RESEARCH AND ENGINEERING COMPANY

(FORMERLY STANDARD OIL DEVELOPMENT COMPANY)

P. O. BOX 121, LINDEN, N. J.

MEDICAL RESEARCH DIVISION

ROBERT E. ECKARDT, PH. D., M.D.
DIRECTOR

N. V. HENDRICKS, CH. E.
HEAD INDUSTRIAL HYGIENIST

HORACE W. GERARDE, PH. D., M.D.
HEAD TOXICOLOGIST

BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

March 20, 1957

Drs: A. W. Horton ✓
R. A. Kehoe
J. J. Phair

The Kettering Laboratory
University of Cincinnati
College of Medicine - Eden Avenue
Cincinnati 19, Ohio

Gentlemen:

This is a reminder to suggest that it would be most helpful to the Subcommittee on Carcinogenicity if we can have in our hands the report which is to be discussed at our second meeting at the Blackstone Hotel in Chicago, by March 25th.

Sincerely yours,

R. E. Eckardt

R. E. ECKARDT, M. D. rjr

REE:cjh
cc: E. W. Adams R. C. Mithoff
C. H. Hine* M. N. Newquist
E. K. Linder A. C. Pabst

* - In Duplicate

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CHIEF CLINICAL RESEARCH PHYSICIAN

February 8, 1957

Messrs: E. W. Adams R. C. Mithoff
C. H. Hine* M. N. Newquist
E. K. Linder A. C. Pabst

Gentlemen:

In accordance with the meeting of the Subcommittee on Carcinogenicity held in Los Angeles on January 31 and February 1, this is to advise that the Subcommittee proposed that the next meeting be held on April 2, 1957 in Chicago at the Blackstone Hotel.

It is proposed by the Subcommittee that the items to be discussed at this time will be a status report by Dr. Horton, a final report by Dr. Phair if possible, and the budget for this project from July 1, 1958 to June 30, 1959 by Dr. Kehoe. It is to be hoped that the three reports from The Kettering Laboratory can be in the hands of the Subcommittee members by March 25, 1957 so that we will have ample time to review them prior to the time of our meeting.

It is planned by the Subcommittee to have its report for the MAC prepared in sufficient time to distribute to the members of the MAC in advance of the meeting in St. Louis. The Subcommittee will plan to hold a meeting at the Jefferson Hotel in St. Louis, Saturday evening, April 20 at 8 p.m. Mr. Stroop has been asked to reserve room for us at this time, relinquishing that which we had previously tentatively reserved for the meeting of the Subcommittee on Friday, April 19.

The plan of this meeting will be to whip up the final draft of the report of the Subcommittee to the MAC into its final form for presentation to the MAC the following day. It is planned to open this meeting to all members of the MAC in order that they might ask questions about our report. In general, however, this Subcommittee meeting will be conducted as other Subcommittee meetings are, the members of the Subcommittee will sit around a table in the center of the room and do most of the discussing of the report. If Dr. Horton, Dr. Phair and Dr. Kehoe are available, they are welcome to sit in on this meeting also, if they so desire.

Sincerely yours,

R. E. Eckardt

R. E. ECKARDT, M. D.

REE:cjh
cc: L. E. Curtis
D. V. Stroop

A. W. Horton
R. A. Kehoe
J. J. Phair

* - In Duplicate

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BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

January 14, 1957

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

Dear Dr. Horton:

The next meeting of the Subcommittee on Carcinogenicity is being scheduled for Thursday and Friday, January 31 and February 1, at the Biltmore Hotel in Los Angeles.

If you wish the subcommittee to consider the new proposal which you suggested in a recent letter of yours to me, I would appreciate it if you would let me have this proposal by January 28, in order that I might take it to the meeting with me. } Mailed Jan. 14

Very truly yours,

R. E. Eckardt

R. E. ECKARDT, M. D.

REE:cjh

February 16, 1957

Members, Subcommittee on Carcinogenicity
API Medical Advisory Committee

Gentlemen:

In accordance with the suggestion by Dr. M. M. Newquist, we have initiated a detailed review of the investigation on the Carcinogenic Action of Mineral Oils, sponsored by the British Medical Research Council. We have fairly complete files on their progress reports. A summary of their experimental findings and a comparison with the results of work at the Kettering Laboratory on the same oils should be ready for distribution some time prior to the meeting in April.

Sincerely yours,

A. Wesley Horton

AWH:mjg
CC: Mr. David V. Stroop

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HEAD TOXICOLOGIST

BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

February 8, 1957

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

Dear Dr. Horton:

The Subcommittee on Carcinogenicity of the American Petroleum Institute's Medical Advisory Committee met in Los Angeles on January 31 and February 1. The proposal for wax carcinogenicity studies attached to your letter of January 14, 1957 was included with six other proposals from other toxicological laboratories.

It was the decision of the Subcommittee that several of the other proposals received by the Subcommittee showed a greater imaginative approach to the solution of the problem and a better understanding of the nature of the problem involved. Hence, the proposal which you submitted to us is no longer under active consideration by the Subcommittee.

I want at this time to express the gratitude and appreciation of the Subcommittee to you for having submitted this proposal. It wasn't that your proposal did not contain very many interesting concepts for the study, but only that other laboratories had proposed studies which we felt were more in keeping with the needs of the Subcommittee.

The Subcommittee holds your laboratories in the highest regard and should other problems arise in the future, I am sure that we would wish to contact you concerning them.

Sincerely yours,

R. E. Eckardt

R. E. ECKARDT, M. D.

REE:cjh
cc: E. W. Adams
C. H. Hine*
E. K. Linder
R. C. Mithoff
M. N. Nexquist
A. C. Pabst

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BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

December 19, 1956

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

Dear Dr. Horton:

I would appreciate it if you would send copies of your letter of December 11, 1956 to me, to each of the members of the Subcommittee on Carcinogenicity, in order that we may discuss it at the next meeting of our Subcommittee.

The Subcommittee would be most happy to receive from you, the memorandum which you refer to in the last paragraph of your letter. I would appreciate it if you would forward this also to each of the members of the Subcommittee in order that it can be included in our discussions on the wax cancer problem.

Very truly yours,

R. E. Eckardt.

R. E. ECKARDT, M. D.

REE:cjh

December 11, 1956

Dr. Robert E. Eckardt, Director
Medical Research Division
Esso Research and Engineering Company
P. O. Box 121
Linden, New Jersey

Dear Doctor Eckardt:

We are heartily in favor of the fullest ... exchange of information on this question of carcinogenicity of petroleum fractions with the Institute of Petroleum. To tell the truth, I was not aware that the erstwhile policy of sending our annual report to Research Committee # 2 had been discontinued.

I presume that it might now be appropriate to send copies of our annual reports on Project MC-1 for 1955 and 1956, together with reprints of our papers on the determination of benzopyrene and carcinogenesis of the skin. I believe that Mr. Stroop has copies of all of these reports.

In connection with the proposed investigation of petroleum waxes, we have given serious consideration to the desirability of dividing the program into two phases, the first of which would involve a relatively rapid screening of pertinent waxes used to coat meat wrapping paper or milk cartons. If positive biological evidence of the presence of carcinogens was obtained in this first phase a second developmental phase to estimate the hazard of internal cancers would be recommended. We have prepared a memorandum to this effect, which we would be glad to send along if you are interested.

Sincerely yours,

A. Wesley Horton

AWH:mjg
extra cc:
CC: Mr. David V. Stroop

ESSO RESEARCH AND ENGINEERING COMPANY

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P. O. Box 121, Linden, N. J.

MEDICAL RESEARCH DIVISION

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HORACE W. GERARDE, PH. D., M.D.
HEAD TOXICOLOGIST

BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

December 6, 1956

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

Dear Dr. Horton:

Periodically, we have received information from the Research #2 Committee of the Institute of Petroleum, outlining the work which they have been doing on various petroleum fractions and their carcinogenicity.

I believe that you have regularly been receiving copies of this from Mr. Stroop. It occurs to me that we have not been forwarding to them anything in the last several years. Perhaps you would like to indicate to me what you think would be appropriate for us to send to their committee.

Very truly yours,

R. E. Eckardt.

R. E. ECKARDT, M. D.

REE:cjh
cc: Mr. D. V. Stroop

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HORACE W. GERARDE, PH.D., M.D.
HEAD TOXICOLOGIST

BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

September 18, 1956

Messrs: E. W. Adams
C. H. Hine
E. K. Linder
R. C. Mithoff
M. H. Newquist
A. C. Fabst

Gentlemen:

This is to confirm that the next meeting of the Subcommittee on Carcinogenicity will be held in Chicago, Saturday, October 20, 1956. The place will be my room at the Drake Hotel. Unfortunately, I was unable to obtain a suite at the Hilton and, so at the suggestion of Dr. Kehoe, I have managed to get a suite at the Drake. Incidently, for those who might not realize it, the Safety Council is meeting in Chicago at this time. For this reason, hotel reservations are scarce for October 20.

If any of you arrive late Friday night, October 19, it is probable that I will have an extra bed in my suite and I would be very happy to have you join me if you are unable to get a reservation. In fact, if necessary, we could probably have a couple of cots put up in the living room, if hotel reservations are that tight.

I am attaching to this letter, a copy of a proposal that was recently made to another company for studies on microcrystalline wax. These studies were really for the purpose of determining the chronic toxicity, in accordance with the recommendations of the FDA, and do not include tests of carcinogenicity. Even so, however, the total possible expenses of these studies comes to about $40,000.

The purposal which is under consideration by the FDA for testing of carcinogenicity, includes 800 rats and 800 mice (2 strains) on feeding experiments for 2 years, plus 400 rats and 400 mice (2 strains) on injection studies, plus 20 dogs on feeding studies for a total of 7 years. At the recent Gordon Research Conference on Toxicology, Dr. Fitzhugh of the FDA suggested that we might consider a compromise on the feeding studies, which would consist of 150 rats for 2 years with an additional 100 controls and 200 mice for 2 years with an additional 200 controls. This would then total some 750 rodents. They might consider 6 dogs with 4 controls for 5-7 years for cancer. In addition, they would probably require the 400 rats and 400 mice on injection studies. It is easy to see that if these recommendations are to be followed, the costs of such studies would be far in excess of the amount suggested in the attached.

I am simply enclosing this attachment in order to give each of you some understanding of the magnitude of the problem we are facing in planning to do carcinogenic studies on waxes. The preliminary discussions which we had with Dr. Kehoe and Dr. Horton in Chicago, suggested a theoretical approach to this problem, which, from a scientific standpoint, might be entirely satisfactory. As yet, I did not obtain any approval for use on milk cartons, at least from the carcinogenic standpoint. I sincerely hope that Dr. Kehoe, when he makes his proposal in Chicago, will indicate the practical facts of life, namely, those dealing with the FDA into consideration of making his proposal. All of us who have had dealings with the FDA in the past have found, at one time or another, that theoretical considerations, although carrying weight with the FDA, must, at times, be supplemented by rather practical considerations of what will be acceptable to the FDA.

It is my desire that Dr. Kehoe will have for us, a write-up of his proposal at least a week in advance of the October 20th meeting of the Subcommittee, in order that each of us may carefully review it prior to the meeting.

Sincerely yours,

R. E. Eckardt

R. E. ECKARDT, M. D. cjh

REE:cjh
Attach. - PROPOSAL FOR STUDIES ON MICROCRYSTALLINE WAX. pp. 1-3.
cc: Dr. L. E. Curtis (w/o attach.)
Mr. A. W. Horton (w/attach.)
Dr. R. A. Kehoe (w/attach.)
Mr. D. V. Streep (wo/attach.)

Dictated, but not read

December 10, 1956

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

Dear Mr. Stroop:

Under separate cover and via Railway Express, I am sending you 75 copies of my report to the Medical Advisory Committee - along with the multilith mats. Individual copies are being sent to Dr. Curtis, Dr. Eckardt, and the members of the Subcommittee on Carcinogenicity.

Sincerely yours,

Jgd.

John J. Phair, M.D.

cc: Dr. Curtis
Dr. Eckardt
Dr. Kehoe
Dr. Horton ✓
report in "report file"

A PROGRAM FOR THE INVESTIGATION OF INTERMEDIATE AND REFINED WAXES

OBJECTIVES: Certain crude paraffinic distillates have been associated with the development of scrotal cancer in wax pressmen. By further refining (essentially deoiling and decolorization processes) the waxy components of these distillates are purified until they meet the specifications for their particular use.

The major objective of the proposed investigation is the determination by suitable biological tests of the stage in the refining process at which the concentration of the components of the paraffinic distillates responsible for their carcinogenic potency for the human skin has been reduced to a negligible level. A correlated and equally important goal will be the development of biological techniques which will yield some estimate of the relative cancer hazard incurred by human beings through the ingestion of these partially or fully refined waxes. Pertinent information on composition obtained in the course of the research on cracked oils and straight run distillates (API Research Project MC-1) will be applicable to the various waxes. Analytical techniques based on these findings will serve as a further check on the extent of the reduction in the concentration of carcinogens present in the crude distillates from which the waxes were derived.

PROCEDURE:

I. Selection of materials

A. Process variables to be considered (partial assembly of this information from individual producers has been carried out in an early phase of Project MC-1)

1. Crude source
2. Preparation of feed to the wax plant
3. Method of deoiling the wax

B. Types of materials under consideration

1. Correlated series of samples
   a. Feed to the wax plant (straight run or extracted paraffinic stocks)
   b. Intermediate scale waxes resulting from sweating or solvent deoiling operations
   c. Refined waxes after final deoiling and decolorization (e.g., MEK-benzol or adsorbents)
2. Waxes of increasing molecular weight (melting point), including those referred to as "microcrystalline"
3. Suitable composites of closely related materials from different producers

C. Pertinent properties by which selected materials may be described

1. Oil content
2. Melting range or molecular weight
3. Content of fluorescent materials (chromatographic)
4. Absorption and mass spectra

II. Biological testing

A. Criteria for selection of experimental conditions

1. Control animals subjected to the administration of vehicles alone, with no added carcinogens, should have a low, essentially negligible incidence of the cancer to be reproduced
2. Positive results should be obtainable if a known carcinogenic hydrocarbon is introduced into the animal under the conditions of the investigation

B. Materials to be tested

1. Solutions of fluorescent fractions (chromatographic) of the waxes, in selected concentrations in the appropriate vehicles
2. Solutions of benzopyrene (BP) or methylcholanthrene (MC) in the same vehicle
3. Vehicles alone
4. Solid solutions of BP or MC in the non-fluorescent fraction (chromatographic) of selected waxes

C. Species of animals to be used

1. Inbred mice for induction of skin cancer
2. Selected species, including mice, which are available from healthy stocks, for induction of cancer of small intestine or other internal organs

II. Biological testing (continued)

D. Experiments involving the induction of skin cancer

1. Tests to determine the relative potencies of liquid fractions of slack waxes which differ with respect to the variables shown in I.A. or I.C.
2. Subsequent tests to determine the relative potencies of liquid fractions, or solutions of fluorescent fractions of related samples of slack wax, intermediate scale waxes, and fully refined wax

E. Experiments involving the induction of intestinal tumors

1. Attempted duplication of published method of induction of intestinal tumors by solutions of MC in olive oil
2. Subsequent attempts to induce similar tumors by solutions of fluorescent fractions of waxes
3. Determination of relative potency to intestine of solid solutions of MC in non-fluorescent fractions of waxes

III. Application of analytical techniques from Project MC-1 to paraffinic oils and separated waxes

Kettering Laboratory
November 1, 1956

MEMORANDUM ON A MEANS OF APPRAISING THE POTENTIAL CANCEROGENIC HAZARD OF THE USE OF PETROLEUM WAXES UNDER CONDITIONS THAT MAY RESULT IN THEIR INTRODUCTION INTO HUMAN FOOD AND BEVERAGES

The question of the safety of the use of refined waxes on food containers was apparently raised in Rome this past summer. According to Dr. Arnold Lehman of the F.D.A., the potential problem was not discussed by Dr. Hueper in his formal paper. (It has since been referred to briefly, among many other sources of contamination of food, in an article in the Saturday Review of literature.) At the same time, the reports in the popular press are sufficient evidence that the subject was discussed informally by some members of the conference. In any event, it seems highly probable that the question will have to be answered eventually by the acquisition and publication of convincing experimental evidence.

On October 4, the following persons participated in an informal discussion of a suitable approach to the problem: Drs. Lehman, Nelson and Voss of the Food and Drugs Administration and Drs. Kehoe and Horton of the Kettering Laboratory. There was unanimous agreement that the somewhat conventional experiment of feeding test materials to rats over a period of two years is not particularly applicable. It was further agreed that the experimental approach to the testing of materials in terms of the responses of animals, must be or, at least, should be controlled in a positive answer by some experimental procedure in which a known carcinogenic hydrocarbon will produce malignant tumors of relevant type and location. In keeping with the sense of the foregoing discussion, and following careful consideration of the entire problem, we propose to investigate the carcinogenic potentialities of

selected materials by introducing them into the forestomach and small intestine of mice (see publications of Lorenz and Stewart of National Cancer Institute) after choosing a suitable solvent for the appropriate experimental material or fraction thereof. The use of positive controls, exposed in corresponding manner to methylcholanthrene in the same solvent, and negative controls, comparably exposed to the solvent alone, would form a necessary part of such a program. (Dr. Lehman and his associates indicated that they would be in substantial agreement with this approach. Dr. Lehman suggested further that, since the methods for developing cancer of the skin from liquid solutions had been worked out, it might be expeditious to apply some of the solutions to the skin, at least in the preliminary phases of the program. The data from the skin, in combination with those from the gastro-enteric tract, would provide a much higher level of confidence in the interpretation of the results then would be possible if only one or the other of the tissues was involved.)

