

Castleman File: American Petroleum Institute
w/c = with cover letter or memo If DATE = 0, undated
CD-ROM Document #: API 24 DATE 1950

- published article from trade journal
- published advertisements
- newspaper article
- published government report
- government inspection results
- unpublished or internal report
- unpublished presentation from conference
- letter
- memorandum
- industry warning labels
- industry sales literature
- industry recommended practices
- ✓ — meeting minutes (with attachments)
- membership list
- BC notes

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

File

January 12, 1950

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

CABLE ADDRESS: KETLAB, CINCINNATI
TELEPHONE: CAPITOL 1414

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

Dear Mr. Stoop:

I herewith acknowledge with thanks receipt of American Petroleum Institute's check in the amount of \$39,963.39, covering expenditures to be made on their behalf for the balance of the year ending June 30, 1950.

Very truly yours,

E. R. Fortlage

E. R. Fortlage, Secretary to
Dr. Kehoe

ef

API 04917

January 10, 1950

Dr. Robert A. Kehoe
Mettering Laboratory of Applied Physiology
College of Medicine
University of Cincinnati
Cincinnati 19, Ohio

Dear Doctor Kehoe:

Pursuant to the terms of the continuation agreement of June 30, 1949 we enclose the Institute's check in the amount of \$38,963.39 to continue the investigation of the toxicity and mode of action of certain petroleum products for the balance of the year ending June 30, 1950.

The figure of \$38,963.39 is the difference between the balance of \$49,412.08 stated in the agreement and the \$10,448.61 unexpended balance as of June 30, 1949.

Very truly yours,

BWS:d
Enclosure

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

February 16, 1951

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

CABLE ADDRESS. KETLAB CINCINNATI
TELEPHONE. CAPITOL 1414

KD
FILE

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

Dear Mr. Stroop:

I am sending you herewith, for your information, a statement of expenditures made on behalf of The American Petroleum Institute for the fourth quarter of 1949. If you have any questions or comments, Doctor Kehoe would appreciate your bringing them to his attention.

Very truly yours,

E. R. Fortlage, Jr.
E. R. Fortlage, Secretary to
Dr. Kehoe

ef

Enc.

UNIVERSITY OF CINCINNATI
KETTERING LABORATORY
ACCOUNT OF AMERICAN PETROLEUM INSTITUTE

For the Fourth Quarter 1949

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

Robert A. Kehoe	- Supervision	17.30
Francis Heyroth	- Chemical and Toxicological Asst.	38.37
Frank Dutra	- Pathological Assistance	14.01
Frank Cleveland	- " "	88.56
A. Wesley Horton	- Chemical Assistance	1800.00
John Phair		1375.02
Dorothy Templeton-a	" "	303.54
Russell Tye	- " "	900.00
Karl Korpi	- Technical Assistance	135.54
Sylvan Witherup	- " "	160.35
Ruth Pierle	- " "	1125.00
Waldo Younker	- " "	47.86
Harold Schlecht	- " "	7.78

6013.33

MISCELLANEOUS EXPENSE

Purchase of Animals	119.21
Laboratory Supplies	328.37
Traveling Expense	1194.02
Proportion of Secretarial, Library, Janitors, Wash Boys, Draftsman, Shipping Clerks, Animal Caretakers, Histopathological Preparation etc	2598.32
Proportion of Heat, Gas, Electricity, Steam, Telephone, Maintenance, Pensions, Annuities etc	2378.38

TOTAL \$12,631. 63

Balance Available for Work in 1949	
at End of 3rd Quarter 1949	\$47,225.78
Expenditures 4th Quarter 1949	<u>12,631.63</u>
Balance Available for Work in 1950	
at End of 4th Quarter	34,594.15

HARVARD UNIVERSITY

OFFICE OF THE ASSISTANT
TO THE PRESIDENT

March 6, 1950

24 MILK STREET
BOSTON 9, MASSACHUSETTS

AD
FILE

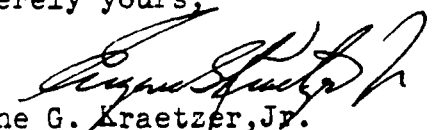
Mr. David V. Stroup, Director
American Petroleum Institute
50 West 50th Street
New York 20, N.Y.

Dear Mr. Stroup:

We are pleased to enclose Harvard's formal acknowledgment for your valued assistance in the matter of the grant to the Department of Industrial Hygiene.

As you requested, I return two copies of the letter of authorization duly accepted on behalf of Harvard.

Sincerely yours,


Eugene G. Kraetzer, Jr.
Recording Secretary

EGKJr/S

API 04921

AMERICAN PETROLEUM INSTITUTE

50 WEST 50TH STREET

NEW YORK 20, N. Y.

DEPARTMENT OF SAFETY
DAVID V. STROOP, DIRECTOR

February 28, 1950

Mr. U. Haskell Crocher
Harvard University
24 Milk Street
Boston 9, Mass.

Dear Mr. Crocher:

This letter is authorization to continue the investigation of permissible concentrations of toxic substances, known as American Petroleum Institute Medical Project No. 2; Professor Philip Brincker, Director, as planned and administered cooperatively with the Subcommittee on Permissible Concentrations of the API Medical Advisory Committee, from March 15, 1950 to June 30, 1950, subject to the following conditions:

1. Budget

Salaries and Expenses \$3,000

2. Our check in the amount of \$3,000 is enclosed. On June 30, 1950 the project is to terminate. As of that date a statement of the amount expended and the balance in the fund will be rendered to Lacey Walker, Secretary, American Petroleum Institute, 50 West 50th Street, New York 20, New York.

3. While it is not anticipated that patentable developments will arise out of this project, it is understood and agreed that if such should arise, the benefits will be dedicated to the public by publication or otherwise.

Very truly yours,

AMERICAN PETROLEUM INSTITUTE

By

W. M. Mays
President
Lacey Walker
Secretary

Accepted by:

President and Fellows of
HARVARD COLLEGE, by

Frederic S. Sturges
Assistant Secretary

BY
DATE

API 04922

AMERICAN PETROLEUM INSTITUTE

50 WEST 50TH STREET

NEW YORK 20, N. Y.

DEPARTMENT OF SAFETY
DAVID V. STROOP, DIRECTOR

February 28, 1950

Mr. U. Haskell Crocker
Harvard University
24 Milk Street
Boston 9, Mass.

Dear Mr. Crocker:

This letter is authorization to continue the investigation of permissible concentrations of toxic substances, known as American Petroleum Institute Medical Project No. 2; Professor Philip Drinker, Director, as planned and administered cooperatively with the Subcommittee on Permissible Concentrations of the API Medical Advisory Committee, from March 15, 1950 to June 30, 1950, subject to the following conditions:

1. Budget

Salaries and Expenses \$3,000

2. Our check in the amount of \$3,000 is enclosed.

On June 30, 1950 the project is to terminate. As of that date a statement of the amount expended and the balance in the fund will be rendered to Lacey Walker, Secretary, American Petroleum Institute, 50 West 50th Street, New York 20, New York.

3. While it is not anticipated that patentable developments will arise out of this project, it is understood and agreed that if such should arise, the benefits will be dedicated to the public by publication or otherwise.