In considering the proper scope of such an investigation, the opinion was general that there is a lack of the data necessary to present a clear picture of the situation rather than an actual or imminent hazard to the public health. Hence, although a fairly detailed examination of the problem seems warranted, it should be carried out in a carefully considered manner and at a logical speed, rather than after the manner of an emergency.

In general, the problem arises out of the fact that refined waxes, as marketed, are faintly to strongly fluorescent under ultraviolet light. While not all fluorescent hydrocarbons are carcinogenic, the converse apparently is true. There is, for example, evidence that the carcinogens responsible for the development of scrotal cancer in wax pressmen are fluorescent.

Since the refined waxes derive from the distillates associated with these occupational skin cancers, the obvious question is raised, since the waxes still fluoresce, whether the carcinogens have been eliminated or to what extent their concentration has been reduced. A program aimed at a qualitative understanding of the composition of the carcinogens in the wax distillates and a quantitative measure of the desired decrease in their concentration during the refining processes seems to be called for.

Although API Research Project MC-1 has been directed primarily at cracked oils, the general principles and techniques developing in that work should be applicable to the wax problem. Biological testing of solutions of suitable fractions of the intermediates and final products in parallel with chemical research on the composition of the fluorescent components should provide the information needed for the long term answer to this problem.

This question concerns every oil company engaged in the production or distribution of petroleum waxes. Since the inclusion of even selected materials from each of these companies would quickly multiply the experimental effort beyond the scope warranted by the nature of the problem, it would seem appropriate to follow the mechanism for sampling used in Project MC-1 in

1949-50. The general boundaries of the investigation would be described by the advisory committee. Guided by this outline, the Kettering Laboratory should assume the responsibility for assembling the necessary confidential information from the individual producers and selecting a representative group of samples. The experience along this line and contacts already established should make this a fairly efficient process of arriving at the desired goal.

As to the general level of the overall effort, an annual expenditure in the neighborhood of $35,000 to $40,000 for about five years would produce the information needed in the most economical and satisfactory manner. It is doubtful in our mind that a higher rate of expenditure initially would be wise or necessary. It will probably be desirable to be able to indicate an early date for the initiation of the investigation. The staff of the Laboratory would be prepared to start the necessary groundwork for the sampling program at a moderate cost, as soon as the decision to proceed has been arrived at.

Robert A. Kehoe

Robert A. Kehoe, M. D.

October 11, 1956

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

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

CABLE ADDRESS: KETLAB, CINCINNATI
TELEPHONE: CAPITOL 1414

October 31, 1956

Members, Subcommittee on Carcinogenicity
Medical Advisory Committee
American Petroleum Institute

Gentlemen:

I am forwarding to you herewith a proposal of a program for the investigation of the paraffin waxes, with respect to the potential hazard of the induction of cancer, through their use on wrappers or containers for food for human consumption. This program is based upon our own judgement as to the needs of the situation, from the aspect of the public health, should the issue be raised in a serious manner, and upon our consideration of the information and views presented to us in a preliminary meeting with members of the Subcommittee on September 6 and in a more recent meeting on October 20th.

In your examination of the proposal stepwise, you will note our adherence to the sequence of experimental steps agreed upon in the meeting of October 20. No reference is made to the preliminary gathering of information on the available products and their usage by the appropriate agency of the API. At the same time, the participation of the staff of the Laboratory in the selection of the materials to be investigated is regarded as a necessity, partly because of the difficulties encountered in our early prosecution of the work on other petroleum products, partly because much, if not the bulk of the information on the processing of the waxes, will have to be obtained, to the extent that it has not been done previously, by ourselves on a confidential basis, and partly because the Laboratory does not undertake to investigate materials about which members of its staff do not have the fullest and most complete information that can be obtained.

No attempt has been made to lay down the precise details of the experimental procedures, in the manner that would be possible if we were planning to undertake a feeding experiment with a known material involving several levels of daily dosage or of concentration in the diet. Rather, in view of the unpredictability of the numbers and the precise types of materials (samples) to be tested, and in view of the fact that the experimental procedures (with the exception of applications upon the skin) are to be tested and, in some degree developed, in the course of the experimental work, the attempt is to outline

briefly the objectives and the philosophy of the experimental approach, and to indicate the character of the initial attempts to solve the problem at issue. The intent behind this general approach is that the staff will report its progress at appropriate intervals and will confer with the Subcommittee (or its designated representatives) concerning the further steps by which the significant questions will be answered.

It is recognized that so-called feeding experiments may be indicated. It is believed, however, that in the interest of economy of effort and expenditure as well as that of definition of purpose and experimental conditions, such experiments should be considered later, when they can be so designed as to have physiological and technical significance.

It seems probable that methods of biological investigation other than those referred to specifically, including other methods of introducing potentially carcinogenic materials into animals of various species, may turn out to be desirable. It is not believed that much effort should be expended in this direction, however, until the procedures which offer the greatest promise of positive results have been explored with some care.

The budget proposed for the conduct of this work during the first year ($35,000 to $40,000) is based, realistically, upon the actual work which can reasonably be done by the members of the staff of the Laboratory that will be assigned to this project, with such augmentation of technical assistance, as seems to be feasible in relation to the available facilities in space and equipment.

I trust that these items of information will be sufficient for your purposes.

Cordially yours,

Robert A Kehoe

Robert A. Kehoe, M. D.

RAK:mjg
CC: Dr. L. E. Curtis
Mr. D. V. Stroop

A PROGRAM FOR THE INVESTIGATION OF INTERMEDIATE AND REFINED WAXES

OBJECTIVES: Certain crude paraffinic distillates have been associated with the development of scrotal cancer in wax pressmen. By further refining (essentially deoiling and decolorization processes) the waxy components of these distillates are purified until they meet the specifications for their particular use.

The major objective of the proposed investigation is the determination by suitable biological tests of the stage in the refining process at which the concentration of the components of the paraffinic distillates responsible for their carcinogenic potency for the human skin has been reduced to a negligible level. A correlated and equally important goal will be the development of biological techniques which will yield some estimate of the relative cancer hazard incurred by human beings through the ingestion of these partially or fully refined waxes. Pertinent information on composition obtained in the course of the research on cracked oils and straight run distillates (API Research Project MC-1) will be applicable to the various waxes. Analytical techniques based on these findings will serve as a further check on the extent of the reduction in the concentration of carcinogens present in the crude distillates from which the waxes were derived.

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II. Biological testing

A. Criteria for selection of experimental conditions

1. Control animals subjected to the administration of vehicles alone, with no added carcinogens, should have a low, essentially negligible incidence of the cancer to be reproduced
2. Positive results should be obtainable if a known carcinogenic hydrocarbon is introduced into the animal under the conditions of the investigation

B. Materials to be tested

1. Solutions of fluorescent fractions (chromatographic) of the waxes, in selected concentrations in the appropriate vehicles
2. Solutions of benzopyrene (BP) or methylcholanthrene (MC) in the same vehicle
3. Vehicles alone
4. Solid solutions of BP or MC in the non-fluorescent fraction (chromatographic) of selected waxes

C. Species of animals to be used

1. Inbred mice for induction of skin cancer
2. Selected species, including mice, which are available from healthy stocks, for induction of cancer of small intestine or other internal organs

II. Biological testing (continued)

D. Experiments involving the induction of skin cancer

1. Tests to determine the relative potencies of liquid fractions of slack waxes which differ with respect to the variables shown in I.A. or I.C.

2. Subsequent tests to determine the relative potencies of liquid fractions, or solutions of fluorescent fractions of related samples of slack wax, intermediate scale waxes, and fully refined wax

E. Experiments involving the induction of intestinal tumors

1. Attempted duplication of published method of induction of intestinal tumors by solutions of MC in olive oil

2. Subsequent attempts to induce similar tumors by solutions of fluorescent fractions of waxes

3. Determination of relative potency to intestine of solid solutions of MC in non-fluorescent fractions of waxes

III. Application of analytical techniques from Project MC-1 to paraffinic oils and separated waxes

Kettering Laboratory
November 1, 1956

For Hueston

October 15, 1956

To the Subcommittee on Carcinogenicity
Medical Advisory Committee
American Petroleum Institute

Dr. R. E. Eckardt
Dr. C. H. Hine
Dr. E. K. Lindner
Dr. R. C. Mithoff
Dr. M. N. Newquist
Mr. A. C. Pabst
Dr. E. W. Adams

Gentlemen:

In response to a direct request, I am submitting herewith a memorandum for your consideration at the meeting of the Subcommittee in Chicago on October 20.

I am fully aware of the fact that this memorandum does not set forth the details of the proposed experimental approach to this problem. It is couched in general rather than specific terms for two reasons; one is concerned with an expression of the underlying purpose of solving this problem rather than that of surrounding it with insulation according to a conventional formula; the other arises from the fact that the procedure of the Laboratory calls for the formal examination of the problem and the preparation of a definitive proposal by the division heads.

Serious thought has gone into the opinions expressed in the memorandum, but there has not been time for formal action, since our thinking has been crystallized by discussion only within the past few days (after an informal discussion with representatives of the Food and Drug Administration.) A more definite proposal will be presented on the 20th, and a more precise estimate of the costs will be made at that time. It is believed, however, that the memorandum will serve a useful purpose in preparation for the consideration of this matter at the Chicago meeting. It is regarded as certain, moreover, that the scope and the details of both procedure and expenditure will have to be determined initially and subsequently through the joint efforts of the Laboratory and the Committee.

Cordially yours,

Robert A. Kehoe, M. D.

RAK ef
Enc. (Memorandum mailed to you on October 11.)

meeting 10-20-56

MEMORANDUM ON A MEANS OF APPRAISING THE POTENTIAL CANCEROGENIC HAZARD OF THE USE OF PETROLEUM WAXES UNDER CONDITIONS THAT MAY RESULT IN THEIR INTRODUCTION INTO HUMAN FOOD AND BEVERAGES

The question of the safety of the use of refined waxes on food containers was apparently raised in Rome this past summer. According to Dr. Arnold Lehman of the F.D.A., the potential problem was not discussed by Dr. Hueper in his formal paper. (It has since been referred to briefly, among many other sources of contamination of food, in an article in the Saturday Review of Literature.) At the same time, the reports in the popular press are sufficient evidence that the subject was discussed informally by some members of the conference. In any event, it seems highly probable that the question will have to be answered eventually by the acquisition and publication of convincing experimental evidence.

On October 4, the following persons participated in an informal discussion of a suitable approach to the problem: Drs. Lehman, Nelson and Voss of the Food and Drugs Administration and Drs. Kehoe and Horton of the Kettering Laboratory. There was unanimous agreement that the somewhat conventional experiment of feeding test materials to rats over a period of two years is not particularly applicable. It was further agreed that the experimental approach to the testing of materials in terms of the responses of animals, must be or, at least, should be controlled in a positive answer by some experimental procedure in which a known carcinogenic hydrocarbon will produce malignant tumors of relevant type and location. In keeping with the sense of the foregoing discussion, and following careful consideration of the entire problem, we propose to investigate the carcinogenic potentialities of

selected materials by introducing them into the forestomach and small intestine of mice (see publications of Lorenz and Stewart of National Cancer Institute) after choosing a suitable solvent for the appropriate experimental material or fraction thereof. The use of positive controls, exposed in corresponding manner to methylcholanthrene in the same solvent, and negative controls, comparably exposed to the solvent alone, would form a necessary part of such a program. (Dr. Lehman and his associates indicated that they would be in substantial agreement with this approach. Dr. Lehman suggested further that, since the methods for developing cancer of the skin from liquid solutions had been worked out, it might be expeditious to apply some of the solutions to the skin, at least in the preliminary phases of the program. The data from the skin, in combination with those from the gastro-enteric tract, would provide a much higher level of confidence in the interpretation of the results then would be possible if only one or the other of the tissues was involved.)

In considering the proper scope of such an investigation, the opinion was general that there is a lack of the data necessary to present a clear picture of the situation rather than an actual or imminent hazard to the public health. Hence, although a fairly detailed examination of the problem seems warranted, it should be carried out in a carefully considered manner and at a logical speed, rather than after the manner of an emergency.

In general, the problem arises out of the fact that refined waxes, as marketed, are faintly to strongly fluorescent under ultraviolet light. While not all fluorescent hydrocarbons are carcinogenic, the converse apparently is true. There is, for example, evidence that the carcinogens responsible for the development of scrotal cancer in wax pressmen are fluorescent.

Since the refined waxes derive from the distillates associated with these occupational skin cancers, the obvious question is raised, since the waxes still fluoresce, whether the carcinogens have been eliminated or to what extent their concentration has been reduced. A program aimed at a qualitative understanding of the composition of the carcinogens in the wax distillates and a quantitative measure of the desired decrease in their concentration during the refining processes seems to be called for.

Although API Research Project MC-1 has been directed primarily at cracked oils, the general principles and techniques developing in that work should be applicable to the wax problem. Biological testing of solutions of suitable fractions of the intermediates and final products in parallel with chemical research on the composition of the fluorescent components should provide the information needed for the long term answer to this problem.

This question concerns every oil company engaged in the production or distribution of petroleum waxes. Since the inclusion of even selected materials from each of these companies would quickly multiply the experimental effort beyond the scope warranted by the nature of the problem, it would seem appropriate to follow the mechanism for sampling used in Project MC-1 in

1949-50. The general boundaries of the investigation would be described by the advisory committee. Guided by this outline, the Kettering Laboratory should assume the responsibility for assembling the necessary confidential information from the individual producers and selecting a representative group of samples. The experience along this line and contacts already established should make this a fairly efficient process of arriving at the desired goal.

As to the general level of the overall effort, an annual expenditure in the neighborhood of $35,000 to $40,000 for about five years would produce the information needed. in the most economical and satisfactory manner. It is doubtful in our mind that a higher rate of expenditure initially would be wise or necessary. It will probably be desirable to be able to indicate an early date for the initiation of the investigation. The staff of the Laboratory would be prepared to start the necessary groundwork for the sampling program at a moderate cost, as soon as the decision to proceed has been arrived at.

Robert A. Kehoe

Robert A. Kehoe, M. D.

October 11, 1956

COPY

Esso Research and Engineering Company
P. O. Box 121, Linden, New Jersey

September 10, 1956

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

Dear Doctor Kehoe:

As a follow-up to the recent meeting of the Subcommittee on Carcinogenicity, I am sending you, for your own information, a copy of a memorandum which I have distributed to the doctors in the affiliates of Standard Oil Company (New Jersey). Assuming that I can get approval, I also plan to send this to all the members of the Medical Advisory Committee.

I believe that it summarizes most of the valid information available on the wax situation. It is, of course, possible that additional information is available in the literature, but I am not sure that it has any great validity in the situation which is under consideration.

Very truly yours,

/s/ R. E. Eckardt
R. E. Eckardt, M. D.

REE:cjh

Attach. - MEDICAL RESEARCH MEMORANDUM ON PARAFFIN (WAX) TOXICITY
R. E. Eckardt, M. D. (September 4, 1956)

MEDICAL RESEARCH MEMORANDUM
ON
PARAFFIN (WAX) TOXICITY

On August 21, 1956, THE NEW YORK TIMES contained the attached article reporting a recent symposium held in Rome by a Committee of the International Union Against Cancer. In addition, TIME MAGAZINE of August 27, 1956, also reported on this Rome meeting.

Of particular importance to the petroleum industry is the suggestion that paraffin used on milk cartons had produced cancer in man and experimental animals. Paraffins have been extensively studied by the Medical Research Division of Esso Research and Engineering Company, working cooperatively with the Institute of Industrial Medicine of New York University-Bellevue Medical Center. The facts of the situation clearly show that paraffins (waxes) used to coat milk cartons have never produced cancer in man or experimental animals.

The facts in the situation are as follows:

The first step in the manufacture of wax from petroleum is to remove the wax from a distillate fraction of crude oil. This is done either by plate and frame filter pressing or by solvent dewaxing. Cancer of the skin has been produced in men exposed intimately for ten years or more to the crude wax separated from the oil by the plate and frame pressing. Such cancers have never been found in the solvent dewaxing process. The crude wax obtained by plate and frame pressing contains as much as 20% - 30% of oil. This crude wax, known in the trade as slack wax, when painted three times a week on the shaved skin of mice, did produce an occasional cancer in these mice. Thus, of 11 such slack waxes painted on 330 animals, 7 cancers were produced after approximately one and one-half years of such painting. Thus, both the human data and the animal data show that this crude slack wax can produce cancer of the skin.