Very truly yours,

AMERICAN PETROLEUM INSTITUTE

By

W. M. K. K.
President
L. Walker
Secretary

Accepted by:

President and Fellows of
HARVARD COLLEGE, by

Frederic S. ...

Assistant Secretary
ASSISTANT SECRETARY
TO THE CORPORATION



President and Fellows of Harvard College

desire to express their gratitude to

American Petroleum Institute

for the generous gift of

three thousand dollars on account of a
renewed grant to continue investigation
of permissible concentrations of toxic
substances, under the direction of Pro-
fessor Philip Drinker.


Recording Secretary

March 6, 1950

February 28, 1950

Professor Philip Brinker
Harvard University
School of Public Health
55 Shattuck Street
Boston 15, Mass.

Dear Professor Brinker:

In response to your letter of February 18 we are enclosing both the letter of authorization (three copies) and our check in the amount of \$3,000 to cover the continuation of Medical Project No. 2 from March 15 until June 30, 1950, at which time it is to terminate.

We trust that the letter of authorization is satisfactory to you and the Treasurer and that two signed copies may be returned to us.

Very truly yours,

DVB:d

Enclosures

cc: Dr. V. S. Baird
Dr. Kleffer Davis
Dr. J. P. Holt
Mr. Lacey Walker

API 04925

February 28, 1970

Mr. U. Marshall Crocker
Harvard University
24 Milk Street
Boston 9, Mass.

Dear Mr. Crocker:

This letter is authorization to continue the investigation of permissible concentrations of toxic substances, known as American Petroleum Institute Medical Project No. 2; Professor Philip Brinker, Director, as planned and administered cooperatively with the Subcommittee on Permissible Concentrations of the API Medical Advisory Committee, from March 15, 1970 to June 30, 1970, subject to the following conditions:

1. Budget

Salaries and Expenses \$3,000

2. Our check in the amount of \$3,000 is enclosed. On June 30, 1970 the project is to terminate. As of that date a statement of the amount expended and the balance in the fund will be rendered to Larry Walker, Secretary, American Petroleum Institute, 50 West 50th Street, New York 20, New York.

3. While it is not anticipated that patentable developments will arise out of this project, it is understood and agreed that if such should arise, the benefits will be dedicated to the public by publication or otherwise.

Very truly yours,

AMERICAN PETROLEUM INSTITUTE

By _____
President

Secretary

Accepted by:
President and Fellows of
HARVARD COLLEGE, by



President and Fellows of Harvard College

desire to express their gratitude to

American Petroleum Institute

for the generous gift of

ten thousand dollars in continued support of investigation of permissible concentrations of toxic substances under the direction of Dr. Philip Drinker, as stated in their letter dated March 14, 1949 to Mr. Claflin.

W. H. C. Carter.

Recording Secretary

March 17, 1949

HARVARD UNIVERSITY

OFFICE OF SPECIAL ADVISER
TO THE PRESIDENT

March 17, 1949

Handwritten: For Mr. Crocker
24 MILK STREET
BOSTON 9, MASSACHUSETTS

Mr. David V. Stroop, Director
Department of Safety
American Petroleum Institute
50 West 50th Street
New York 20, N.Y.

Dear Mr. Stroop:

This will acknowledge receipt of the letter of March 14 from the American Petroleum Institute to Mr. Claflin, who resigned as Treasurer last June 30.

I take pleasure in enclosing herewith our formal acknowledgment for the very welcome gift of \$10,000 for the continuation of the investigation which is being carried on under the direction of Dr. Philip Drinker. We are indeed grateful to the American Petroleum Institute for this additional assistance.

I also return herewith two copies of the letter setting forth the conditions on which this project is being undertaken. I have indicated Harvard's acceptance by signing this letter as Assistant Secretary.

Sincerely yours,

U. Haskell Crocker

U. Haskell Crocker
Recording Secretary

S

AMERICAN PETROLEUM INSTITUTE

50 WEST 50TH STREET

NEW YORK 20, N. Y.

March 14, 1949

DEPARTMENT OF SAFETY
DAVID V. STROOP, DIRECTOR

Mr. William E. Claflin, Jr.
Treasurer of Harvard University
24 Milk Street
Boston, Mass.

Dear Mr. Claflin:

This letter is authorization to continue the investigation of permissible concentrations of toxic substances, known as American Petroleum Institute Medical Project No. 2; Professor Philip Brinker, Director, as planned and administered cooperatively with the Subcommittee on Permissible Concentrations of the API Medical Advisory Committee, from March 15, 1949 to March 14, 1950, subject to the following conditions:

1. Budget

Salaries and Expenses \$10,000

2. Our check in the amount of \$10,000 is enclosed. As of March 14, 1950, a statement of the amount expended and the balance in the fund will be rendered to Lacey Walker, Secretary, American Petroleum Institute, 50 West 50th Street, New York 20, N.Y.

3. If the work under this project should terminate on or before March 14, 1950, it is understood that any unexpended balance in the fund will be returned to the Institute. If the work is to be continued on and after March 15, 1950, any unexpended balance in the fund shall become available for and be added to the budget for the ensuing year.

4. While it is not anticipated that patentable developments will arise out of this project, it is understood and agreed that if such should arise, the benefits will be dedicated to the public by publication or otherwise.

Very truly yours,

AMERICAN PETROLEUM INSTITUTE

By W. E. Claflin, Jr. President
Lacey Walker Secretary

Accepted by:
President and Fellows of
HARVARD COLLEGE, by

W. Haskell Currier

U. HASKELL CURRIER

Assistant Secretary

API 04929

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

March 14, 1949

DEPARTMENT OF SAFETY
DAVID V. STROOP, DIRECTOR

Mr. William H. Claflin, Jr.
Treasurer of Harvard University
24 Milk Street
Boston, Mass.

Dear Mr. Claflin:

This letter is authorization to continue the investigation of permissible concentrations of toxic substances, known as American Petroleum Institute Medical Project No. 2; Professor Philip Brinker, Director, as planned and administered cooperatively with the Subcommittee on Permissible Concentrations of the API Medical Advisory Committee, from March 15, 1949 to March 14, 1950, subject to the following conditions:

1. Budget
Salaries and Expenses \$10,000

2. Our check in the amount of \$10,000 is enclosed. As of March 14, 1950, a statement of the amount expended and the balance in the fund will be rendered to Lacey Walker, Secretary, American Petroleum Institute, 50 West 50th Street, New York 20, N.Y.

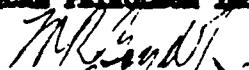
3. If the work under this project should terminate on or before March 14, 1950, it is understood that any unexpended balance in the fund will be returned to the Institute. If the work is to be continued on and after March 15, 1950, any unexpended balance in the fund shall become available for and be added to the budget for the ensuing year.

4. While it is not anticipated that patentable developments will arise out of this project, it is understood and agreed that if such should arise, the benefits will be dedicated to the public by publication or otherwise.

Very truly yours,

AMERICAN PETROLEUM INSTITUTE

By



President



Secretary

Accepted by:
President and Fellows of
HARVARD COLLEGE, by



Assistant Secretary

API 04930

March 14, 1949

Professor Philip Drinker
Harvard University
School of Public Health
55 Shattuck Street
Boston 15, Mass.

Dear Professor Drinker:

We have been delayed in the negotiation of our continuing agreement on Medical Project No. 2; therefore, we are enclosing both the letter of authorization (3 copies) and our check in the amount of \$10,000.

We trust that both are in good form and acceptable to you and the Treasurer of Harvard University.

If, as, and when accepted, please return two signed copies of the letter for our use and files.

Very truly yours,

DVS:d

Enclosures

cc: Dr. V. C. Baird
Dr. A. E. Houg
Dr. J. P. Holt

From the office of

DAVID V. STROOP

9/14/49

To WRB Jr

PLEASE SIGN 4 COPIES OF
THIS AGREEMENT WHICH COVERS
CONTINUATION OF MEDICAL
RESEARCH PREVIOUSLY APPROVED
BY EXECUTIVE COMMITTEE
AND FINANCED BY SPECIAL
FUNDS CONTRIBUTED IN 1948

①/2

Feb-1950
~~March 14, 1949~~ 1950
1950 to June 30 1950

Mr. William H. Claflin, Jr.
Treasurer of Harvard University
24 Milk Street
Boston, Mass.

Dear Mr. Claflin:

This letter is authorization to continue the investigation of permissible concentrations of toxic substances, known as American Petroleum Institute Medical Project No. 2; Professor Philip Drinker, Director, as planned and administered cooperatively with the Subcommittee on Permissible Concentrations of the API Medical Advisory Committee, from March 15, 1949 to March 14, 1950, subject to the following conditions:

1. Budget 3000
Salaries and Expenses ~~(10,000)~~

2. Our check in the amount of ~~3000~~ ~~(10,000)~~ is enclosed. As of March 14, 1950, a statement of the amount expended and the balance in the fund will be rendered to Lacey Walker, Secretary, American Petroleum Institute, 50 West 50th Street, New York 20, N.Y.

3. If the work under this project should terminate on or before March 14, 1950, it is understood that any unexpended balance in the fund will be returned to the Institute. If the work is to be continued on and after March 15, 1950, any unexpended balance in the fund shall become available for and be added to the budget for the ensuing year.

4. While it is not anticipated that patentable developments will arise out of this project, it is understood and agreed that if such should arise, the benefits will be dedicated to the public by publication or otherwise.

Very truly yours,

AMERICAN PETROLEUM INSTITUTE

By _____
President

Secretary

Accepted by:
President and Fellows of
HARVARD COLLEGE, by

For Information Only - Not For Publication

AMERICAN PETROLEUM INSTITUTE

SUBCOMMITTEE ON CARCINOGENICITY

Minutes of Meeting
March 25, 1950
Kettering Laboratory
College of Medicine
University of Cincinnati
Cincinnati, Ohio

Members Present

McIver Woody (Chairman)
Marshall Clinton
T. M. Frank
A. E. Hoag
J. P. Holt (Rep. by R. E. Eckardt)
T. J. Kelly
J. W. Long
M. N. Newquist

Associates Present

L. C. Beard, Jr.
L. C. Crockett
R. M. Landon
E. P. Lankeima
K. G. Mackenzie
R. M. Shepardson

Visitors

T. E. Allen
F. F. Boys
J. W. Crockshank
Kieffer Davis
E. K. Linder
B. B. Reeve

E. W. Adams
R. D. Bent
R. C. Cole
T. E. DeVilliers
L. M. Henderson

Guests

Lewis J. Cralley - U. S. Public Health Service
Francis Heyroth - University of Cincinnati
A. W. Horton - University of Cincinnati
R. A. Kehoe - University of Cincinnati
John J. Phair - University of Cincinnati
D. V. Stroop - American Petroleum Institute
J. G. Townsend - U. S. Public Health Service
E. R. Warrick - The Texas Company

Members Absent

L. E. Curtis
W. R. Levis
Chas. A. Swan

Associates Absent

R. W. Faulk
E. G. M. Fischer
Allen E. Docley

.....

THE KETTERING LABORATORY OF APPLIED PHYSIOLOGY

Dr. Robert A. Kehoe, Director, welcomed the members and guests and gave them an historical review of the origin and growth of the Kettering Laboratory.

He expressed appreciation for the contribution of capital funds made by the petroleum industry and described the facilities which had been made possible by those funds.

He mentioned the types of industrial problems which are studied at the laboratory and reviewed in detail those problems which are under investigation for the petroleum industry.

He emphasized the exceptional character of the API project on carcinogenicity because it constitutes an organized study of a problem prior to the occurrence of trouble. Usually the trouble occurs before any investigation is made.

PROGRESS REPORT

1. Dr. A. Wesley Horton presented and discussed his report of March 15th, a copy of which is attached.
2. Dr. John J. Phair discussed progress and plans being made on the epidemiological studies for the project. See attached copy of Dr. Phair's report.
3. For the information of those present, D. V. Stroop read draft of progress report which was in preparation for John R. Suman, Chairman of the Safety Committee of the Board of Directors, to present to the Board at its meeting to be held in Houston, Texas on April 3rd.

A copy of the report as presented by Mr. Suman is attached.

GUESTS

Dr. Woody introduced Dr. J. G. Townsend, Chief, Division of Industrial Hygiene, Public Health Service, who reviewed the division's long experience with scrotal and other forms of cancer incidental to workers in wax-pressing operations.

He reminded the members that the Public Health Service is not empowered to control or regulate industrial operations; it can only suggest or recommend precautionary and remedial measures to improve industrial hygiene conditions.

He called attention to the U. S. Public Health laboratory in Cincinnati and tendered the services of a liaison officer to work with Dr. Kehoe and to correlate plans so as to avoid duplication of work with that now being conducted for the Bureau of Mines on shale oil.

He expressed his appreciation of the opportunity to attend the meeting and to obtain first-hand information on the work being done by the industry at Kettering Laboratory.

Dr. Townsend introduced Dr. Cralley, who spoke briefly about his interest in the project.

TOUR OF LABORATORIES

Following a splendid luncheon served in the University of Cincinnati dining room, Drs. Kehoe and Heyroth conducted the members and guests on extended tours of inspection of the Kettering Laboratories.

EXECUTIVE SESSION

The members held a short executive session to discuss matters of business relating to the administration of the carcinogenicity project.

D. V. Stroop
Acting Secretary

Approved:

McIver Woody, M.D.
Chairman

For Information Only - Not For Publication

Report to Subcommittee on Carcinogenicity
of the

API Medical Advisory Committee

on

PROJECT ON CARCINOGENICITY AT THE
UNIVERSITY OF CINCINNATI

Operating data on the various cracking and lube refining processes have been received from over 90 per cent of the cooperating oil companies. Collection of the samples listed in Table 1 is under way, the materials being held temporarily in storage at the refineries until requested by the Kettering Laboratory for animal testing. Corresponding to each of the product samples listed, a sample of the feed stock to the particular unit is being collected at the same time. Thus, if any one of the products is found to have unusual carcinogenic properties, it will be possible to go back and determine the potency of the feed stream for a direct comparison.

Up to the present time, spectral analysis has continued to prove a reliable tool for the prediction of the carcinogenic potency of the various petroleum products to which it has been applied. Accordingly, it has been requested that this procedure be applied to each of the product samples listed in Table 1 by the company collecting it.

With all of the analytical and spectral absorption properties of the samples as well as the operating data on the units producing them before us, it will be possible to select the materials for animal testing in such a way that complete coverage of the various processes can be given and, at the same time, the validity of the spectral method of analysis for carcinogen concentration can be determined rigorously. The latter is a most important point since without a reliable analytical tool it might be necessary to keep a large scale animal testing program going continuously for several years.