This crude slack wax cannot be used on milk cartons because it is too soft, and has a yellow color and oily odor which would be found unacceptable to the consumer. Consequently, the crude wax is purified further. The first step in the purification of a pressed slack wax is sweating. In this process, the crude wax is heated to just below its melting point, which causes the oil in the wax to "sweat" out. This sweating process reduces the oil content of the wax from 20% - 30% to about 1% - 2%. Extensive studies of workmen exposed to the sweated wax revealed that no cancers had been produced in these men.

This sweated wax is further refined either by acid treating and bauxite filtering or by hydrogenation, to produce a white refined wax which has an oil content of about 0.05% - 0.2%. Men exposed to this refined wax have likewise been thoroughly examined, and have never developed skin cancer as a result of their exposure. In addition, five refined waxes have been painted on 150 mice for as long as 477 days without the production of any cancers.

This data on both humans and animals very clearly shows, therefore, that although the crude wax containing 20% - 30% of oil has produced cancer in

both man and animals the refined wax - that wax which gets onto milk cartons - containing 0.05% - 0.2%oil, has produced cancer neither in man nor in experimental animals. The data shows that the cancer-producing agent contained in the original crude wax must have been present in the oil, and that as this oil was removed from the wax by the usual refining steps, so was the carcinogenic property of the wax eliminated. As further evidence of this fact, when the aromatics (contained in the oil) of eight slack waxes were painted on 240 animals, 26 cancers were produced. This compares with 7 cancers in 330 animals painted with 11 slack waxes and no cancers in 150 animals painted with refined waxes. This data shows that as the carcinogenic agent is removed from the slack wax, it is concentrated in that portion removed from the wax (in the oil), and since the oil does not get on the milk carton, the milk carton is coated with a material which has never caused cancer in man or in experimental animals.

In addition, in the United States, paraffin for use on food containers must meet the definition of paraffin given in the U. S. Pharmacopoeia. Included in this definition is an acid test, the USP acid test for paraffin, which, in essence is a repetition of the acid treatment to which the wax is subjected during refining. This test is a measure of the oil content of the wax, and when the wax meets this specification it is of such a sufficiently high degree of purity, and low oil content, that it can be used for medicinal purposes.

Finally, the author of this memo discussed this situation with Dr. W. C. Hueper at the recent Gordon Research Conference on Cancer held in New London, N. H. Dr. Hueper said that no data, manuscripts, or press releases were given to reporters in Rome, and that he did not talk with reporters so that the information in THE NEW YORK TIMES article was not based on factual releases of the Rome Conference. He indicated that paraffin which meets the USP specification, and which is the paraffin used on milk cartons, would constitute no hazard, although he pointed out that in certain foreign countries, no standard of identity or purity, such as is contained in the U. S. Pharmacopoeia, has been established for paraffins used on milk cartons.

An additional piece of interesting data has just been made known. Certain plastics, such as cellophane, nylon, paper, polyvinylchloride, polymethyl methacrylate, polystyrene, teflon, and even silver foil and vitalliumfoil, when implanted subcutaneously in rats produce malignant tumors (Sarcomas). Paraffin pellets when so implanted have produced no such malignant tumors, which is additional evidence for the non-carcinogenicity of paraffin.

The second point of interest to the petroleum industry is the report that several detergents had co-carcinogenic and promoting effects. This may have been based on observations that dodecyl benzene, a detergent alkylate, has such co-carcinogenic or promoting properties in animals (mice). However, the detergent is formed by sulfonating the alkylate and mouse tests of the sulfonate (as well as commercial detergents) by Dr. Shubik of Chicago Medical School, have shown that the sulfonation step destroys the co-carcinogenic or promoting action of the alkylate.

It thus appears that the symposium in Rome was provided inadequate or incomplete data on which to base its report, or that newspaper or other public press reports of the Rome proceedings were based on reportorial fancy rather than facts provided by the symposium.

R. E. ECKARDT/cjh
Director, Medical Research Division
September 4, 1956.

KETTERING LABORATORY

SPONSOR: **American Petroleum Institute Paraffins - ESTIMATE**

DATE: 10-11-1956

DIRECT CHARGES			
Supplies	2000.00		
Animals	560.00		
Animal Care	288.00		
Histopath. Prep.	1700.00		
Travel	1500.00		
TOTAL DIRECT CHARGES	6048.00		
DIRECT SALARIES			
Toxicology - Gen'l.			
- C Div.			
- H Div.	14,498.80		
- S Div.			
- T Div.			
- W Div.			
Analytical Laboratory			
Pathology	152.00		
Epidemiology			
Clinic			
Dermatology			
Direction and Editing	100.00		
Engineering			
Library			
Statistics	300.00		
Computing			
Shop			
Duplicating and Drafting	18.00		
Other			
TOTAL DIRECT SALARIES	15,068.80		
OVERHEAD 120 %	18,058.56		
SUMMARY			
Direct Charges	6,048.00		
Direct Salaries	15,068.80		
Overhead	18,058.56		
TOTAL EXPENDITURES	39,175.36		

AMERICAN PETROLEUM INSTITUTE

PARAFFIN PROPOSAL

10-11-1956

SALARIES

Investigator (W.H.) - 15% for 1 year	$1976.40
Chemist - full time	7000.00
Chemical Technician - full time	3000.00
Biologist - (MJG) - 20% for one year	1022.40
Biological Technician - 20% for one year	720.00
Secretary - 1/4 time for one year	780.00
Editing	100.00
Statistician	300.00
Multilithing - 2 days	18.00
Pathology - Reading of Slides and Reporting	152.00
	15,068.80
Supplies	2,000.00
Animals - 800 mice	560.00
Animal Care - 800 mice	288.00
Pathology - Gross on 400 mice 1200.00 Micro on 200 mice (full) 400.00 Micro on 200 mice (skins) 100.00	1,700.00
OVERHEAD - 120% of Total Salaries	18,058.56
TOTAL ESTIMATE	39,175.36

PROPOSAL FOR STUDIES ON MICROCRYSTALLINE WAX

The following is a proposed outline of the toxicity studies for microcrystalline wax:

I. Acute Oral Toxicity

A. Determination of the LD_{50} in albino rats.

It is anticipated that the microcrystalline wax will have a very low oral toxicity; therefore, five rats will be administered the highest practical dose. In addition to the test compound, five rats will be administered the highest practical dose of U.S.P. paraffin.

It is estimated that the cost of determining the oral toxicity in the 10 rats will be approximately $100.00. In the event that toxicity is exhibited by the rats receiving the microcrystalline wax, three lower dosage levels of five rats each will be initiated, in order to determine an LD_{50}. The additional three levels would increase the estimated cost to approximately $325.00.

B. Determination of the LD_{50} in dogs.

Four dogs will be administered the highest practical dose of microcrystalline wax and four dogs will be administered the equivalent dosage of U.S.P. paraffin.

It is estimated that the cost for the eight dogs will be approximately $350.00. In the event that toxicity is exhibited by the dogs receiving the test compound, three additional levels of four dogs each will be initiated. The addition of the three extra levels will increase the cost to approximately $925.00.

II. Two-Year Chronic Feeding - Albino Rats

A. Five groups of rats, designated as two control groups and three experimental groups, will be initiated as follows:

Group 1 - Control, 25 males and 25 females.

Group 2-- Positive control, 25 males and 25 females to receive U.S.P. paraffin at the same dosage level as Group 5.

Group 3 - 25 males and 25 females on a low dietary level of microcrystalline wax.

Group 4 - 25 males and 25 females on an intermediate dietary level of microcrystalline wax.

Group 5 - 25 males and 25 females on a high dietary level of microcrystalline wax.

B. All animals will be individually housed and body weight and food consumption will be recorded at weekly intervals. In addition, records will be kept of the general physical condition and behavior of each animal. Fresh diets will be prepared weekly.

C. Gross autopsies will be performed on five males and five females from each group at 12 months, and on all surviving animals at 24 months. In addition, autopsies will be performed on all animals which die during the course of the study. Organ weights of liver and kidneys will be determined from each animal sacrificed. Thirteen tissues will be preserved from five males and five females from each level. The following tissues from three males and three females per group will be submitted for histological examination: lung, liver, adrenal, kidney, stomach, large and small intestine, bladder, and gonads.

D. The estimated cost for this portion of the study will be approximately $31.700.00.

III. Twelve-Month Chronic Oral Administration - Male and Female Dogs

A. Five groups of dogs, designated as two control groups and three experimental groups, will be initiated as follows:

Group 1 - Control, two males and one female.

Group 2 - Positive control, two males and one female to receive U.S.P. paraffin at the same dosage level as Group 5.

Group 3 - Two males and one female on low dietary level of microcrystalline wax.

Group 4 - Two males and one female on an intermediate dietary level of microcrystalline wax.

Group 5 - Two males and one female on a high dietary level.

B. All animals will be individually housed. Records of individual compound consumption and body weights will be kept. In addition, records of the general physical condition and behavior of each animal will be kept at weekly intervals. The compound will be administered by capsule five days per week.

C. The following clinical studies will be run initially and at four, eight, and 12 months: complete blood counts; sedimentation rates; hematocrits; blood-urea-nitrogen determinations; bromsulphalein liver function tests, and urine analyses. Gross autopsies will be performed on each animal sacrificed and routine organ weights will be determined. Thirteen tissues will be preserved from each animal sacrificed and the following tissues will be submitted for histological examination: lung, liver, adrenal, kidney, stomach, large and small intestine, urinary bladder, and gonads.

D. The cost for this portion of the study will be approximately $15,400.00.

The cost estimates given above are based on past experience and the assumption that no unusual difficulty will be encountered in the administering or feeding of the microcrystalline wax. Should additional studies be included during the progress of the investigations, the costs would be determined on the standard laboratory procedures but no estimate is possible at this time.

ESSO RESEARCH AND ENGINEERING COMPANY

(FORMERLY STANDARD OIL DEVELOPMENT COMPANY)

P. O. BOX 121, LINDEN, N. J.

MEDICAL RESEARCH DIVISION
ROBERT E. ECKARDT, PH.D., M.D.
DIRECTOR
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HEAD INDUSTRIAL HYGIENIST
HORACE W. GERARDE, PH.D., M.D.
HEAD TOXICOLOGIST
BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

August 29, 1956

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

Dear Dr. Kehoe:

reprint file

The attached news article from THE NEW YORK TIMES, of August 21, 1956, may not have been brought to your attention. A subsequent article in the August, 27th issue of TIME magazine also suggests that milk carton paraffins are carcinogenic.

I would greatly appreciate it if you would give some thought to this situation and be prepared to advise the Subcommittee on Carcinogenicity as to what action and/or statement should be made by the API in an attempt to refute that which we believe is a misstatement. This situation is somewhat acute and critical as a reaction has already begun to be felt by milk dealers who market their products in waxed cartons.

In addition, the section dealing with detergents might require consideration by the Subcommittee at its meeting in Chicago.

Your serious consideration of this most pressing problem would be very greatly appreciated.

Very truly yours,

R. E. ECKARDT, M. D.

REE:eh
cc - Dr. W. A. Horton
Attach. - Article from THE NEW YORK TIMES, August 21, 1956.
Cancer is Traced to Food Additives.

COPY
8/29/56 (Original to Dr. Horton
at Detroit, Michigan)

Chicago trip

ESSO RESEARCH AND ENGINEERING COMPANY

P.O. Box 121, Linden, N. J.

Medical Research Division

August 20, 1956

Messrs: E. W. Adams
C. H. Hine
E. K. Linder
R. C. Mithoff
M. N. Newquist
A. C. Pabst

Gentlemen:

Having talked with Charlie Hine in New Hampshire, it now appears that the best time for the Subcommittee meeting is Thursday, September 6, in Chicago.

I will attempt to get reservations at the Conrad Hilton Hotel. The meeting will start at 9:00 A.M. in my room, and the Kettering Lab group will join us at 10:00 A.M.

It is my understanding that Dr. Hine is calling a meeting of the C9C12 Subcommmittee for Wednesday, September 5, which will also be held in the Conrad Hilton Hotel. This will make it possible for members of both subcommittees to attend both meetings and will be a great convenience to those from the West Coast who find it difficult to get in and out of Cincinnati.

I trust that you will be able to make it and I am looking forward to seeing you on the 6th.

Sincerely yours,

R. E. Eckardt (s)

R. E. ECKARDT, M. D.

REE:cjh

cc - Messrs: L. E. Curtis
A. W. Horton
R. A. Kehoe
J. J. Phair
D. V. Stroop

ESSO RESEARCH AND ENGINEERING COMPANY

(FORMERLY STANDARD OIL DEVELOPMENT COMPANY)

P. O. Box 121, Linden, N. J.

MEDICAL RESEARCH DIVISION

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HORACE W. GERARDE, PH.D., M.D.
HEAD TOXICOLOGIST

BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

August 6, 1956

Messrs: E. W. Adams
C. H. Hine
E. K. Linder
R. C. Mithoff
M. N. Newquist
A. C. Pabst

Gentlemen:

I have been informed that neither Dr. Kehoe nor Dr. Horton will be available during the month of August for a meeting of the subcommittee. Ergo, no meeting in August.

Now Charlie Hine has proposed the date of September 14, in order to tie in the meeting of the Subcommittee on Carcinogenicity with the meeting of the C_9C_{12} Subcommittee on September 15. He does not, however, make it clear whether he wishes the subcommittee to meet in Dallas, Texas; Cincinnati, Ohio or Timbuktu, so I am unable to determine where he proposes the meeting to be held. I trust that he will pick this up in his copy of this letter and inform each of you where he suggests that the meeting be held.

It has been my understanding in the past, that the subcommittee always meets in Cincinnati for the convenience of the Kettering group in order not to take that group away from their laboratories. In this way, we can hold a two-day meeting of the subcommittee and yet only require one-half day, plus or minus, of the Kettering group's time.

It would appear to me that it would be quite a trip from a meeting in Cincinnati on the 14th to Dallas on the 15th, but if this is the wish of those members of the subcommittee which must attend both meetings, I am willing to attempt it. However, I do not believe that it is feasible for the Kettering Lab group to meet in Dallas and I would appreciate it if they would so express themselves in reply to this inquiry.

Very truly yours,

R. E. Eckardt

R. E. ECKARDT, M. D.

REE:cjh

cc - Messrs: L. E. Curtis
W. A. Horton
R. A. Kehoe
J. J. Phair
D. V. Stroop

ESSO RESEARCH AND ENGINEERING COMPANY

(FORMERLY STANDARD OIL DEVELOPMENT COMPANY)

P. O. BOX 51, LINDEN, N. J.

MEDICAL RESEARCH DIVISION
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HORACE W. GERARDE, PH.D., M.D.
HEAD TOXICOLOGIST
BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

July 30, 1956

Messrs: E. W. Adams
C. H. Hine
E. K. Linder
R. C. Mithoff
H. H. Newquist
A. C. Pabst

Gentlemen:

At the present time, I have heard from five members of the subcommittee, pressing their desires for a meeting of the subcommittee. The vote looks somewhat as follows:

September 4	September 7 and 8	September 10
2 - no	1 - questionable	2 - no
2 - yes	4 - yes	3 - yes
1 - questionable		

Dr. Kehoe has indicated September 7 or 8 would be satisfactory for him, but that September 4 or 10 would be less convenient.

In the meantime, Dr. Hine has suggested that we meet sometime in relationship to the Gordon Research Conference in New Hampshire. I presume he refers to the Gordon Research Conference on Toxicology, which is to be held the week of August 13-17. This would suggest that we meet sometime in the early part of the week of August 20 or the latter part of the week of August 6. For my own wishes, I would prefer the 20th or the 21st to the 10th or 11th. I, personally, cannot make the meeting during the week of the 27th. I would, therefore, appreciate hearing from each of you what your preferences would be for holding the meeting of the Subcommittee on Carcinogencity in Cincinnati, on August 20 or August 10 or 11, as opposed to the presently selected date of September 7 or 8. Since time isshort, I would appreciate it if each of you would let me have this information by return mail so that we can make plans for the subcommittee meeting.

By the way of general information, we are all in favor of Dr. Horton presenting his manuscript to the American Chemical Society in the fall and you all out-voted me in that you wished to continue the support of the epidemiological work until January 1, 1957.

By carbon copy of this letter to Dr. Curtis, I am so informing him of the decision of the subcommittee in order that they immediately proceed with the obtaining of the opinion of the total Medical Advisory Committee and instructing the Kettering Laboratory in accordance with the questions of the MAC.

I am looking forward to seeing you all again soon.

Very truly yours,

R. E. Eckardt

R. E. ECKARDT, M. D.

REE:cjh
cc - L. E. Curtis
A. W. Horton ✓
R. A. Kehoe
D. V. Stroop

July 24, 1956

Dr. Robert E. Eckardt
Esso Research & Engineering Company
P. O. Box 121
Linden, N. J.

Dear Dr. Eckardt:

I will be leaving for a trip to the Middle East on September 12th, returning October 4th. I understand that Dr. L.E. Curtis will leave for the Middle East and points in the Far East on September 7th.