This tentative sample list for the period, July 1950 to July 1951, is being submitted at this time for discussion and comments by the Members and Associates of the Medical Advisory Committee. We shall welcome any suggestions as to its organization. The complete list of the samples which are under study at the present time will be included in our April report which will be circulated in advance of the Chicago meeting. Doctor J. J. Phair will outline at that meeting the status of his epidemiological study.

A. Wesley Horton

AWE:fe
March 15, 1950

TABLE 1

UNIT	PRODUCTS							
	Heavy Gas Oils	Tars	Synthetic Bottoms	Slurry (Decanted Oil)	Coke	Slack Wax	Press Oil	Solvent Extracts
Gas Oil Cracking	5	23						
Viscosity Breaking	3	8						
Naphtha Reforming		4						
Coking	4				4			
Polyforming	1	4						
Houdry	5		8					
TCC	6		17					
FCC	12			10				
Cycloversion	2							
Hydroformer		2						
Wax Pressing						4	2	
Furfural Extraction								5
Phenol Extraction								15
Duosol Extraction								3
Nitrobenzene Extraction								1

TOTAL PRODUCT SAMPLES 148

For Information Only - Not for Publication

THE PROJECT ON CARCINOGENICITY
PROPOSED EPIDEMIOLOGICAL STUDIES

Objectives

Possible Approaches

Implementation

Preliminary Outline
for
The Subcommittee on Carcinogenicity
of the
API Medical Advisory Committee

March 25, 1950

OBJECTIVES

- I. To determine as accurately as possible, the prevalence and incidence rates of retrograde, hypertrophic, and/or neoplastic responses in man following various degrees of exposure during production, processing, transportation and consumption to:-
 - A. petroleum products obtained by catalytic cracking processes.
 - B. petroleum products obtained by thermal cracking processes.
 - C. products encountered in wax extraction.
 - D. special chemical products.
 - E. various crude oils.
- II. To compare, insofar as possible, the prevalence and incidence rates found with similar rates of:-
 - A. groups of workers in the petroleum industry not directly in contact with petroleum or its products.
 - B. groups not employed in the petroleum industry, such as:-
 1. the general population
 - a. of the nation.
 - b. of the same geographic areas.
 2. the employees of other industries
 - a. of the nation.
 - b. of the same geographic areas.

III. To ascertain and evaluate, insofar as possible, the relative values of control procedures that are:-

- A. accepted and employed at the present time by essentially the entire industry.
- B. recommended but not adopted or employed except by a few companies.
- C. additional measures which may become important during the course of this investigation.

IV. To recommend for consideration of all interested parties, employing the results of the laboratory and epidemiological studies, standardized safety and control procedures provided that:-

- A. unusual incidence or prevalence rates are found justifying the control procedures.
- B. the measures increase the safety and efficiency of the operation even though the rates might not indicate a significant hazard.

POSSIBLE APPROACHES

I. Historical

Under this approach, the cooperating companies will forward to the University of Cincinnati all available clinical and employment records of proven or suspected cases of neoplastic disease which have been reported among their employees during the past insofar as records are available.

II. Current Registry

A. Clinical and Employment Record Study

A central registry will be established by the University of Cincinnati group to receive reports of neoplastic disease as they are discovered by and/or reported currently to the various Medical Departments. With this plan, the various cooperating companies would submit a fairly complete clinical report and an adequate employment record using standardized record forms. These records can be expected to be somewhat more reliable than those forwarded under the Historical Approach, since they would be completed immediately upon the report of a case.

B. Central Pathology Service

As an adjunct to the central registry, it would seem desirable to plan for the establishment of a central pathology service so that a uniform tissue diagnosis would be available both for the study purposes and to stimulate the interest and cooperation of the various Medical Departments.

III. Employee Health Record Study

In this investigation the epidemiological team of the University of Cincinnati would attempt a review of the employee health benefit records, not only of the various companies of the petroleum industry but certain other cooperating industries, to establish, insofar as possible, comparable incidence rates for all diseases. This approach, with due regard for the many variables, should develop certain useful intra- and extra-mural comparisons.

IV. Dermatological Field Study

This plan envisions field studies among various groups of workers employed not only in the petroleum industry but also in other industries with the objective of establishing comparable incidence rates for retrograde or hyperkeratotic lesions on the exposed skin surfaces. The groups to be surveyed by a trained team from the University of Cincinnati should be selected by an authorized committee familiar with all the possible variables and capable of securing adequate cooperation by all interested groups. These rates, if some degree of correlation is shown, could be used to determine susceptibility of individuals or groups, to estimate the degree of hazard in various situations and to evaluate control procedures that may be proposed.

V. Slack Wax Study

An investigation by one of the interested members of this group has pointed out an unusual hazard in their slack wax process. In view of this finding, it would be desirable for the survey group of the University of Cincinnati, working either independently or with some other company and/or companies, to repeat this investigation.

IMPLEMENTATION

I. Historical Approach

This approach was approved in principle at the November, 1949 meeting of the Medical Advisory Committee following the report of the Subcommittee. Actual work was held up until the various Medical Directors and Technical Advisors could be contacted individually for their suggestions regarding the clinical and employment records to be employed. It was necessary also to determine legal right of the various Medical Departments to release clinical records of their employees to an independent agency.

These questions have been fully clarified, and the new record forms embodying the various suggestions are being drafted. The proposed handling of the individual records so that the Medical Departments will not incur a liability because of their release to an independent agency with the standard records will be included in the formal report to be made at the April meeting in Chicago.

II. Current Registry

A. Clinical and Employment Record Study

Since the records and questions involved under this plan are very similar to those found with the Historical Approach, this effort has likewise awaited completion of the various interviews, although the concept was approved in principle at the November meeting. It is hoped that this work can begin early this summer.

II. Current Registry (Cont.)

B. Central Pathology Service

This is a new venture and one that is favored by many of the Medical Directors. Before it can be placed into operation, however, it will be necessary to determine if all believe that it is desirable and an acceptable method of financing.

III. Employee Health Record Study

This plan has been discussed only with a few of the Medical Directors. Before definitive action can be taken, this approach should be discussed thoroughly by the Medical Advisory Committee, since a great deal of effort will be required both from the various companies as well as the University of Cincinnati to bring it to a successful termination.

IV. Dermatological Field Survey

This, too, is a concept which has not been completely discussed and must be explored thoroughly by all interested parties. Financing and staffing would be problems, but this approach could be tested thoroughly within a very short time. If proven valid, it should give answers to the proposed objectives much more quickly and easily than any other method.

V. Slack Wax Study

It is apparent now that the probable implementation of this approach will require the cooperation of one or two companies in the industry. If the Medical Advisory Committee approves and interested companies can be found, this investigation could get under way very shortly without too much trouble.

SAFETY COMMITTEE OF BOARD OF DIRECTORS

REPORT OF CHAIRMAN - JOHN R. SUMAN

Concurrently with important developments in refining methods, processes, and products, the industry's toxicological problems are growing in number and complexity. Oil companies are making substantial increases in their medical staffs and facilities.