I could attend a meeting on September 4th and possibly Dr. Curtis could attend a meeting on that date, although he has a meeting to attend in New York City on either the 5th or 6th of September.

I could also attend a meeting the last week of August if you so decided.

The 4th of September may not be a good date since it would cut in on the Labor Day week-end for those who had to travel a long distance.

My next choice would be Saturday, September 8th.

Very truly yours,

M. N. NEWQUIST

M. N. NEWQUIST, M. D.

MNN:RMS

Messrs. L.E. Curtis
A. W. Horton
R. A. Kehoe
J. J. Phair
D. V. Stroop

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HEAD TOXICOLOGIST

BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

June 21, 1956

Messrs.: E. W. Adams R. C. Mitoff
C. E. Kine M. H. Newquist
E. K. Linder A. C. Pabst

Dear Sirs:

Dr. Mitoff has proposed that our subcommittee hold its next meeting on either September 4, 7, 8, or 10. I would appreciate hearing from each of you, which of these dates would be most satisfactory for you. The purpose of holding the meeting on one of these four dates is so that Dr. Curtis can join the meeting of the subcommittee.

Very truly yours,

R. E. ECKARDT, M. D.

REE:ejh
cc - Messrs.: L. E. Curtis J. J. Phair
A. W. Horton ✓ D. V. Streep
R. A. Kehoe

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

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

CABLE ADDRESS: KETLAB, CINCINNATI
TELEPHONE: CAPITOL 1414

June 14, 1956

Dr. Robert E. Eckardt
Medical Research Division
Esso Research and Engineering Company
P. O. Box 151
Linden, New Jersey

Dear Doctor Eckardt:

Attached is a copy of the manuscript of a paper we propose to present as part of the Symposium on Polycyclic Hydrocarbons at the national meeting of the American Chemical Society in September. The chairman of the symposium, Dr. H. Pines of Northwestern University, has kindly agreed to an extension of the deadline for receipt of the manuscript, which was officially May 25.

It is the practice in the Petroleum Division of the American Chemical Society to distribute preprints of symposia a couple weeks before the meetings. Hence, we shall appreciate very much anything you are able to do to expedite the processing of this paper.

With best personal regards,

Sincerely yours,

A. Wesley Horton

AWH:mjg
CC: Dr. E. W. Adams
Dr. L. C. Beard, Jr.
Dr. C. H. Hine
Dr. R. C. Mithoff
Dr. M. N. Newquist
Mr. A. C. Pabst
Mr. D. V. Stroop
Dr. R. A. Kehoe

ESSO RESEARCH AND ENGINEERING COMPANY

(FORMERLY STANDARD OIL DEVELOPMENT COMPANY)

P. O. BOX 121, LINDEN, N. J.

MEDICAL RESEARCH DIVISION
ROBERT E. ECKARDT, PH.D., M.D.
DIRECTOR
NATHAN V. HENDRICKS, CH.E.
HEAD INDUSTRIAL HYGIENIST
HORACE W. GERARDE, PH.D., M.D.
HEAD TOXICOLOGIST
BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

February 20, 1956

Messrs. E. W. Adams
C. H. Hine
E. K. Linder
R. C. Mithoff
M. N. Newquist
A. C. Pabst

Gentlemen:

In response to my letter of February 9, 1956, I have heard from every member of the Subcommittee on Carcinogenicity, except one, concerning a meeting of this Subcommittee for some time in March or April. Furthermore, I have heard from the Kettering Laboratory and it has been indicated to me that Dr. Kehoe would be unable to attend the meeting on April 20, 1956 in Philadelphia. In view of this, I propose a meeting of the Subcommittee on Carcinogenicity for Friday, March 23, in Cincinnati to begin at 9:00 a.m. in my room at the Hotel Terrace Plaza, and to be continued at the Kettering Laboratory at about 10:30 or 11:00 the same day. I would suggest that the Subcommittee members plan to stay overnight in Cincinnati on Friday, March 23, and that they meet again on Saturday morning, March 24, in order to frame its report to the Medical Advisory Committee for the MAC's meeting in April.

Very truly yours,

R. E. ECKARDT, M. D.

REE:mak

cc: Mr. D. W. Streep
Dr. A. W. Korten ✓
Dr. R. A. Kehoe
Dr. J. J. Phair
Dr. L. G. Beard, Jr.

THE TEXAS COMPANY
135 EAST 42ND STREET
NEW YORK 17, N. Y.

M. N. NEWQUIST, M. D.
MEDICAL DIRECTOR

February 24, 1956

Dr. R. E. Eckardt
Esso Research & Engineering Company
P. O. Box 121
Linden, N. J.

Dear Dr. Eckardt:

In connection with your letter of February 20, 1956, I plan on attending the meeting of the Subcommittee on Carcinogenicity in Cincinnati on March 23rd and 24th.

Very truly yours,

M. N. NEWQUIST, M. D.

MNN:RMS

cc: Mr. D. V. Stroop
Mr. A. W. Horton
Dr. R. A. Kehoe
Dr. J. J. Phair
Dr. L. C. Beard, Jr.

Call Rhair's secy and ask about his schedule - 19th or 20th available

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BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

February 9, 1956

Messrs. E. W. Adams
L. C. Beard, Jr.
C. H. Hine
E. K. Linder
M. M. Marisic
R. C. Mithoff
M. N. Newquist
A. C. Pabst

Gentlemen:

It has been suggested that we hold a meeting of the Subcommittee on Carcinogenicity in Cincinnati on March 22 or March 23. In particular, this has been done to accommodate Dr. Linder who will be returning from a visit to the west coast at that time. I realize that this is close to April 21 when the Industrial Health Conference will be held in Philadelphia, so that it may be that you would prefer to have a meeting of the Subcommittee immediately preceding the Industrial Health Conference. Then Dr. Hine will not have to make two trips to the east. As a tentative suggestion I would propose an all-day meeting of the Subcommittee on Friday, April 20, 1956, if this appears preferable to the March 22 or 23 date. I would be interested in hearing from each of you, by return mail if possible, which of the two dates are best for you and any other possible dates if neither of these are good.

Very truly yours,

Mar 23

R. E. ECKARDT, M. D.

REE:mak

Out
Mar 20, 21, 22

23: OK
OK for Phair

Apr. 20

cc: Mr. D. V. Stroop
Dr. A. W. Norton
Dr. R. A. Kehoe
Dr. J. J. Phair

23

24th Sbr
30 Rockefeller Plaza
Library 10 AM
Feb 23

Manuscript on Acceleration will be ready and distributed prior to meeting
Westfield 2-7939 M

Meeting 4-25-55

EXHIBIT A

TO MINUTES OF MEETING OF MEDICAL ADVISORY COMMITTEE
April 25, 1955

REPORT OF THE SUBCOMMITTEE ON CARCINOGENICITY
Robert E. Eckardt, M. D., Chairman

I. Status of Publications

The manuscript on the method of determining benzpyrene is published. A slight modification of the method, which is attached as Appendix A, will be attached to reprints of this publication.

The manuscript on Carcinogenesis of the Skin was returned to Kettering Laboratory with suggestions for condensation of portions of the paper, and expansion of the introduction so it will have more meaning to cancer research workers. This expansion of the introduction and other modifications is attached as Appendix B.

II. Status of the Biological and Chemical Work

The interim report of the Laboratory is attached as Appendix C.

The original concept that petroleum products in the boiling range of 450-650°F or 700°F all contained significant quantities of accelerators now appears untenable. Rather it appears that in this range, there are variations in accelerator content which the laboratory is now in the process of working out. It is felt by the laboratory that this is important because a comparison of mouse data with available human data, suggests to the laboratory that accelerators may have significance in human skin carcinogenesis. This may be even more important in the petroleum industry than the coal tar industry.

Work to date suggests that petroleum cuts boiling in the range 625-650°F may be low in their accelerator content. On the other hand, above 650°F there appears to be another surge of accelerators.

Present work also suggests that alkyl naphthalenes are very potent accelerators, far more so than straight chain paraffins. Furthermore, they may not be as easily reduced in their activity by dilution as the straight chain paraffins.

Washing experiments suggest there is no advantage, and possibly a distinct disadvantage to using a petroleum material as a rinse prior to washing.

III. Future Chemical and Biological Work

About 55% of the effort of the laboratory in this direction will be in chasing down the nature of the carcinogens in the 700-725-750° F boiling range. To date 3 classes of carcinogens have been identified: (1) Benzpyrene types, (2) Types which form an adduct with maleic anhydride, presumably benzanthracenes, and (3) the as yet unidentified types in the 700-725-750° F range.

About 35% of the effort of the laboratory in this direction will be devoted to separating and characterizing the properties of accelerators. For this, boiling range, gravity, refractive index and aniline point have been

found to be useful tools. Liquid thermal diffusion as another useful tool will be investigated.

To date four types of accelerators are known: (1) straight chain paraffins, (2) Alkyl benzenes, (3) Alkyl naphthenes and (4) Alkyl naphthalenes. It appears that there is a chain length in each type which gives optimum accelerating properties. Further work on the definition of optimum chain length is planned.

From what has been said, it is evident that accelerators are major components of petroleum. In contrast, carcinogens constitute only minor components.

IV. Epidemiology

A progress report by Dr. Phair is attached as Appendix D.

500 new cases have been reported, bringing the total to 1800. The data on all 1800 of these are now being transferred from the previous manual sort cards to electronic sort cards. It is anticipated that this transfer, and initial correlations will be available by the next meeting of the Medical Advisory Committee. It is possible that preliminary incidence figures will also be available at that time.

The medical directors are again encouraged by the subcommittee to continue and extend whenever possible, their reporting of cases to Dr. Phair.

V. Budget

The budget for July 1, 1955 to June 30, 1956 is $65,000, to be expended as follows:

Biological Work	$20,000
Technical Work	32,250
Epidemiological Work	12,750

The subcommittee has requested of the Kettering Laboratory that a complete status report of the work be prepared in advance of the next Medical Advisory Committee Meeting. This status report should include significant conclusions of the work to date, with supporting data, grouped in accordance to important individual conclusions. In addition, a brief outline of future objectives should be included.

Recommendation:

The Subcommittee recommends that this work be continued with a budget of $58,500 for the period July 1, 1956 to June 30, 1957. Of this budget, from $15,000 to $20,000 shall be expended in the epidemiological work.

April 25, 1955

APPENDIX A

MODIFICATION OF METHOD DESCRIBED ON PAGE 252 OF THE REPRINT FROM ANALYTICAL CHEMISTRY, VOLUME 27, PAGE 248 TO 253, FEBRUARY 1955

Certain materials failed to give qualitatively satisfactory difference spectra by the routine method of analysis (see page 252). Amongst these are crude petroleum or shale oil and fractions of coal tar or cracked petroleum relatively rich in anthracenes. A substantial removal of the interfering substances from the sample may be accomplished by the action of concentrated sulfuric acid.

A 200 mg. sample is dissolved in 100 ml. of C.P. thiophene free benzene and shaken vigorously with 100 ml. of concentrated H_2SO_4 in a separatory funnel at 25-28°C. The contents of the funnel are then allowed to stand for ten minutes, during which time separation of layers should have occurred. The H_2SO_4 layer is allowed to run out over 500 g. of cracked ice. agitated by a glass stirring rod. The aqueous acid is then extracted by 100 ml. of benzene. The aqueous layer and any interfacial scums are then discarded (these scums will commonly constitute a volume of 5-10 ml. and contain approximately 5% of the benzopyrene). The benzene solution is now washed with 200 ml. of 5% NaOH in water, and again the aqueous layer and interfacial scums are discarded, with similar losses.

The benzene solution is now evaporated down to a volume of approximately 5 ml. and diluted with 5 ml. of isooctane. The resulting solution is then treated by the usual analytical process. The percent benzopyrene indicated may then appropriately be adjusted by the addition of 15% of the answer obtained.

Appendix B

CARCINOGENESIS OF THE SKIN. A reexamination of Basic Experimental Methods, and the Use of Reference Standards in Expressing the Relative Potencies of Complex Tars and Oils!

by A. Wesley Horton and Dorothy Templeton Denman

(Kettering Laboratory, University of Cincinnati, Cincinnati, Ohio)

The investigation of cancer in this Laboratory has been directed toward the estimation of the potential hazards of various forms of this disease which sometimes arise in industrial operations. This paper deals with one essential phase of such appraisals, namely, the experimental determination of the relative carcinogenic potency of selected materials for the tissue in question, in this case the skin.

In certain situations, it may be sufficient to measure the order of magnitude of the activities of a pertinent series of samples. Such would perhaps be the situation if, in the industrial operation in question, a mixture is produced, the composition of which is relatively simple and can reasonably be expected to remain constant indefinitely. However, in the case of the materials with which we have been primarily concerned, complexity and change have been the rule rather than the exception. Our investigative program was, therefore, directed toward the development of a qualitative picture and a subsequent quantification of the basic relationships between the chemical composition and the relative carcinogenic potency of various complex tars and oils. Through this approach, it is hoped that the results will have continuing significance in a changing technology.

The chance that a logical program of chemical and biological investigation would successfully resolve this complex problem depended heavily upon the accuracy with which the potencies of the various samples could be determined. This need was particularly emphasized by the findings in the course of this work that, while in the case of many of the mixtures tested, potency was independent of the quantity used for each application, certain important materials exhibited as much as four times the potency when the dose of 100 mg. was applied each time than when that of 15 mg. was so applied.

Recent analyses of the variability of the latent periods to the appearance of papillomas led to an estimate by Blanding and coworkers (3) that the "tumor potency" of a given material to the skin could be measured within +31 percent or -24 percent (approximately +50 percent or -30 percent in terms of arithmetic dose) in tests involving 30 stock mice each. Shimkin and Andervont (23) had shown earlier that the rate of induction of sarcomas could be defined more accurately by using the inbred C3H strain rather than stock mice. However, they obtained discrepant results even with C3H mice in repeated tests of solutions of dibenzanthracene (24) which may have been partly responsible for the more conservative estimate by Bryan and Shimkin (7) of the possible error as +100 percent or -50 percent for assays involving 100 animals (see also, 22). Although one of the pertinent experiments in which this unexplained variation occurred was complicated by the occurrence of intercurrent infection among the animals (page 58 of reference 23), Shimkin and Andervont did not relate this phenomenon to the observed retardation of tumor induction.

In this Laboratory, in which the minute and sometimes insidious effects of prolonged exposure to potentially injurious agents have been under investigation, the rate of growth of experimental animals has been measured with

regularity. The availability of such data in a large number of experiments involving application of a variety of potentially carcinogenic materials has enabled us to explain certain discrepancies comparable to those reported by Shimkin and Andervont. Examples in the body of this text will show that combinations of systemic intoxication and intercurrent disease sufficient to cause significant aberration of the growth of the animals are capable generally of exercising an inhibitory effect upon the experimental induction of cancer of the skin of the mouse.

It has been our experience that neither the incidence of tumors nor the standard deviation of the latent period of their appearance will necessarily be changed by this slowing down of their growth. Hence, although appropriate statistical treatment of these data is useful and necessary, it may fail utterly to reveal the intrinsic error introduced by this variable. Along with all proper precautions to minimize the toxicity of the applied material and to prevent intercurrent disease of any type, the animals should be weighed at regular intervals. Then, before the results are used for quantitative comparison with those of other tests, the investigator must assure himself that the average growth of each group of animals was normal at least during the relevant periods of the experiments.

In the course of this experimental program, solutions of synthetic carcinogens in pure solvents have been used as external standards of reference. Results of these tests have been correlated to provide certain dosage-response relationships, discussed in the section on Reference Standards.

EXPERIMENTAL METHODS

The validity of the use of data obtained from experiments with small animals to provide some indication of potential hazards to men in specific occupations depends upon the extent of correlated experience. The use of mice in the estimation of the relative carcinogenic potency of various materials for the skin of men can be justified on such a basis. The similarity of response of the skin of these two species to carcinogenic materials, such as shale oils from Scottish refineries and certain spindle oils used in the spinning of cotton in Lancashire, is well documented (14,15,18,20).

To obtain reasonably close definition of relative potencies with a minimum number of mice in each experiment, males of the highly inbred C3H strain have been used in most of our work. The docility of this animal has proved important in obtaining reproducible results as compared to other work in this Laboratory with CFW and Swiss males. Thus, in experiments which were satisfactory from the standpoint of growth and survival, 20 C3H mice were usually sufficient to define the mean time of appearance of tumors within confidence limits of ±15 percent (95 percent probability).

The general procedure may be summarized briefly. Mice were received from the Jackson Memorial Laboratory at six to eight weeks of age. They were placed under observation for four weeks to eliminate any in which there was evidence of poor health.

The actual tests of various synthetic solutions and complex oils followed the time-honored procedure of repeated application upon the fur and skin in the interscapular region (see for example, 20). The usual schedule consisted of three 100 mg. applications each week. The average quantity used in each painting has proved a most important variable in the case of certain complex oils and, therefore, was kept within reasonable limits. In testing certain materials of

moderate toxicity, it was necessary to reduce the severity of the exposure (dosage per application or frequency of application) to obtain satisfactory results.

On an unrestricted diet of Purina Laboratory Chow and water, the C3H mice in the satisfactory tests reached an average weight of 28 to 31 g. at six months of age. Experience has shown that, even when the mortality among an experimental group was low, the mean time of appearance of tumors was sometimes delayed seriously (as much as 50 percent) by conditions of variable or uncertain origin which also interrupted the normal growth of the animals. As a measure of such conditions, therefore, the mice were weighed at frequent intervals throughout the experiments. Precautions were taken to minimize infections and to prevent their spread from one group to another.

In general, under the conditions of these experiments one of two results has been obtained in response to repeated applications of any one of a long series of materials, i.e., most of the animals which lived long enough developed tumors of the skin at the site of the application, or none of them did so. The outcome of the experiments, therefore, has been essentially unequivocal, and the relative potencies of the different active materials could be expressed in terms of the relative rates of induction of tumors. For comparison, these rates may be conveniently expressed by what amounts to their reciprocals, the means[1] of the observed times of appearance of tumors. When deaths of tumor-free mice occur after the first tumor has appeared in a group, an improved estimate of the mean may be obtained by actuarial techniques ( ). A useful scale of relative carcinogenic potencies, based upon the relationship of these average times to the concentrations of carcinogen involved, is discussed in a later section.

CLASSIFICATION OF EXPERIMENTAL RESULTS ON THE BASIS OF THE HEALTH OF THE MICE

The success of a program aimed at the development of useful correlations between chemical composition and biological potency will depend largely upon the validity of the experimental data. Hence, it is essential to distinguish between the expected variation due to differences in the susceptibility of individual mice and occasional aberrant results due to other variables of unpredictable effect. Limits of confidence obtained by statistical methods (e.g., 5) usually provide an adequate measure of the possible error in a given determination. However, the toxicity of a complex oil, which is not directly related to its carcinogenic potency, and the occurrence of incidental disease among the animals may introduce important variables which cannot be given proper weight in the calculations.

A parallel examination of accumulated data on the growth and survival of the mice and the rate of induction of tumors in a large number of experiments on oils of widely varying composition and toxicity has proved most educational in this respect. The experience gained from this study has provided certain biological criteria for classifying a given test involving C3H mice as satisfactory (B) or unsatisfactory (X) for quantitative interpretation. Experiments have been placed in the X category if conditions resulted in excessive mortality or significant inhibition of growth during the critical period, the interval of about 15 weeks preceding the mean time of appearance of tumors. In tests on oils of moderately high potency, such conditions have frequently been accompanied by an increase in the mean of as much as eight weeks, equivalent to a reduction in relative potency of 40 to 50 percent (see discussion of potency scale below). An even more serious error may enter the interpretation of the results of Class X

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1 Since recording of the times of appearance of tumors has been on an intermittent (weekly) rather than a continuous basis, the calculated means have been arbitrarily reduced by one-half week.

experiments on materials of relatively low carcinogenic activity ($P_{MC} \leq 0.1$). The tendency in such cases is toward high non-tumor mortality, sometimes to the degree that the improper assumption could easily be made that the material involved is of negligible potency to mice.

These considerations have led to the general use in our program of data sheets on the individual tests, which permit a direct visual comparison of the growth and survival of the mice and the distribution in time of the induced tumors[2], (as shown in Figures 1 and 2). The oil involved in these examples was a high boiling residuum from a catalytic cracking unit, from which benzo[a]pyrene has been isolated (19). The carcinogenic properties of similar materials have been the subject of a number of recent papers (see for example,).

In the two examples, the same frequency of mortality among mice which had not developed skin tumors was experienced. However, the growth of the surviving animals in Experiment 8A approximated that of normal controls, whereas in 8B recovery from an apparent infection in the 12th to 14th weeks of the test was shortlived and there was a general decline after the 20th week. The accompanying increase in the mean time of appearance of tumors has been typical of tests in which this pattern of growth is observed. As in this instance, the standard deviation was unusually large in the majority of such experiments, although the reverse was the case in a few. The latter result might have been expected in Experiment 8B had the onset of the infection occurred two to three weeks earlier.

From the experimental data of Shimkin and Andervont, it is evident that a similar increase in the mean latent period to sarcoma after single subcutaneous injections of carcinogens in C3H mice may occur if infection interferes during critical periods. In a series of experiments on MC, BP, and DBA, reported in 1940 ( ), an intercurrent infection caused seven deaths among mice exposed to the latter carcinogen. The mean latent period after injection of 0.5 mg of DBA was 23.3 weeks. In a test performed a year later ( ) with the same dosage of DBA, no animals died before developing sarcomas and the mean latent period was 16.6 weeks. On the other hand, no discrepancy occurred in parallel experiments on 0.5 mg. doses of MC. Since the means in the latter tests were only 9.5 weeks, it is probable that the infection in the 1940 series occurred after most of the MC mice had developed tumors. Information on the growth curves of the mice injected with BP would be necessary to judge the relative significance of the mean latent periods obtained in the 1940 tests with this carcinogen.

To sum up, the results of tests on small populations may be seriously biased by variables not directly related to carcinogenic potency. Hence, it is important that data be collected on the health as well as on the survival and frequency of tumors among the test animals. Quantitative comparisons of biologically unsatisfactory data are unwarranted and may be quite misleading if not properly qualified.

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2 The cumulative frequency plots were based upon general principles outlined by Bliss (4). The normal distribution in time, shown for Experiment 8A, is typical. Logarithmic transformation of the time scale (3) has not been required.

Appendix C

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.

			Mice	Human Experience
Material	Relative Carcinogen Content	Maximum Probable Percentage of Long-chain Accelerators	Average Latent Period* (weeks)	Average Exposure Period (years)
Paraffin Distillate (Slack Wax)	Low	60	20-35	20 or more
Spindle Oil	Low	40	60	40 (Henry)
Coal Tar	High	Negligable	12-27	23 (Henry)
Pitch	Very High	Negligable	-	
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.

ESSO RESEARCH AND ENGINEERING COMPANY

(FORMERLY STANDARD OIL DEVELOPMENT COMPANY)

P. O. BOX 51, LINDEN, N. J.

MEDICAL RESEARCH DIVISION

ROBERT E. ECKARDT, PH.D., M.D.
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HORACE W. GERARDE, PH.D., M.D.
HEAD TOXICOLOGIST

BERTRAND E. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

April 12, 1955

Dr. E. W. Adams
Dr. L. C. Beard, Jr.
Mr. Allan E. Dooley
Dr. F. D. Gassaway
Dr. C. H. Hine
Dr. E. K. Linder
Dr. M. M. Marisic
Dr. R. C. Mithoff
Dr. M. N. Newquist
Dr. James W. Osborn
Dr. F. J. Sanders

Gentlemen:

Attached is the agenda for the meeting of the Subcommittee on Carcinogenicity of the API Medical Advisory Committee to be held on Saturday, April 23, 1955 at the Hotel Statler in Buffalo.

Sincerely yours,

R. E. Eckardt

R. E. ECKARDT, M. D.

REE/mak
Att.

cc: Mr. D. V. Stroop
Dr. A. W. Horton ✓
Dr. R. A. Kehoe
Dr. J. Phair

AGENDA FOR THE MEETING OF THE SUBCOMMITTEE ON CARCINOGENICITY
OF THE API MEDICAL ADVISORY COMMITTEE

Saturday, April 23, 1955

Detroit Room, Hotel Statler, Buffalo

9:30-10:30 a.m. - Executive Session - Subcommittee Members Only

10:30 a.m. - Subcommittee Meeting - Medical Advisory Committee Members and Guests Welcome

I. Approval of Minutes of Previous Meeting

II. Progress Report by Dr. A. W. Horton

III. Progress Report by Dr. J. Phair

IV. Comments, if any, by Dr. R. A. Kehoe

V. Efficiency of Solvent Extraction in Removing Carcinogens from Lubricating Oils

VI. Emulsion Techniques

VII. Possible Lung Carcinogenicity of Lubricating Oil Mists

VIII. Any Other New Business

IX. Executive Session if Necessary

X. Adjournment

Vitamin A in squamous or columnar

ESSO RESEARCH AND ENGINEERING COMPANY

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HORACE W. GERARDE, PH.D., M.D.
HEAD TOXICOLOGIST

BERTRAND K. BENNISON, M.D.
CHIEF CLINICAL RESEARCH PHYSICIAN

March 16, 1955

Messrs. E. W. Adams
L. C. Beard, Jr.
Allan A. Dooley
F. D. Gerarde
L. M. Henderson
C. E. Kline
E. K. Linder
R. C. Mitkoff
M. M. Neuquist
James W. Osborn
F. J. Sanders

Gentlemen:

This letter will serve simply as a reminder that the next meeting of the Subcommittee on Carcinogenicity is scheduled for April 23rd in the Statler Hotel in Buffalo. Since the time is rapidly drawing near for this meeting, I would like to urge each of you to send me the items which you would like to have included on the agenda of this meeting so that I may circulate the agenda to each of you well in advance of the meeting and you can each have the opportunity to think over those items on the agenda and organize any discussion which you might wish to prepare for the meeting.

In addition, this letter will serve as a reminder to the group at Kettering who I hope will have a progress report in our hands sufficiently in advance of the April meeting so that we can each have an opportunity to study it in detail and be prepared to make our comments, criticisms and suggestions at the time of the Subcommittee meeting. I am sure each of you realizes that this approach is much more productive at the actual Subcommittee meeting than if we attempt to hold a meeting in which we have had insufficient time to review the agenda and Subcommittee reports.

I am looking forward to seeing each of you again in Buffalo.

Sincerely yours,

R. K. ECKARDT, M. D.

RKE:ilk

cc: Messrs. D. V. Stroop
J. J. Muir
R. A. Kehoe
A. Wesley Morton

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

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

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

Delaware and Niagara Sq.
Buffalo, N.Y.

January 14, 1955

Messrs. E. W. Adams
L. C. Beard, Jr.
Allan E. Dooley
F. D. Gassaway
L. M. Henderson
C. H. Hine
E. K. Linder
R. C. Mithoff
M. N. Newquist
James W. Osborn
F. J. Sanders

Gentlemen:

At the January 10th meeting of the Steering Committee, it was recommended that the Subcommittee on Carcinogenicity be composed of the following people: E. W. Adams, L. C. Beard, Jr., R. E. Eckardt, C. H. Hine, E. K. Linder, R. C. Mithoff and M. N. Newquist, with an ex officio member, the Chairman of the Lubrication Committee, Division of Marketing. Whether or not this is now the official membership of our subcommittee, I am not sure, and therefore I am sending this letter to each of the members indicated in Mr. Stroop's memorandum of February 17, 1954.

I have so far heard from the following people concerning the meeting in April: Messrs. Adams, Hine, Mithoff, Linder, Gassaway, Newquist and Beard. Of this group, four said that either April 22nd or April 23rd would be satisfactory to them. Two gave a preference for April 23rd and one gave a preference for April 22nd. As far as I personally am concerned, either day is satisfactory. Therefore, I believe that our meeting should be called for Saturday, April 23, 1955 in Buffalo. By carbon copy of this letter to Mr. Stroop, I am asking that he arrange a room for us to hold this meeting. By carbon copy of this letter to the Cincinnati group, I am informing them of the arrangements.

It is my hope to have an agenda and progress report from the Kettering Laboratory for distribution to each of you at least a week in advance of this meeting so that you will have an opportunity to read the progress report and organize your thoughts on the topics to be included in the agenda. In the meantime, I would appreciate it if each of you would let me know of any topics which you would wish to have included on the agenda of this meeting in April.

Sincerely yours,

R. E. ECKARDT, M. D.

REE:ilk

cc: Messrs. D. V. Stroop
R. A. Kahoe
J. J. Fhair
A. Wesley Horton

ESSO LABORATORIES

STANDARD OIL DEVELOPMENT COMPANY

P. O. BOX 51, LINDEN, N.J.

MEDICAL RESEARCH DIVISION

ROBERT E. ECKARDT, PH.D., M.D.
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HEAD TOXICOLOGIST

INDUSTRIAL HYGIENE SECTION

NATHAN V. HENDRICKS, CH.E.
HEAD OF SECTION

FRANKLIN W. CHURCH, M.S.

GEORGE M. WILKENING, M.S.
INDUSTRIAL HYGIENISTS

December 21, 1954

Messrs. E. W. Adams
L. C. Beard, Jr.
Allan K. Dooley
F. D. Gammeter
L. M. Henderson
C. H. Hine
E. K. Linder
R. C. Mitheff
M. W. Newquist
James W. Osborn
F. J. Sanders

Gentlemen:

As you all know, the Industrial Medical Association and the AIHA are holding their annual meeting in Buffalo beginning Monday, April 25, 1955. At the last meeting of our subcommittee, it was suggested that we meet at about the time of this Industrial Health Meeting in April. In order to arrange for a definite date for a meeting of the subcommittee, I am proposing two dates, namely, Friday, April 22, or Saturday, April 23. Meeting in advance of the actual Industrial Health Meeting would permit us more time to discuss the work of the subcommittee and have our meeting completed prior to the meeting of the whole Medical Advisory Committee. I would appreciate hearing from each of you as soon as possible which of these two dates, namely, Friday, the 22nd, or Saturday, the 23rd, would be most satisfactory for you for holding a meeting of the Subcommittee on Carcinogenicity. When I have heard from each of you, I will send you a letter setting forth the definite date of the meeting.

May I take this opportunity to wish you all A Very Merry Christmas and A Happy New Year.

Sincerely yours,

R. E. ECKARDT, M. D.

REE:ilk

cc: Messrs. D. V. Stroop
R. A. Kehoe
J. J. Phair
A. Wesley Horton

ESSO RESEARCH AND ENGINEERING COMPANY

(FORMERLY STANDARD OIL DEVELOPMENT COMPANY)

P. O. BOX 45, LINDEN, N. J.

MEDICAL RESEARCH DIVISION
ROBERT E. ECKARDT, PH. D., M. D.
DIRECTOR
BERTRAND E. BENNISON M. D.
ASSISTANT DIRECTOR
N. V. HENDRICKS, CH. E.
HEAD INDUSTRIAL HYGIENIST
HORACE W. GERARDE, PH. D., M. D.
HEAD TOXICOLOGIST

September 25, 1958

TO: SUBCOMMITTEE ON CARCINOGENICITY

Gentlemen:

As you all may have noticed a meeting of the Subcommittee on Carcinogenicity is scheduled in Chicago for the afternoon of November 7.

It is my personal impression that it will not be necessary to schedule a meeting of this Subcommittee a month in advance of the Medical Advisory Committee as has been done in the past since the Kettering Laboratory is presumably in the finalizing stages of the final report of their work. In view of this, I would propose that we suggest that the Kettering group meet with our Subcommittee in Chicago on November 7 and that no additional meeting of the Subcommitee be scheduled.

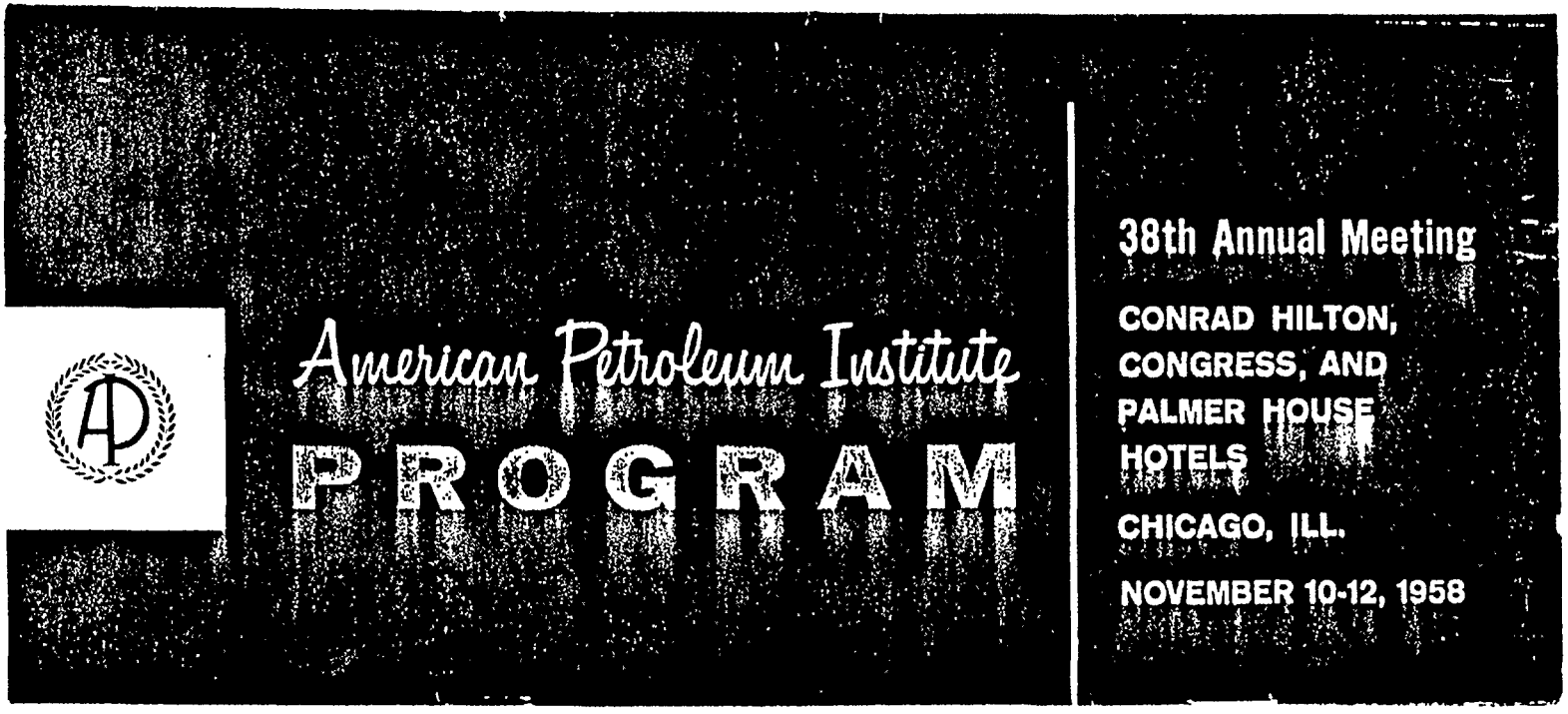
Unless I hear to the contrary from each of you by October 15, I will plan to proceed in this way.