These developments led to the creation of the Institute's Medical Advisory Committee in 1945. Since then the committee has served constructively by making useful information available to oil companies for their protection of employees and customers against accidental injury and for the defense of industry against unreasonable and unnecessary laws and regulations, as well as unjustified and false claims for damages.

The organization of this committee and its semiannual meetings have facilitated an informal exchange of medical information of intangible but substantial value in the prevention and treatment of industrial injuries and occupational disease.

The committee also has been instrumental in organizing special studies and investigations on important toxicological problems with cooperative grants-in-aid at the University of Cincinnati and Harvard University.

The initiation of this work promptly after the end of the war has placed the industry in a favorable position at a time when numerous proposals are being made to give government new and far-reaching controls in the field of industrial medicine and hygiene.

The individual members of the committee, through their several professional channels and associations, acquire valuable information regarding these trends in regulatory legislation. The pooling of the information thus obtained clearly indicates trends which are disquieting.

Highlighted by the California smog problems and supplemented by the reports on the Donora situation, there is an active drive to impose an American Standard Code on Industrial Hygiene. This proposal is put forward by the American Conference of Governmental Industrial Hygienists, which has drafted a code that is far from realistic and shows little sympathy for the practical needs of industry. If adopted generally, such an arbitrary code would impose unreasonable and unnecessary restrictions upon industry, and might readily become the basis for state laws and regulations.

Another indication of the growing interest of government is a letter recently received from the Chief, Division of Industrial Hygiene, Public Health Service. He suggested a meeting with the Medical Advisory Committee to discuss potential health hazards and possible control procedures in the petroleum industry. The committee has invited him to attend its regular mid-year meeting in April and has held some preliminary discussions with his representatives at a recent subcommittee meeting held at Kettering Laboratory in Cincinnati.

Because of enforcement difficulties it may be safe to assume that statutory and regulatory control of industrial hygiene will be unreasonably restrictive and unnecessarily so for responsible and progressive companies which voluntarily are adopting policies to insure hygienic working conditions.

It is encouraging to note the number of companies which are adopting such progressive policies because it suggests the possibility of avoiding some or most statutory and regulatory controls.

AMERICAN PETROLEUM INSTITUTE

50 WEST 50TH STREET

NEW YORK 20, N. Y.

April 11, 1950

To Members and Associates
Subcommittee on Carcinogenicity

Gentlemen:

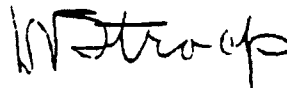
For your consideration in advance of your meeting to be held April 23, there is enclosed copy of Doctor Horton's report on the Institute's carcinogenicity project at the University of Cincinnati, with copy of his letter dated April 7th.

You will note that the report contains data which is to be published as provided for in the contract between the Institute and the University.

Pursuant to action taken by the Executive Committee of the Board of Directors on November 10, 1949, John R. Suman, Chairman, Safety Committee of the Board of Directors, has instructed me to send copies of this report to the members of the General Committee, Division of Refining.

Copies of the report also are being sent to members of the Safety Committee of the Board and to all members and associates of the Medical Advisory Committee.

Very truly yours,



D. V. Stroop

DVS:d
Enclosures

MC: Members, Safety Committee of the Board of Directors.
Members, General Committee, Division of Refining.
Members and Associates, Medical Advisory Committee.
Mr. W. T. Gunn
Dr. A. Wesley Horton (5 copies)

C O P Y

C O P Y

C O P Y

UNIVERSITY OF CINCINNATI

Department of Preventive Medicine and Industrial Health

April 7, 1950

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

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

Dear Mr. Stroop:

Attached is our report on the technological, biological and chemical aspects of the carcinogenicity project. If possible, will you please have this progress report duplicated for distribution to each of the members and associates of the API Medical Advisory Committee prior to the meeting in Chicago on April 23? I should appreciate if you could let me have five copies for distribution to the various people here at the Kettering Laboratory. At least twenty additional copies should be brought to the committee meeting on April 23 for those members who will not have theirs before them.

We should like to submit for publication in the journal "Cancer Research" the data in Table II of the report with the dose-response curves of the two strains of mice to the various concentrations of methylcholanthrene. Will you please advise the members of the Medical Advisory Committee of our intentions in accordance with the machinery set up for publications at the recent meeting at the Kettering Laboratory? We shall conform to the suggested 30-day waiting period before submitting our paper to the editor of the journal.

The fact has already been published in this journal that high-boiling catalytically cracked oils have a marked carcinogenic potency toward mice, (see, for example, Sugiura, Smith and Sunderland, "Cancer Research" vol. 9, p. 631, 1949). Hence we consider it highly desirable to include in our paper the TI curves for Oils No. 8 and No. 9 in order to demonstrate that while it is true that some high-boiling catalytically cracked oils have a high potency, an equal number will be found to have a relatively low position on the scale. For the time being, these oils will be designated simply as typical oils of this type.

Very truly yours,

/s/ A. W. Horton

A. Wesley Horton

AWH ef

Enc.

C.C.: Dr. McIver Woody
Dr. Kieffer Davis

API 04949

C O F Y

C O P Y

C O F Y

For Information Only - Not for Publication

Report to Subcommittee on Carcinogenicity

of the

API Medical Advisory Committee

PROJECT ON CARCINOGENICITY AT THE
UNIVERSITY OF CINCINNATI

A tentative list of samples to be studied during the period, July 1950 to July 1951, was attached to the progress report which was distributed prior to the recent interim meeting on March 25, 1950. The collection of these refinery products is well under way, and programs have been set up at the various laboratories of the companies concerned to carry out the distillations and spectral analyses desired. A fair proportion of this work has already been completed and the spectra received seem very satisfactory for the prediction of the carcinogenic potencies of the oils. As rapidly as the facilities and the availability of animals permit, samples selected on the basis of the process and analytical data are being forwarded to Cincinnati for testing. At the same time we are making it a practice to advise each company of the interpretation of the spectral data submitted in order that they might know as early as possible the processes and products in their refineries which represent the greatest potential hazards from the cancer standpoint.

The biological experiments employing refinery samples, and fractions derived therefrom in the laboratory, are listed in the attached Table I. The potency PMC is defined as that concentration (in grams/100 ml.) of methylcholanthrene in benzene which has the same carcinogenic action on the mice as the oil in question. The values of PMC for those oils on which the tests are essentially complete are presented in Table I.

The concentration standards employing solutions of methylcholanthrene and 9,10-dimethyl-1,2-benzanthracene are listed in Table II. It will be recalled that the tumor index, TI, has been defined by the following relation:

$$TI = \frac{\text{Number of mice which have developed tumors}}{\text{"Effective group"}}$$

"Effective Group" = Number of mice given adequate exposure =

Original number of mice employed - Number of mice which have died without tumors prior to the appearance of tumor in the "average tumor-bearing mouse"

The "average mouse" is designated as the median in a simple arithmetic array of the times of appearance of tumors.

It will be noted from the times required to reach tumor indices of 50% that the albino CFW mice are much more susceptible to the carcinogenic action of methylcholanthrene than are the brown C3H mice when treated with the lower concentrations. Thus the CFW strain proves a very useful tool to determine the relative carcinogenicities of low potency oils in the shortest time. However, it has been found that the concentrations of methylcholanthrene greater than 0.15 gm./100 ml. give very ambiguous results with this strain. These undesirable side effects are not as disturbing in the brown C3H mice, and hence this strain is used for the higher potency oils almost exclusively.