Sincerely yours,

R. E. Eckardt

R. E. ECKARDT, M. D.

REE/bpj
cc: Dr. A. W. Horton
Dr. R. A. Kehoe
Mr. E. O. Mattocks


American Petroleum Institute
PROGRAM
38th Annual Meeting
CONRAD HILTON, CONGRESS, AND PALMER HOUSE HOTELS
CHICAGO, ILL.
NOVEMBER 10-12, 1958

This program has been prepared in two complete sections: -

Calendar of Events. A chronological listing of all events by days appears on pages 4-7. To facilitate easy reference, each meeting is illustrated with its respective symbol. The general sessions and group sessions appear in boldface type.

Divisional Listings are indicated by the tabs at the right margin of this program. All events concerning each division are listed under their respective tabs and are broken down by group sessions and committee meetings.

HEADQUARTERS

REGISTRATION AND INFORMATION
Conrad Hilton—Foyer Grand Ballroom
Palmer House—Private Dining Room 11

PRESS HEADQUARTERS
Conrad Hilton—Room 556A

PRODUCTION DIVISION HEADQUARTERS
Conrad Hilton—Room 515A

REFINING DIVISION HEADQUARTERS
Conrad Hilton—Room 551A

MARKETING DIVISION HEADQUARTERS
Congress Hotel—Caucus Room

TECHNICAL SERVICES HEADQUARTERS
Conrad Hilton—Room 530A

PUBLIC AFFAIRS COMMITTEE HEADQUARTERS
Conrad Hilton—Room 537A

TRANSPORTATION HEADQUARTERS
Palmer House—Private Dining Room 11

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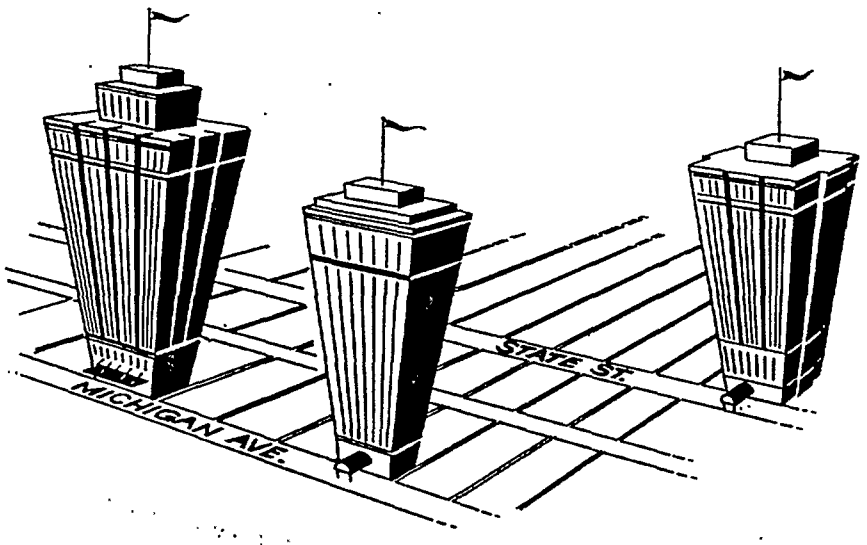
Non-divisional	18-21

PRODUCTION
REFINING
MARKETING
TRANSPORTATION
FINANCE and ACCOUNTING
NON-DIVISIONAL



CONRAD HILTON . . . Telephone: WAbash 2-4400
Michigan Boulevard, 7th-8th Streets
Chicago 5, Illinois

CONGRESS HOTEL . . . Telephone: HArrison 7-3800
500 South Michigan Avenue
Chicago 5, Illinois

PALMER HOUSE . . . Telephone: RAndolph 6-7500
State Street at Monroe
Chicago 90, Illinois

GENERAL SESSIONS

Monday, November 10, 1958

2:00 PM

General Session: (Conrad Hilton—Grand Ballroom)
Presiding: H. S. M. Burns, Chairman, API Board of Directors; President, Shell Oil Co., New York, N. Y.

Invocation.
Dr. Harold Blake Walker, Pastor of The First Presbyterian Church of Evanston, Evanston, Ill.

Remarks:
Frank M. Porter, President, American Petroleum Institute.

Presentation of Gold Medal for Distinguished Achievement.

Response by Recipient.

Address:
George Romney, President, American Motors Corp., Detroit, Mich.

Wednesday, November 12, 1958

10:00 AM

General Session: (Conrad Hilton—Grand Ballroom)
Presiding: H. S. M. Burns, Chairman, API Board of Directors; President, Shell Oil Co., New York, N. Y.

Invocation.
Dr. Charles Ray Goff, Pastor of The First Methodist Church, Chicago, Ill.

Report of Board of Councillors and Election of Directors.

Address:
Morgan J. Davis, President, Humble Oil and Refining Co., Houston, Texas.

Fifth World Petroleum Congress.
E. V. Murphree, President, Fifth World Petroleum Congress; President, Esso Research and Engineering Co., Linden, N. J.

Address:
Lee A. DuBridge, President, California Institute of Technology, Pasadena, Calif.

BOARD OF DIRECTORS

Tuesday, November 11, 1958

10:00 AM

Board of Directors Meeting:
(Conrad Hilton—Parlor B)

12:30 PM

Board of Directors Luncheon:
(Conrad Hilton—Parlor C)

2:00 PM

Board of Directors Meeting:
(Conrad Hilton—Parlor B)

Wednesday, November 12, 1958

12:30 PM

Board of Directors Luncheon:
(Conrad Hilton—Parlor C)

2:00 PM

Board of Directors Meeting:
(Conrad Hilton—Parlor B)

Note: The Program and Budget Review Committee and the Executive Committee of the Board of Directors will meet jointly immediately following this session of the Board of Directors.

BOARD OF COUNCILLORS

Monday, November 10, 1958

4:30 PM

Board of Councillors Meeting:
(Conrad Hilton—Waldorf Room)
To Nominate Candidates for Election as Members of the Board of Directors.

CALENDAR OF EVENTS

Thursday, November 6, 1958

9:00 am Joint Meeting (CRE) (All Day); Subcommittee of Refinery Inspection Supervisors; Designers' Subcommittee on Refinery Inspections (Conrad Hilton—PDR 2)

9:00 am Subcommittee on Instruments (CRE) (All Day) (Conrad Hilton—PDR 3)

9:00 am Manufacturers' Subcommittee on Tanks and Vessels (CRE) (All Day) (Conrad Hilton—PDR 10)

9:00 am Manufacturers' Subcommittee on Refinery Valves (CRE) (Conrad Hilton—Room 14)

9:00 am Manufacturers' Subcommittee on Heat Exchanger Tubing (CRE) (Conrad Hilton—PDR 4)

2:00 pm Manufacturers' Subcommittee on Fired Heater Tubing (CRE) (Conrad Hilton—Room 14)

2:00 pm Manufacturers' Subcommittee on Gaskets (CRE) (Conrad Hilton—PDR 4)

Friday, November 7, 1958

9:00 am Subcommittee on Tubing (CRE) (All Day) (Conrad Hilton—PDR 1)

9:00 am Manufacturers' Subcommittee on Safety and Relief Valves (CRE) (All Day) (Conrad Hilton—Room 18)

9:00 am Subcommittee on Corrosion (CRE) (All Day) (Conrad Hilton—PDR 2)

9:00 am Subcommittee on Instruments (CRE) (All Day) (Conrad Hilton—PDR 3)

9:00 am Subcommittee on Oil Storage Tanks (CRE) (All Day) (Conrad Hilton—Room 14)

9:00 am Joint Meeting (CRE) (All Day); Subcommittee on Mechanical Equipment; Manufacturers' Subcommittee on Centrifugal Compressors; Manufacturers' Subcommittee on Mechanical-Drive Turbines (Conrad Hilton—PDR 4)

9:00 am Panel on Hurricanes (All Day) (Conrad Hilton—PDR 5)

9:00 am Task Force on Stainless Steel Valves (CRE) (All Day) (Conrad Hilton—Room 12)

2:00 pm Subcommittee on Fuel Surveys (ARC) (Conrad Hilton—PDR 10)

Saturday, November 8, 1958

9:00 am Planning Task Group Subcommittee on Corrosion (CRE) (All Day) (Conrad Hilton—Room 12)

9:00 am Subcommittee on Refinery Piping (CRE) (All Day) (Conrad Hilton—PDR 1)

9:00 am Committee on Petroleum Products (Conrad Hilton—Parlor B)

9:00 am Joint Meeting (CRE) (All Day); Subcommittee on Mechanical Equipment; Contractors' Subcommittee on Refinery Construction; Manufacturers' Subcommittee on Centrifugal Pumps (Conrad Hilton—Parlor A)

9:00 am Advisory Committee on Fundamental Research on Occurrence and Recovery of Petroleum (All Day) (Conrad Hilton—PDR 2)

9:00 am Research Project 44 Advisory Committee (All Day) (Conrad Hilton—PDR 3)

9:00 am Committee on Positive Displacement Metering Measurement (All Day) (Conrad Hilton—Bel Air Room)

2:00 pm Subcommittee on Pressure-relieving Systems (CRE) (Conrad Hilton—PDR 4)

2:00 pm Automotive Research Committee (Conrad Hilton—Parlor B)

Sunday, November 9, 1958

9:00 am Interdivisional Committee on Labeling (Conrad Hilton—PDR 3)

9:00 am Committee on Crude-Oil Measurements (All Day) (Conrad Hilton—Parlor B)

9:00 am Program Committee, Division of Refining (Conrad Hilton—PDR 2)

9:00 am Publications Committee (S and F) (Conrad Hilton—PDR 8)

9:00 am Subcommittee on Unfired Pressure Vessels (CRE) (All Day) (Conrad Hilton—Parlor A)

9:00 am Subcommittee on Electrical Equipment (CRE) (All Day) (Conrad Hilton—Bel Air Room)

9:00 am Research Project 6 Advisory Committee (Conrad Hilton—Room 18)

9:00 am Research Project 45 Advisory Committee (Conrad Hilton—Room 19)

9:30 am Committee on Petroleum Statistics (All Day) (Conrad Hilton—Parlor C)

10:00 am Organization Committee, Division of Finance and Accounting (Conrad Hilton—PDR 9)

12:30 pm Organization Committee, Division of Finance and Accounting (Luncheon) (Conrad Hilton—PDR 10)

1:00 pm Advisory Committee on Fundamental Research on Weather Forecasting (Conrad Hilton—PDR 4)

2:00 pm Technical Advisory Committee (S and F) (Conrad Hilton—PDR 2)

2:00 pm Advisory Committee, Division of Refining (Conrad Hilton—PDR 1)

2:00 pm Engineering and Technical Section (Pipeline) (Palmer House—PDR 8)

2:00 pm Government Regulation Section (Pipeline) (Palmer House—PDR 14)

2:00 pm Operating Section (Pipeline) (Palmer House—PDR 7)

2:00 pm Coordinating Committee (Highway) (Palmer House—PDR 6)

2:00 pm Committee on Agriculture (Conrad Hilton—Room 18)

2:00 pm Corporate Accounting Committee (Conrad Hilton—Room 19)

4:00 pm Executive Committee (CRE), Division of Refining (Conrad Hilton—PDR 8)

4:00 pm Nominating Committee, Division of Finance and Accounting (Conrad Hilton—PDR 3)

4:00 pm Executive Committee (of the Advisory Committee on Fundamental Research on Composition and Properties of Petroleum) (Conrad Hilton—PDR 9)

4:30 pm Nominating Committee, Division of Transportation (Palmer House—PDR 9)

8:00 pm Joint Meeting; Coordinating Committee (Pipeline); Conference Steering Committee (Palmer House—PDR 9)

Monday, November 10, 1958

8:00 am Nominating Committee, Division of Marketing (Breakfast and Meeting) (Congress Hotel—Music Room)

8:30 am Joint Meeting; Central Committee on Accident Prevention; Central Committee on Fire Protection (Conrad Hilton—Beverly Room)

9:00 am Subcommittee on Recovery Efficiency (Conrad Hilton—Room 12)

9:00 am Central Committee on Training (Conrad Hilton—Upper Tower)

9:00 am Manufacturers' Subcommittee on Pump Manuals (CTR) (All Day) (Conrad Hilton—PDR 5)

9:00 am Committee on Refinery Equipment (Conrad Hilton—PDR 2)

9:00 am Smoke and Fumes Committee (Conrad Hilton—Parlor B)

9:00 am NEC Coordinating Committee (All Day) (Conrad Hilton—Room 19)

9:00 am Operating Committee of Lubrication Committee (Congress Hotel—Washington Room)

9:00 am Service Station Advisory Committee (All Day) (Congress Hotel—Florentine Room)

9:00 am Aviation Technical Service Committee (All Day) (Conrad Hilton—Bel Air Room)

9:00 am Advisory Committee on Fundamental Research on Occurrence and Recovery of Petroleum (Conrad Hilton—PDR 4)

9:00 am Research Project 42 Advisory Committee (Conrad Hilton—PDR 8)

9:00 am Committee on Petroleum Statistics (Conrad Hilton—Parlor C)

10:00 am Group Session—Transportation (Palmer House—Red Lacquer Room)

10:00 am Group Session—Finance and Accounting (Conrad Hilton—Waldorf Room)

10:00 am Committee on Gas and Electric Cutting and Welding (Conrad Hilton—Room 13)

10:00 am Committee on Off-the-Job Safety (Conrad Hilton—PDR 3)

10:00 am Committee on Safety Awards (Conrad Hilton—PDR 1)

10:00 am Agricultural Advisory Committee (Conrad Hilton—Room 18)

10:00 am Asphalt Committee (Conrad Hilton—Room 14)

11:00 am Group Session—Committee on Public Affairs (Conrad Hilton—Grand Ballroom)

12:00 N Publications Committee (of the Central Committee on Drilling and Production Practice) (Luncheon) (Conrad Hilton—PDR 10)

Monday, November 10, 1958

12:00 N Marketing Membership Committee (Luncheon) (Congress Hotel—Purkview Room)

12.00 N Program Committee Division of Marketing (Luncheon) (Congress Hotel—Victorian Room)

12.00 N Medical and Health Committee of the Board of Directors (Luncheon) (Conrad Hilton—PDR 9)

12:30 pm Aviation Technical Service Committee (Luncheon) (Conrad Hilton—Bel Air Assembly)

1:30 pm Committee on Fire-Protection Engineering (Conrad Hilton—Beverly Room)

2:00 pm Commission Wholesale Marketers Advisory Committee (Congress Hotel—Glass Hat)

2:00 pm Fuel Oil Committee (Congress Hotel—Francis I Room)

2:00 pm Corporate Finance Committee (Conrad Hilton—Room 13)

2:00 pm Advisory Committee on Fundamental Research on Composition and Properties of Petroleum (Conrad Hilton—PDR 2)

2:00 pm Forum on Refining Operating Practices (Conrad Hilton—Parlor C)

2:00 pm General Session (Conrad Hilton—Grand Ballroom)

2:00 pm Committee on Personal Protective Equipment (Conrad Hilton—PDR 1)

2:30 pm Committee on Law and Regulation (Palmer House—Crystal Room)

4:00 pm Nominating Committee, Division of Production (Conrad Hilton—Room 18)

4:00 pm Nominating Committee, Division of Refining (Conrad Hilton—PDR 8)

4:30 pm Board of Councillors Meeting (Conrad Hilton—Waldorf Room)

7:00 pm Committee on Fire-Protection Engineering (Conrad Hilton—Beverly Room)