The preliminary results with 9,10-dimethyl-1,2-benzanthracene (DMBA) indicate that it may be an equally satisfactory carcinogenic standard. Experiments 211 through 213 employing the nonvolatile solvent, dodecylbenzene, have run into serious difficulties because of a severe crusting effect of the skin of the mice caused by the solvent. Sample 218 is being tested to determine the effect of the viscosity of the solvent on the response to methylcholanthrene application.

In Table III are listed the painting and washing experiments being run at the present time. More severe tests are planned employing a frequency of application of three times per week.

The following four samples have been selected for exchange experiments to be run concurrently by the group at New York University:

Oils Nos. 8, 8-4, 25, and 25-1.

A standard solution of 0.1 grams/100 ml. of methylcholanthrene in benzene will be included for further correlation. We have discussed the desirability of communicating with representatives of the Institute of Petroleum to arrange a three-way exchange program employing these same oils.

To date in the chemical laboratory the presence of the following polycyclics in high-boiling catalytically cracked oil has been determined with a good degree of certainty:

perylene, 4-methylpyrene and chrysene.

From preliminary data on the distillation fractions it would appear that the pyrene and the perylene nuclei predominate among the polycyclic aromatic hydrocarbons in these oils boiling from 750° to 1100°F. A continued effort is being made to isolate the compound responsible for the absorption peak at 430 millimicrons. This material has an extremely high boiling point, and it seems not unlikely that isolation and characterization will prove it to be one of the highly carcinogenic dibenzpyrenes.

A. Wesley Horton

AWH ef
April 7, 1950

Table I
Skin Painting Experiments on High Boiling
Samples

API Sample Number	Process	Product	Gravity	Boiling Range ° F.			Sulfur %	P _{MC}
				10%	90%	E.P. % - °F.		
5	Straight Run Distilla- tion	Residuum From Wilmington Crude 11885	12.8			59-940	1.97	0
6	Thermal Cracking	Tar W-3631	5.2	586		58-666	1.55	40.03
6-1*	Dilution	77% Oil No. 6 23% Benzene						--
7	TCC	Bottoms N8295-2	20.2	463	570		0.39	40.01
8	FCC	Decanted Oil W-3632	11.1	550	760		1.01	0.6
8-1*	3-phase Deasphalt- ing With Mixed Hexanes	Oil re- covered From Upper Liquid Phase						0.3
8-2*	Same as 8-1	Oil re- covered From Lower Liquid Phase						0.15
8-3	Filtration Dewaxing of No. 8	Press Oil (85% of Original)	11.3				0.94	--
8-4	Dilution	50% Oil No. 8 (White Oil 50% (W. Texas Resid.						--
9	TCC	Syn. Tower Bottoms	18.4	488	608	98-756	0.43	0.02

Table I

API Sample Number	Process	Product	Gravity	Boiling Range			Sulfur	P _{MC}
				10%	90%	E.P. ° F. % - ° F.		
10	TCC	Fuel Oil	11.6	630	757		0.53	0.41
11	Houdry	Syn. Tower Bottoms	4.3	548		81-700		0.11
12	FCC	Decanted Oil	18.1	450	912		0.54	0.65
12-1*	Pentane Deasphalt- ing	Asphalt in benzene (2.3 g./ 100 ml.)						--
12-2*	Chromato- graphy (Silica gel)	Non-Aromatics (Cut with 20% Heptane)						--
12-3*	Pentane Deasphalt- ing	2nd Asphalt in benzene (2. g./100 ml.)						--
12-4*	Distilla- tion (1-plate vac.)	Aromatics Boiling 510- 710° F. (Corr.)						--
12-5*	Same as 12-4	Fraction boiling 1010- 1065° (6 g./ 100 ml. benzene)						--
12-6*	Same as 12-4	Residue boil- ing > 1065° (5 g./100 ml. benzene)						--
13	Polyforming	Tar	9.7			75-740		--
14	Solvent Extraction (Furfural)	Extract from Kansas 200 stock	10.3	762	869	98-920	1.43	--
15	Same as 14	Extract from Okla. 400 pale	10.9	853	960		0.81	--

Table I

API Sample Number	Process	Product	Gravity	Boiling Range ° F.			Sulfur	P _{MC}
				10%	90%	E.P. % - °F.		
16	Solvent Extraction (Phencl)	Extract from Coastal 900-X	11.0			50-915	--	--
17	Solvent Extraction (Duosol)	Extract from Calif. waxy residuum	7.0			50-950	0.9	--
18	Viscosity Breaking	Cracked Residuum	6.0				0.85	--
19	Naphtha Reforming	Tar	17.0	420	706		0.46	--
20	Thermal Cracking (15% Cat. G.O. in Feed)	Tar	4.7			83-930	--	0.18
20-1*	Dilution	50% Oil No. 20 50% Dodecyl- benzene					--	--
21	Desulfuri- zation of No. 8-3 by catalytic hydrogena- tion	Hydrogenated Heavy gas oil	18.1	595	870		0.15	--
22	Cyclover- sion	Heavy gas oil	24.0	572	686	98-722	0.2	--
23	FCC	Heavy cycle gas oil	26.1	611	769	98-828	0.71	--
24	Thermal Cracking of No. 23	Tar	13.5	564	930	98-1050	1.26	--
25	FCC	700° + Bottoms from Heavy Cycle Gas Oil						
25-1	Dilution	50% oil No. 25 (White Oil - 50% (W. Texas (Resid.						

* Sample prepared in laboratory.

API 04954

Table II

CONCENTRATION STANDARDS WITH METHYLCHOLANTHENE (MC)
AND 9, 10 - DIMETHYL - 1, 2 - BENZANTERACENE (DMBA)

API Sample Number	Carcinogen	Solvent	Concentration (g./100 ml.)	Frequency of Application	Time After 1st Painting Required to Reach 50% T.I.	
					C3H	CFW
201	MC	Benzene	0.010	3X/week	--	--
202	MC	Benzene	0.038	3X/week	216 days	140 days
203	MC	Benzene	0.075	3X/week	181 days	116 days
204	MC	Benzene	0.15	3X/week	108 days	78 days
205	MC	Benzene	0.30	3X/week	77 days	84 days
206	MC	Benzene	0.60	3X/week	39 days	87 days
207	MC	Benzene	1.00	3X/week	64 days	67 days
209	MC	Benzene	0.45	3X/week	--	
210	MC	Benzene	0.02	3X/week		--
211	MC	Dodecylbenzene	0.10	3X/week	--	--
212	MC	Dodecylbenzene	0.30	3X/week	--	
213	MC	Dodecylbenzene	0.04	3X/week		--
218	MC	API-5	0.30	3X/week	--	--
214	DMBA	Benzene	0.30	3X/week	48 days	
215	DMBA	Benzene	0.10	3X/week	--	--
216	DMBA	Benzene	0.05	3X/week	--	--
217	DMBA	Benzene	0.01	3X/week		--

Table III

Skin Painting and Washing Experiments (CFW Mice)

API Sample Number	Oil Applied	Frequency of Application	Period of Exposure to Oil Before Re- moval By Washing With Soap and Water	Time After 1st Painting Required to Reach 50% T. I.
8	8	1X/week	Control (no washing)	112 days
300	8	1X/week	10 min.	No tumors in 219 days
301	8	1X/week	1 hr.	No tumors in 219 days
302	8	1X/week	4 hrs.	No tumors in 219 days

AMERICAN PETROLEUM INSTITUTE

SUBCOMMITTEE ON CARCINOGENICITY

Minutes of Meeting
April 23, 1950
Hotel Sherman
Chicago, Illinois

Members Present

McIver Woody (Chairman)
Marshall Clinton
T. M. Frank
A. E. Hoag
J. P. Holt (Rep. by R. E. Eckardt)
T. J. Kelly
J. W. Long
M. N. Newquist
Chas. A. Swan

Associates Present

L. O. Crockett
Allan E. Dooley
R. W. Faulk
R. M. Landon
H. P. Lankelma
K. G. Mackenzie (Rep.
by H. R. Warrick)
R. M. Shepardson

Members and Associates of Medical Advisory Committee

W. O. Armstrong	E. W. Adams
V. C. Baird	R. D. Bent
F. F. Boys	R. C. Cole
Kieffer Davis	T. E. DeVilliers
E. K. Linder	L. M. Henderson
E. P. Luongo	C. A. Neilson
B. B. Reeve	F. M. Watkins
E. R. Ware	

Guests

N. W. Bolyard - Standard Oil Co. (Ind)
Philip Drinker - Harvard School of Public Health
J. W. Hammond - Humble Oil and Refining Co.
Howard Hansen - Esso Standard Oil Co.
A. W. Horton - University of Cincinnati
W. C. Hueper - National Cancer Institute, Bethesda. Md.
R. A. Kehoe - University of Cincinnati
R. C. Page - Standard Oil Co. (N. J.)
J. J. Phair - University of Cincinnati
H. G. S. van Raalte - Shell Oil Co., Curacao, N. Ant.
W. E. Smith - New York University
D. V. Stroop - American Petroleum Institute
P. M. Waddill - Phillips Petroleum Co.

Total in attendance - 44

Members Absent

L. E. Curtis
W. R. Levis

Associates Absent

L. C. Beard, Jr.
H. G. M. Fischer

The minutes of the November 10, 1949 meeting were approved.

Dr. A. W. Horton presented a progress report, copies of which had been sent to all members and associates on April 11. This report was supplemented by a series of lantern slides showing potencies of some of the oils which have been tested. With respect to the analytical phases, Dr. Horton stated that many compounds had been isolated but very few had been identified as yet. Perylene, 4-methyl pyrene and chrysene have been definitely identified as constituents of high-boiling catalytically cracked oils.

Dr. Horton described the data which was to be submitted for publication in "Cancer Research". The potency curves of oils 8 and 9 (see Table I of Dr. Horton's report) would be included as being typical examples of the oils being studied.

In the discussion which followed, many of the members and associates voiced a request that a complete and detailed report be prepared by Dr. Horton. It was pointed out that such a report would be of particular benefit to new members and associates.

Dr. Horton's report was accepted and approved.

Mr. R. M. Shepardson described the work of his company on the development of a quick laboratory test for measuring the potential carcinogenicity of petroleum products. As a numerical expression of potential carcinogenicity, the number of days required for 50 per cent of the mice to develop tumors after discarding all mice which had died

without tumors, has been tentatively chosen. Of 64 samples tested to date, a satisfactory correlation has been found between the biological tests and the ultra-violet absorption measured at 360 mu on the portion of the sample separated by distillation and boiling between 650° and 950° F., when correcting for difference in viscosity, mid-boiling point and concentration of the 650-950° F. material. This study is being continued on a larger number of samples.

The subcommittee expressed its thanks to Mr. Shepardson for his presentation.

Dr. R. E. Eckardt reported on some of the work* being done at Memorial Hospital. Cancers have been produced in two monkeys out of six who had been painted with a high-boiling oil twice a week for about five years. This is the first time that skin cancers have been produced experimentally in monkeys.

Dr. Eckardt reporting on washing experiments said that results to date indicate that washing offers some protection but not absolute protection. With groups of 30 mice, application of the oil and washing after five minutes resulted in a reduction in the number of tumors and no cancers after one year. Washing the mice one hour after application produced tumors in four mice and cancer in one mouse of the group of thirty. Washing the mice six hours after application resulted in the development of cancer in three mice.

In a group of sixty mice which were painted with only one application of a high-boiling oil, tumors were produced in two mice

* See attached copy of paper "Experimental Analysis of the Carcinogenic Activity of Certain Petroleum Products" for additional information on this work.

and cancers in two additional mice. The first tumor appeared after 92 days and the first cancer after 274 days. No tumors or cancers appeared in a control group on 100 mice.

This subcommittee expressed its thanks to Dr. Eckardt for his presentation.

Dr. J. J. Phair presented a progress report on the epidemiological study which he plans to get under way about July 1, 1950. Dr. Phair distributed mimeographed copies of his report. During the discussion it was brought out that, to date, there have been no cases of skin cancer in which the employe has claimed that exposure to these high-boiling oils was the cause.

Dr. Phair's report was accepted and approved with the understanding that the word "approved" would be changed to "needed" where it fits the context of the report.

Dr. H. G. S. van Raalte told about a fishing village on the island of St. Martin where the inhabitants, all of Danish ancestry, can trace their ancestry back about 200 years on the island. He stated that most of the men develop skin cancers by the time they reach age 40. Most work at fishing and handle tarred nets and tackle. A few who have worked in the refinery or at Aruba apparently have not had skin cancers.

Dr. W. C. Hueper (National Cancer Institute) said that he had talked to a nurse in an asphalt shingle plant in the western part of the United States and that the nurse had reported cases of cancer on the dorsum of the hands. Dr. Hueper said that a petroleum asphalt

was being used and that it would be well to keep an eye on this material with respect to both producers and consumers.

The subcommittee recommended to the Medical Advisory Committee that it should approve:

1. Publication of the report as described by Dr. Horton in his letter of April 7, 1950 to D. V. Stroop.
2. The proposed epidemiological study as described by Dr. Phair.

McIver Woody, M.D.
Chairman

Allan E. Dooley
Secretary

For Information Only - Not for Publication

EXPERIMENTAL ANALYSIS OF THE CARCINOGENIC
ACTIVITY OF CERTAIN PETROLEUM PRODUCTS*

William E. Smith, M.D., Douglas A. Sunderland, M.D.,
and Kanematsu Sugiura, D.Sc.

from the Institute of Industrial Medicine, New York
University-Bellevue Medical Center, and the Sloan-
Kettering Institute for Cancer Research, New York,
U.S.A.

As part of the preventive medical program of a petroleum
company, we conducted tests for carcinogenic activity on approximately
400 samples from refinery, laboratory and wax works operations. Each
sample was tested by painting on a group of 30 mice.

Oils from Catalytic Cracking Process: Carcinogenic activity
was found only in fractions distilling above 700° F. The carcinogeni-
city of the most potent oils studied was markedly reduced by dilution
to approximately 10% concentration with non-carcinogenic oils. Blends
containing not more than 10% of potent oils elicited only a few tumors
and these were benign.

Waxes: Unrefined petroleum waxes elicited cancers late and
infrequently, but their aromatic extracts were very active. The hazard
in wax works thus appears to be associated with the aromatic compounds
in unpurified wax and not with the paraffins.