Tuesday, November 11, 1958

8:00 am Highway Coordinating Committee (Breakfast) (Conrad Hilton—Astoria Room)

8:30 am Committee on Tanks (All Day) (Conrad Hilton—PDR 1)

8:30 am Committee on Safety and Fire Protection in Drilling and Production Operations (All Day) (Conrad Hilton—PDR 3)

9:00 am Committee on Traffic Safety (Conrad Hilton—PDR 4)

9:00 am Executive Committee (of the Central Committee on Drilling and Production Practice) (Conrad Hilton—Parlor A)

9:00 am Jobber Advisory Committee (Congress Hotel—Gold Room)

9:00 am Lubrication Committee (Congress Hotel—Francis I Room)

9:00 am Marketing Personnel Development Committee (Congress Hotel—Washington Room)

9:00 am Research Projects 48 and 52 Advisory Committees (All Day) (Conrad Hilton—PDR 2)

9:00 am Joint Meeting: (Palmer House—PDR 8) Coordinating Committee (Water); Program Committee

9:00 am Central Committee on Pipeline Transportation (Palmer House—Red Lacquer Room)

9:00 am Central Committee on Radio Facilities (All Day) (Palmer House—PDR 9)

9:00 am Committee on Railroad Equipment (Palmer House—Crystal Room)

9:00 am Central Committee on Highway Transportation (All Day) (Palmer House—PDR 14)

9:30 am Aviation Advisory Committee (Conrad Hilton—Bel Air Room)

10:00 am Group Session—Statistics (Conrad Hilton—Waldorf Room)

10:00 am Group Session—Refining (Conrad Hilton—Grand Ballroom)

10:00 am Group Session—Finance and Accounting (Conrad Hilton—Beverly Room)

10:00 am Board of Directors Meeting (Conrad Hilton—Parlor B)

10:00 am Defense Services Committee (Conrad Hilton—PDR 8)

12:00 N Program Committee (of the Central Committee on Drilling and Production Practice) (Luncheon) (Conrad Hilton—PDR 9)

12:00 N Safety Committee of the Board of Directors (Luncheon) (Conrad Hilton—PDR 10)

12:00 N Oil Marketers Get-Together—"Dutch-Treat" Buffet Luncheon (Congress Hotel—Michigan Room and Glass Hat)

12:30 pm Board of Directors Luncheon (Conrad Hilton—Parlor C)

1:30 pm Committee on Fire-Protection Regulations (Conrad Hilton—Upper Tower)

1:45 pm Group Session—Production (Conrad Hilton—Grand Ballroom)

2:00 pm Group Session—Petroleum-Industry Buyers (Conrad Hilton—Boulevard Room)

2:00 pm Group Session—Marketing (Congress Hotel—Gold Room)

2:00 pm Board of Directors Meeting (Conrad Hilton—Parlor B)

2:00 pm General Committee, Division of Refining (Conrad Hilton—Bel Air Room)

2:00 pm General Committee, Division of Finance and Accounting (Conrad Hilton—Parlor A)

2:00 pm Committee on Petroleum Statistics (Conrad Hilton—Astoria Room)

2:00 pm General Committee, Division of Marketing (Congress Hotel—Gold Room)

2:00 pm Central Committee on Transportation by Water (Palmer House—Crystal Room)

2:00 pm Central Committee on Railroad Transportation (Palmer House—Red Lacquer Room)

2:00 pm Forum on Refining Operating Practices (Conrad Hilton—Waldorf Room)

2:30 pm Safety and Fire-Protection Program Committee (Conrad Hilton—Room 12)

2:30 pm Committee on Liquefied Petroleum Gas (Conrad Hilton—Beverly Room)

4:00 pm Committee on Visual Aids (Conrad Hilton—PDR 4)

5:30 pm Committee on Visual Aids (Film Presentation) (Conrad Hilton—Waldorf Room)

Wednesday, November 12, 1958

8:30 am Committee on Safety and Fire Protection in Manufacturing Operations (Conrad Hilton—Parlor A)

8:30 am Committee on Safety and Fire Protection in Pipeline Operations (Conrad Hilton—PDR 4)

9:00 am Committee on Accident Statistics (Conrad Hilton—Astoria Room)

9:00 am Coordinating Committee (Pipeline) (Palmer House—PDR 9)

9:00 am Coordinating Committee (Highway) (All Day) (Palmer House—PDR 8)

9:00 am Central Committee on Radio Facilities (All Day) (Palmer House—PDR 14)

10:00 am General Session (Conrad Hilton—Grand Ballroom)

12:00 N General Committee, Division of Production (Luncheon) (Conrad Hilton—Bel Air Room)

12:00 N Research Committee of the Board of Directors (Luncheon) (Conrad Hilton—PDR 1)

12:00 N General Committee, Division of Transportation (Luncheon) (for 1958 members only) (Palmer House—Crystal Room)

12:30 pm Board of Directors Luncheon (Conrad Hilton—Parlor C)

1:30 pm Committee on Static Electricity and Stray Currents (Conrad Hilton—Parlor A)

1:30 pm Committee on Safety and Fire Protection in Marketing Operations (Conrad Hilton—PDR 2)

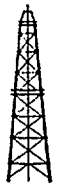
2:00 pm Committee on Safety and Fire Protection in Geophysical Operations (Conrad Hilton—PDR 4)

2:00 pm Board of Directors Meeting (Conrad Hilton—Parlor B)

Thursday, November 13, 1958

8:30 am Joint Meeting (All Day): Central Committee on Accident Prevention; Central Committee on Fire Protection (Conrad Hilton—PDR 2)

DIVISION OF PRODUCTION



GROUP SESSION

Tuesday, November 11, 1958

1:45 PM

Production Session:
(Conrad Hilton–Grand Ballroom)

Presiding: D. L. Connelly, Vice President for Production, American Petroleum Institute; Senior Vice President, Warren Petroleum Corp., Houston, Texas.

Presentation of the API "Certificate of Appreciation."
By D. L. Connelly, Vice President for Production.

Address:
L. F. McCollum, President, Continental Oil Co., Houston, Texas.

Presentation of Carl A. Young Memorial Award.

Why Conservation.
Charlton H. Lyons, Sr., Lyons and Logan, Shreveport, La.

Address:
Hon. Thomas C. Mann, Assistant Secretary of State, Washington, D. C.

Report of Division's Nominating Committee.
T. H. Acres, Sunray Mid-Continent Oil Co., Los Angeles, Calif., Chairman.

Election of Members of the General Committee of the Division of Production.

COMMITTEE MEETINGS

Monday, November 10, 1958

MORNING

9:00 am Central Committee on Training
(Conrad Hilton–Upper Tower)
Chairman: R. E. Foss

9:00 am Subcommittee on Recovery Efficiency
(Conrad Hilton–Room 12)
Chairman: Edgar Kraus

AFTERNOON

12:00 N Publications Committee (of the Central Committee on Drilling and Production Practice)
(Luncheon) (Conrad Hilton–PDR 10)
Chairman: Earle Hellums

4:00 pm Nominating Committee, Division of Production (Conrad Hilton–Room 18)
Chairman: T. H. Acres

COMMITTEE MEETINGS (continued)

Tuesday, November 11, 1958

MORNING

9:00 am Executive Committee (of the Central Committee on Drilling and Production Practice)
(Conrad Hilton–Parlor A)
Chairman: Harold Denton

AFTERNOON

12:00 N Program Committee (of the Central Committee on Drilling and Production Practice)
(Luncheon) (Conrad Hilton–PDR 9)
Chairman: S. C. Oliphant

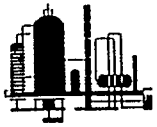
COMMITTEE MEETINGS (continued)

Wednesday, November 12, 1958

AFTERNOON

12:00 N General Committee, Division of Production
(Luncheon) (Conrad Hilton–Bel Air Room)
Chairman: D. L. Connelly

DIVISION OF REFINING



GROUP SESSION

Tuesday, November 11, 1958

10:00 AM

Refining Session: (Conrad Hilton–Grand Ballroom)
Presiding: H. W. Ferguson, Vice President for Refining, American Petroleum Institute; Vice President, Humble Oil and Refining Co., Houston, Texas.

Report of Division's Nominating Committee.
L. C. Burroughs, Shell Oil Co., New York, N. Y., Chairman.

Election of Members of the General Committee of the Division of Refining.

Refining Flexibility and the Problems of Seasonal Demand.
H. W. Ferguson, Vice President for Refining.

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COMMITTEE MEETINGS

Thursday, November 6, 1958

MORNING

9:00 am Joint Meeting (CRE) (All Day): (Conrad Hilton–PDR 2)
Subcommittee of Refinery Inspection Supervisors
(R. B. Sykes, Chairman)
Designers' Subcommittee on Refinery Inspections
(J. H. Rickerman, Chairman)
Presiding: R. B. Sykes

9:00 am Subcommittee on Instruments (CRE) (All Day) (Conrad Hilton–PDR 3)
Chairman: G. N. Ehly

9:00 am Manufacturers' Subcommittee on Tanks and Vessels (CRE) (All Day) (Conrad Hilton–PDR 10)
Chairman: C. W. Wheatley

9:00 am Manufacturers' Subcommittee on Refinery Valves (CRE) (Conrad Hilton–Room 14)
Chairman: W. P. Kliment

9:00 am Manufacturers' Subcommittee on Heat Exchanger Tubing (CRE) (Conrad Hilton–PDR 4)
Chairman: R. K. Tyson

COMMITTEE MEETINGS (continued)

Thursday, November 6, 1958

AFTERNOON

2:00 pm Manufacturers' Subcommittee on Fired Heater Tubing (CRE) (Conrad Hilton–Room 14)
Chairman: E. H. Palchik

2:00 pm Manufacturers' Subcommittee on Gaskets (CRE) (Conrad Hilton–PDR 4)
Chairman: H. H. Dunkle

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Friday, November 7, 1958

MORNING

9:00 am Subcommittee on Tubing (CRE) (All Day) (Conrad Hilton–PDR 1)
Chairman: L. G. Molique

9:00 am Manufacturers' Subcommittee on Safety and Relief Valves (CRE) (All Day) (Conrad Hilton–Room 18)
Chairman: L. P. Stillman

9:00 am Subcommittee on Corrosion (CRE) (All Day) (Conrad Hilton–PDR 2)
Chairman: F. A. L. Holloway

9:00 am Subcommittee on Instruments (CRE) (All Day) (Conrad Hilton–PDR 3)
Chairman: G. N. Ehly

9:00 am Subcommittee on Oil Storage Tanks (CRE) (All Day) (Conrad Hilton–Room 14)
Chairman: C. V. Lynn

9:00 am Joint Meeting (CRE) (All Day): (Conrad Hilton–PDR 4)
Subcommittee on Mechanical Equipment
(E. F. Voss, Chairman)
Manufacturers' Subcommittee on Centrifugal Compressors
(W. O. Lowell, Chairman)
Manufacturers' Subcommittee on Mechanical-Drive Turbines
(P. R. Darling, Chairman)
Presiding: E. F. Voss

9:00 am Task Force on Stainless Steel Valves (CRE) (All Day) (Conrad Hilton–Room 12)
Chairman: William Hellig

AFTERNOON

2:00 pm Subcommittee on Fuel Surveys (ARC) (Conrad Hilton–PDR 10)
Chairman: J. B. Duckworth

COMMITTEE MEETINGS (continued)

Saturday, November 8, 1958

MORNING

9:00 am Planning Task Group of Subcommittee on Corrosion (CRE) (All Day) (Conrad Hilton–Room 12)
Chairman: F. A. L. Holloway

9:00 am Subcommittee on Refinery Piping (CRE) (All Day) (Conrad Hilton–PDR 1)
Chairman: J. P. Mooney

9:00 am Committee on Petroleum Products (Conrad Hilton–Parlor B)
Chairman: C. B. Gale

9:00 am Joint Meeting (CRE) (All Day): (Conrad Hilton–Parlor A)
Subcommittee on Mechanical Equipment
(E. F. Voss, Chairman)
Contractors' Subcommittee on Refinery Construction
(R. N. Hancock, Chairman)
Manufacturers' Subcommittee on Centrifugal Pumps
(G. V. Shaw, Chairman)
Presiding: E. F. Voss

AFTERNOON

2:00 pm Subcommittee on Pressure-relieving Systems (CRE) (Conrad Hilton–PDR 4)
Chairman: E. D. Underwood

2:00 pm Automotive Research Committee (Conrad Hilton–Parlor B)
Chairman: W. J. Sweeney

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Sunday, November 9, 1958

MORNING

9:00 am Program Committee, Division of Refining (Conrad Hilton–PDR 2)
Acting Chairman: D. L. Campbell

9:00 am Publications Committee (S and F) (Conrad Hilton–PDR 8)
Chairman: W. H. Claussen

9:00 am Subcommittee on Unfired Pressure Vessels (CRE) (All Day) (Conrad Hilton–Parlor A)
Chairman: N. J. Rees

9:00 am Subcommittee on Electrical Equipment (CRE) (All Day) (Conrad Hilton–Bel Air Room)
Chairman: E. R. Hoyle

COMMITTEE MEETINGS (continued)

Sunday, November 9, 1958

AFTERNOON

2:00 pm Technical Advisory Committee (S and F) (Conrad Hilton–PDR 2)
Chairman: Jerry McAfee

2:00 pm Advisory Committee, Division of Refining (Conrad Hilton–PDR 1)
Chairman: C. H. Thayer

4:00 pm Executive Committee (CRE), Division of Refining (Conrad Hilton–PDR 8)
Chairman: J. C. Ducommun

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Monday, November 10, 1958

MORNING

9:00 am Manufacturers' Subcommittee on Pump Manuals (CTR) (All Day) (Conrad Hilton–PDR 5)
Chairman: G. V. Shaw

9:00 am Committee on Refinery Equipment (Conrad Hilton–PDR 2)
Chairman: J. C. Ducommun

9:00 am Smoke and Fumes Committee (Conrad Hilton–Parlor B)
Chairman: C. C. Tate

AFTERNOON

2:00 pm Forum on Refining Operating Practices–A Panel Discussion on "Hazards of Water in Refining Operations" (Conrad Hilton–Parlor C)
Presiding: F. H. Blunck
Moderator: A. H. Hayes

4:00 pm Nominating Committee, Division of Refining (Conrad Hilton–PDR 8)
Chairman: L. C. Burroughs

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Tuesday, November 11, 1958

AFTERNOON

2:00 pm General Committee, Division of Refining (Conrad Hilton–Bel Air Room)
Chairman: H. W. Ferguson

2:00 pm Forum on Refining Operating Practices–A Panel Discussion on "Hazards of Air or Oxygen in Refining Operations" (Conrad Hilton–Waldorf Room)
Presiding: F. H. Blunck
Moderator: R. H. Jacobs

DIVISION OF MARKETING

GROUP SESSIONS

Tuesday, November 11, 1958

12:00 Noon

Oil Marketers Get-Together—"Dutch-Treat" Buffet Luncheon:
(Congress Hotel—Michigan Room and Glass Hat)
All persons interested in oil marketing are invited to attend this "Dutch-treat" luncheon.

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2:00 PM

Open Meeting of General Committee:
(Congress Hotel—Gold Room)
Presiding: Dwight T. Colley, Vice President for Marketing, American Petroleum Institute; Vice President, The Atlantic Refining Co., Philadelphia, Pa.

Open Business Session.
(Open meeting at which Division of Marketing business will be transacted by the General Committee. In addition to discussion of current matters, reports will be heard from various committees and study groups of the Division of Marketing.)

Presentation of the API "Certificate of Appreciation."
By J. G. Jordan, Chairman, API Marketing Committee on Awards; Vice President, Shell Oil Co., New York, N. Y.

Report of Division's Nominating Committee.
H. L. Moir, Assistant Vice President, Retail Marketing, The Pure Oil Co., Chicago, Ill., Chairman.

Election of Members of the General Committee of the Division of Marketing.

COMMITTEE MEETINGS

Monday, November 10, 1958

MORNING

8:00 am Nominating Committee, Division of Marketing (Breakfast and Meeting)
(Congress Hotel—Music Room)
Chairman: H. L. Moir

9:00 am *Operating Committee of Lubrication Committee* (Congress Hotel—Washington Room)
Chairman: G. H. Osborne

9:00 am Service Station Advisory Committee (All Day) (Congress Hotel—Florentine Room)
Chairman: L. J. Hoar

9:00 am Aviation Technical Service Committee (All Day) (Conrad Hilton—Bel Air Room)
Chairman: Aubrey Kelf

COMMITTEE MEETINGS (continued)

Monday, November 10, 1958

AFTERNOON

12:00 N Marketing Membership Committee (Luncheon) (Congress Hotel—Parkview Room)
Chairman: E. K. Ketcham

12:00 N Program Committee, Division of Marketing (Luncheon)
(Congress Hotel—Victorian Room)
Chairman: E. M. Toby, Jr.

12:30 pm Aviation Technical Service Committee (Luncheon)
(Conrad Hilton—Bel Air Assembly)
Chairman: Aubrey Kelf

2:00 pm Commission Wholesale Marketers Advisory Committee
(Congress Hotel—Glass Hat)
Chairman: George M. Sullivan

2:00 pm Fuel Oil Committee
(Congress Hotel—Francis I Room)
Chairman: C. M. Blickensderfer

COMMITTEE MEETINGS (continued)

Tuesday, November 11, 1958

MORNING

9:00 am Jobber Advisory Committee
(Congress Hotel—Gold Room)
Chairman: R. O. Goodykoontz

9:00 am Lubrication Committee
(Congress Hotel—Francis I Room)
Chairman: G. H. Osborne

9:00 am Marketing Personnel Development Committee (Congress Hotel—Washington Room)
Chairman: V. A. Bellman

AFTERNOON

2:00 pm General Committee, Division of Marketing
(Congress Hotel—Gold Room)
Chairman: Dwight T. Colley

DIVISION OF TRANSPORTATION

GROUP SESSION

Monday, November 10, 1958

10:00 AM

Transportation Session:
(Palmer House–Red Lacquer Room)

Presiding: Charles E. Spahr, Vice President for Transportation, American Petroleum Institute; President, The Standard Oil Co. (Ohio), Cleveland, Ohio.

Report of Division's Nominating Committee.

A. E. Pecore, Humble Pipe Line Co., Houston, Texas, Chairman.

Election of Members of the General Committee of the Division of Transportation.

Modern Transport and Archaic Controls.

John S. Burchmore, General Counsel, National Industrial Traffic League, Chicago, Ill.

Presentation of the API "Certificate of Appreciation."

By Charles E. Spahr, Vice President for Transportation.

How Vehicles Stretch Our Reach in Geophysics.

Athelstan F. Spilhaus, Dean, Institute of Technology, University of Minnesota, Minneapolis, Minn.

Movies:

1. "An Antarctic Traverse."
2. "Some Scenes of the U. S. IGY Satellite Program."

COMMITTEE MEETINGS

Sunday, November 9, 1958

AFTERNOON

2:00 pm **Engineering and Technical Section (Pipeline)** (Palmer House–PDR 8)
Presiding: J. W. Emison

2:00 pm **Government Regulations Section (Pipeline)** (Palmer House–PDR 14)
Presiding: R. K. Paine

2:00 pm **Operating Section (Pipeline)** (Palmer House–PDR 7)
Presiding: D. F. Sears

2:00 pm **Coordinating Committee (Highway)** (Palmer House–PDR 6)
Presiding: L. E. Reed

4:30 pm **Nominating Committee, Division of Transportation** (Palmer House–PDR 9)
Chairman: A. E. Pecore

EVENING

8:00 pm **Joint Meeting:** (Palmer House–PDR 9)
Coordinating Committee (Pipeline)
(R. H. Lynch, Chairman)
Conference Steering Committee
(J. W. de Groot, Chairman)

Monday, November 10, 1958

AFTERNOON

2:30 pm **Committee on Law and Regulation** (Palmer House–Crystal Room)
Chairman: Fayette B. Dow

COMMITTEE MEETINGS (continued)

Tuesday, November 11, 1958

MORNING

9:00 am **Joint Meeting:** (Palmer House–PDR 8)
Coordinating Committee (Water)
(R. K. Kelly, Chairman)
Program Committee
(William G. Anderson, Chairman)

9:00 am **Central Committee on Pipeline Transportation** (Palmer House–Red Lacquer Room)
Chairman: R. H. Lynch

9:00 am **Central Committee on Radio Facilities (All Day)** (Palmer House–PDR 9)
Chairman: R. D. Wyckoff

9:00 am **Committee on Railroad Equipment** (Palmer House–Crystal Room)
Chairman: E. E. Wickman

9:00 am **Central Committee on Highway Transportation (All Day)** (Palmer House–PDR 14)
Chairman: L. E. Reed

AFTERNOON

2:00 pm **Central Committee on Transportation by Water** (Palmer House–Crystal Room)
Chairman: R. K. Kelly

2:00 pm **Central Committee on Railroad Transportation** (Palmer House–Red Lacquer Room)
Chairman: A. G. Anderson

COMMITTEE MEETINGS (continued)

Wednesday, November 12, 1958

MORNING

9:00 am **Coordinating Committee (Pipeline)** (Palmer House–PDR 9)
Chairman: R. H. Lynch

9:00 am **Coordinating Committee (Highway) (All Day)** (Palmer House–PDR 8)
Chairman: L. E. Reed

9:00 am **Central Committee on Radio Facilities (All Day)** (Palmer House–PDR 14)
Chairman: R. D. Wyckoff

AFTERNOON

12:00 N **General Committee, Division of Transportation (Luncheon) (For 1958 Members Only)** (Palmer House–Crystal Room)
Chairman: Charles E. Spahr

DIVISION of FINANCE and ACCOUNTING



GROUP SESSIONS

Monday, November 10, 1958

10:00 AM

Finance and Accounting Session:
(Conrad Hilton–Waldorf Room)

Presiding: A. A. Buzzi, Vice President for Finance and Accounting, American Petroleum Institute; Controller, Shell Oil Co., New York, N. Y.

Presentation of the API "Certificate of Appreciation."

Determining the Cost of Finding and Producing Gas under Federal Power Commission Regulation.
S. P. Porter, Arthur Young and Co., Tulsa, Okla.

GROUP SESSIONS (continued)

Tuesday, November 11, 1958

10:00 AM

Finance and Accounting Session:
(Conrad Hilton–Beverly Room)

Presiding: A. A. Buzzi, Vice President for Finance and Accounting, American Petroleum Institute; Controller, Shell Oil Co., New York, N. Y.

Report of Division's Nominating Committee.
P. C. Salman, Socony Mobil Oil Co., Inc., New York, N.Y., Chairman.

Election of Members of the General Committee of the Division of Finance and Accounting.

What Price Inflation?
Milton Friedman, Professor of Economics, University of Chicago, Chicago, Ill.

COMMITTEE MEETINGS

Sunday, November 9, 1958

MORNING

10:00 am Organization Committee, Division of Finance and Accounting (Conrad Hilton–PDR 9)
Chairman: C. J. Senger

AFTERNOON

12:30 pm Organization Committee, Division of Finance and Accounting (Luncheon)
(Conrad Hilton–PDR 10)
Chairman: C. J. Senger

2:00 pm Corporate Accounting Committee
(Conrad Hilton–Room 19)
Chairman: O. L. Luper

4:00 pm Nominating Committee, Division of Finance and Accounting (Conrad Hilton–PDR 3)
Chairman: P. C. Salman

COMMITTEE MEETINGS (continued)

Monday, November 10, 1958

AFTERNOON

2:00 pm Corporate Finance Committee
(Conrad Hilton–Room 13)
Chairman: A. E. Wolf

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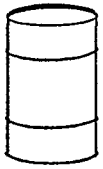
Tuesday, November 11, 1958

AFTERNOON

2:00 pm General Committee, Division of Finance and Accounting (Conrad Hilton–Parlor A)
Chairman: A. A. Buzzi

FINANCE and ACCOUNTING
NON-DIVISIONAL

NON-DIVISIONAL



GROUP SESSIONS

Committee on Public Affairs

Monday, November 10, 1958

11:00 AM

Open Meeting: (Conrad Hilton—Grand Ballroom)

Presiding: H. S. M. Burns, Chairman, API Board of Directors; President, Shell Oil Co., New York, N. Y.

Brief Review of Committee's Activities.
Kerryn King, Chairman, API Committee on Public Affairs; Vice President, The Texas Co., New York, N. Y.

The Oil Industry as Viewed by Two of the Nation's Top Editors.
Lyle C. Wilson, Vice President and Washington Manager, United Press International, Washington, D. C.
Louis B. Seltzer, Editor, The Cleveland Press, Cleveland, Ohio.

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Committee on Petroleum Statistics

Tuesday, November 11, 1958

10:00 AM

Open Session: (Conrad Hilton—Waldorf Room)

Presiding: Maynard I. Landa, Chairman, API Committee on Petroleum Statistics; Petroleum Economics Coordinator, Cities Service Co., New York, N. Y.

The Economic Outlook for 1959 and Its Impact on Automobile Sales.
R. J. Eggert, Marketing Research Manager, Ford Motor Co., Dearborn, Mich.

U. S. Petroleum Forecast and Dynamic World Growth in Petroleum Demands.
Austin Cadle, Manager, Economics Dept., Standard Oil Co. of California, San Francisco, Calif.

Oil's Challenge to the Economist.
Robert G. Dunlop, President, Sun Oil Co., Philadelphia, Pa.

GROUP SESSIONS (continued)

Petroleum-Industry Buyers

Tuesday, November 11, 1958

2:00 PM

Petroleum-Industry Buyers Session: (Conrad Hilton—Boulevard Room)

Presiding: D. A. Monro, Chairman, Petroleum-Industry Buyers Group of the National Association of Purchasing Agents; Director of Purchases, Standard Oil Co. (Indiana), Chicago, Ill.

Tangible and Intangible Values.
Hon. Charles E. Wilson, former Secretary of Defense and former President of General Motors Corp., Bloomfield Hills, Mich.

The Biggest Management Job Ahead.
Lemuel R. Boulware, Vice President, General Electric Co., New York, N. Y.

Inventory Utilization Program—Panel Discussion.

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COMMITTEE MEETINGS

Friday, November 7, 1958

MORNING

9:00 am Panel on Hurricanes (All Day) (Conrad Hilton—PDR 5)
Chairman: M. H. Parks

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Saturday, November 8, 1958

MORNING

9:00 am Advisory Committee on Fundamental Research on Occurrence and Recovery of Petroleum (All Day) (Conrad Hilton—PDR 2)
Chairman: J. E. Sherborne

COMMITTEE MEETINGS (continued)

Saturday, November 8, 1958

MORNING

9:00 am Research Project 44 Advisory Committee (All Day) (Conrad Hilton—PDR 3)
Chairman: C. E. Moser

9:00 am Committee on Positive Displacement Metering Measurement (All Day) (Conrad Hilton—Bel Air Room)
Chairman: M. L. Barrett

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Sunday, November 9, 1958

MORNING

9:00 am Research Project 6 Advisory Committee (Conrad Hilton—Room 18)
Chairman: C. W. Montgomery

9:00 am Research Project 45 Advisory Committee (Conrad Hilton—Room 19)
Chairman: E. C. Hughes

9:00 am Interdivisional Committee on Labeling (Conrad Hilton—PDR 3)
Chairman: M. D. Gjerde

9:00 am Committee on Crude-Oil Measurements (All Day) (Conrad Hilton—Parlor B)
Chairman: F. H. Warren

9:30 am Committee on Petroleum Statistics (All Day) (Conrad Hilton—Parlor C)
Chairman: Maynard I. Landa

AFTERNOON

1:00 pm Advisory Committee on Fundamental Research on Weather Forecasting (Conrad Hilton—PDR 4)
Chairman: F. L. Hartley

2:00 pm Committee on Agriculture (Conrad Hilton—Room 18)
Chairman: E. P. Williams, Jr.

4:00 pm Executive Committee (of the Advisory Committee on Fundamental Research on Composition and Properties of Petroleum) (Conrad Hilton—PDR 9)
Chairman: A. L. Lyman

COMMITTEE MEETINGS (continued)

Monday, November 10, 1958

MORNING

8:30 am Joint Meeting: (Conrad Hilton—Beverly Room)

Central Committee on Accident Prevention
(J. B. DeLaune, Chairman)

Central Committee on Fire Protection
(W. Boon, Chairman)

(*Note:* Premiere showing of film—DANGER!!! WATER!!!—at 11:30 am.)

9:00 am Advisory Committee on Fundamental Research on Occurrence and Recovery of Petroleum (Conrad Hilton—PDR 4)
Chairman: J. E. Sherborne

9:00 am Research Project 42 Advisory Committee (Conrad Hilton—PDR 8)
Chairman: G. H. Denison

9:00 am Committee on Petroleum Statistics (Conrad Hilton—Parlor C)
Chairman: Maynard I. Landa

9:00 am NEC Coordinating Committee (All Day) (Conrad Hilton—Room 19)
Chairman: E. R. Hoyle

10:00 am Committee on Gas and Electric Cutting and Welding (Conrad Hilton—Room 13)
Chairman: A. G. Ford

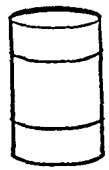
10:00 am Committee on Off-the-Job Safety (Conrad Hilton—PDR 3)
Chairman: J. H. McKenzie

10:00 am Committee on Safety Awards (Conrad Hilton—PDR 1)
Chairman: H. T. Markee

10:00 am Agricultural Advisory Committee (Conrad Hilton—Room 18)
Chairman: W. W. Vandeveer

10:00 am Asphalt Committee (Conrad Hilton—Room 14)
Chairman: Glenn E. Nielson

NON-DIVISIONAL (continued)



COMMITTEE MEETINGS (continued)

Monday, November 10, 1958

AFTERNOON

12:00 N Medical and Health Committee of the Board of Directors (Luncheon) (Conrad Hilton–PDR 9)
Chairman: D. T. Staples

1:30 pm Committee on Fire-Protection Engineering (Conrad Hilton–Beverly Room)
Chairman: J. E. Hill

2:00 pm Advisory Committee on Fundamental Research on Composition and Properties of Petroleum (Conrad Hilton–PDR 2)
Chairman: A. L. Lyman

2:00 pm Committee on Personal Protective Equipment (Conrad Hilton–PDR 1)
Chairman: W. E. Lovejoy

7:00 pm Committee on Fire-Protection Engineering (Conrad Hilton–Beverly Room)
Chairman: J. E. Hill

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Tuesday, November 11, 1958

MORNING

8:00 am Highway Coordinating Committee (Breakfast) (Conrad Hilton–Astoria Room)
Chairman: T. S. Petersen

8:30 am Committee on Tanks (All Day) (Conrad Hilton–PDR 1)
Chairmen: H. K. Ball
J. Howard Myers

8:30 am Committee on Safety and Fire Protection in Drilling and Production Operations (All Day) (Conrad Hilton–PDR 3)
Chairman: H. H. Myers

9:00 am Committee on Traffic Safety (Conrad Hilton–PDR 4)
Chairman: J. C. Wilson

9:00 am Research Projects 48 and 52 Advisory Committees (All Day) (Conrad Hilton–PDR 2)
Chairmen: C. E. Johnson
G. R. Lake

COMMITTEE MEETINGS (continued)

Tuesday, November 11, 1958

MORNING

9:30 am Aviation Advisory Committee (Conrad Hilton–Bel Air Room)
Chairman: Edward Keightley

10:00 am Defense Services Committee (Conrad Hilton–PDR 8)
Chairman: H. S. Merriman

AFTERNOON

12:00 N Safety Committee of the Board of Directors (Luncheon) (Conrad Hilton–PDR 10)
Chairman: R. G. Follis

1:30 pm Committee on Fire-Protection Regulations (Conrad Hilton–Upper Tower)
Chairman: C. D. Norris

2:00 pm Committee on Petroleum Statistics (Conrad Hilton–Astoria Room)
Chairman: Maynard I. Landa

2:30 pm Committee on Liquefied Petroleum Gas (Conrad Hilton–Beverly Room)
Chairman: G. R. Benz

2:30 pm Safety and Fire-Protection Program Committee (Conrad Hilton–Room 12)
Chairman: B. G. Crane

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Tuesday, November 11, 1958

AFTERNOON

4:00 pm Committee on Visual Aids (Conrad Hilton–PDR 4)
Chairman: R. D. Swanson

5:30 pm Committee on Visual Aids (Film Presentation) (Conrad Hilton–Waldorf Room)
Chairman: R. D. Swanson

COMMITTEE MEETINGS (continued)

Wednesday, November 12, 1958

MORNING

8:30 am Committee on Safety and Fire Protection in Manufacturing Operations (Conrad Hilton–Parlor A)
Chairmen: P. F. Lindemann
R. A. Randels

8:30 am Committee on Safety and Fire Protection in Pipeline Operations (Conrad Hilton–PDR 4)
Chairman: C. H. Lindberg

9:00 am Committee on Accident Statistics (Conrad Hilton–Astoria Room)
Chairman: H. T. Markee

AFTERNOON

12:00 N Research Committee of the Board of Directors (Luncheon) (Conrad Hilton–PDR 1)
Chairman: M. E. Spaght

1:30 pm Committee on Static Electricity and Stray Currents (Conrad Hilton–Parlor A)
Chairman: J. C. Howard

1:30 pm Committee on Safety and Fire Protection in Marketing Operations (Conrad Hilton–PDR 2)
Chairman: F. R. McLean

2:00 pm Committee on Safety and Fire Protection in Geophysical Operations (Conrad Hilton–PDR 4)
Chairman: Fred Clairborne

COMMITTEE MEETINGS (continued)

Thursday, November 13, 1958

MORNING

8:30 am Joint Meeting (All Day): (Conrad Hilton–PDR 2)
Central Committee on Accident Prevention
(J. B. DeLaune, Chairman)
Central Committee on Fire Protection
(W. Boon, Chairman)