* These studies were carried out under a grant from the Standard Oil
Co. (N.J.) and certain affiliates in cooperation with the Medical
Department of that company. All samples were prepared and supplied by
the Standard Oil Development Company.

For Information Only - Not for Publication

REVISED DRAFT

EXPERIMENTAL ANALYSIS OF THE CARCINOGENIC
ACTIVITY OF CERTAIN PETROLEUM PRODUCTS.

William E. Smith, M. D., Douglas A. Sunderland, M. D.
and Kanematsu Sugiura, D.Sc.

from the Institute of Industrial Medicine, New York
University-Bellevue Medical Center, and the Sloan-
Kettering Institute for Cancer Research, New York,
U. S. A.

Occupational tumor problems have been much less commonly observed in the petroleum industry than in the Scottish shale oil trade. Occasional tumors have, however, been described, and some petroleum oils have been shown to elicit tumors in experimental animals. For these reasons, the Standard Oil Company (New Jersey) and certain affiliated companies began a general investigation into the question of possible occupational tumor hazards for workers in refineries. In collaboration with this study, we have carried out tests for carcinogenicity on approximately 400 samples of oils and waxes derived from various phases of plant and laboratory processes. The samples were prepared by the Standard Oil Development Company.

The first group of materials studied were from an experimental catalytic cracking operation. In this process, developed extensively during the past ten years, oils are cracked at a relatively high temperature in contact with a catalyst generally composed of mixtures of silica and alumina. From the classic experiments of Kennaway, Cook, Twort and others, it was known that petroleum, like coal and other

bituminous materials, may acquire carcinogenic properties as a result of reactions brought about by extensive thermal decomposition.

Our first tests were conducted with samples of high boiling, catalytically cracked oils. These proved highly potent in bringing about cancer when painted on the skins of mice. They also elicited papillomas and occasional cancers from the skins of rabbits, and, after years of painting, from the skins of monkeys.

Preliminary tests showed that white mice obtained from a commercial breeder (Rockland Farms) gave tumors somewhat more quickly than dark-skinned C57 mice, and we have routinely used white male mice from this breeder. It was found that for practical purposes essentially comparable information could be gained from mice tested in a group of 30 as compared with a group of 100 animals. We have therefore tested each sample on a group of 30 mice. If groups much smaller than this are used, difficulties may arise from loss of animals in the course of the necessarily long-term experiments.

The mice are painted with the test material three times a week throughout their lives, unless the experiment is discontinued earlier. Very potent samples have elicited papillomas as early as 29 days and cancer after 70 days; but for moderately potent materials a period of 250 days is usually necessary to gain an impression of their activity, and many samples must be painted much longer before tumors appear.

(slide)
#5

Statistical methods proposed by the Standard Oil Development Company have been adopted which permit the data from each sample to be charted graphically in a manner that permits one to see at a glance the non-tumor mortality, the number of animals developing benign papillomas, the number developing cancers, and the rate at which the tumors appear. This slide shows such a graph, on which is given data obtained from mice painted with an acetone solution containing 0.3% of the pure carcinogen, methylcholanthrene. The days at which the animals were observed are indicated along the bottom. The percentage of survivors with or without tumors at any given time can be read off the scale at the right. The percentage of animals dying with or without tumors can be read off the scale at the left. The shaded area indicates the time of appearance of the first cancer and the number of cancers that developed. The percentage of animals dying without tumors can be read by reference to the lowest line on the chart. It may be guide to toxicity of the sample but often connotes deaths from fighting or intercurrent infection.

(slide)
#6

The next slide gives the results of painting a sample of high boiling catalytically cracked oil. It shows a carcinogenic activity not greatly less than that of the 0.3% solution of methylcholanthrene just shown. A mixed colony consisting of 13 male and 12 female mice was used in this experiment.

(slide)
#7

The data for each sample under test is entered from month to month on graphs such as these.

For convenience in comparing the carcinogenicity of large numbers of samples, two indices have been employed. The Tumor Index is the percentage of animals, surviving 90 days or longer, that develop either papillomas or cancers. The Cancer Index is the percentage of animals, surviving 90 days or longer, that develop cancers. The activity of each sample can then be rated by a simple numerical fraction, the Cancer Index over the Tumor Index.

(slide)
#8

The next slide, divided into two groups, shows results at 250 days on 10 samples of catalytically cracked oils received from refinery operations. The first group, consisting of five samples, contained relatively little high boiling material (less than 30% distilling above 700° F.). It is seen that they were practically devoid of carcinogenic activity. Only two of the five induced any cancers and then in only a small percentage of animals. It is of interest to note that the most active sample in this group (207) contained the greatest percentage of high-boiling material (28%). By contrast, the second group of five samples gives the results on catalytically cracked oils that contained large amounts of high-boiling materials (over 45% distilled above 700° F.). It is seen that all of these possessed a very high carcinogenic potency.

(slide)
#9

The carcinogenicity of such high-boiling oils can be effectively reduced by dilution with non-carcinogenic oils. Here is a set of tests on blends containing varying proportions of high-boiling material. No reduction in potency was

found when the blend contained 67% of the active oil. When only 55% was present, the carcinogenicity fell off; and when the amount was reduced to 29%, no cancers whatsoever resulted at 250 days, though a considerable percentage of animals still yielded benign papillomas. Further experiments with dilutions of another oil of this type have shown comparable results and are also shown in Slide #9. In these experiments it is indicated that when the concentration of the active oil was reduced by dilution to somewhere between 10 and 20% (8 and 16% boiling above 700° F.), the carcinogenicity of the oil is abolished in that no cancers are produced.

(slide)
#10 The carcinogenicity of these oil samples has thus been shown to be associated with the high boiling material. The problem has been further narrowed down by demonstrating that the carcinogenic activity resides in the aromatic fraction of the oils. Here are tests on fractions of a high boiling oil subjected to chromatographic separation on silica gel. It is seen that the paraffinic components were devoid of carcinogenicity whereas the cumene eluate, which contained the aromatics, was extremely potent.

(slide)
#11 This finding has been applied in the study of materials from wax-works. In the manufacture of waxes, certain oils are cooled and the solid material, or wax, which separates out is collected in a press. Samples of these crude waxes were melted at 60° and planted on mice. After 250 days, very few animals thus painted showed any tumors. When the painting was kept up for 450 days, however, tumors were induced by all

of 8 samples of crude waxes but the percentage of animals that developed tumors was small. Often, merely papillomas and no cancers resulted. By contrast, the aromatics extracted by silica gel from these crude waxes possessed very marked carcinogenic potency. In every instance, they elicited considerably more tumors than the whole crude wax from which they were obtained. Furthermore, the aromatic fractions regularly produced one or more malignant tumors.

It therefore appears that the carcinogenic hazard in the case of crude waxes is due to the presence in them of aromatic components, and not to the paraffins which compose the final purified waxes.

LIST OF SLIDES

1. Cancer and papilloma as seen on a mouse painted with a sample of high boiling catalytically cracked oil (color photo).
2. Histological section of tumor shown in Slide 1.
3. Papillomas on ear of rabbit painted with same material applied to mouse shown in Slide 1.
4. Ditto (monkey)
5. Graph showing data from painting methylcholanthrene (Exp. 22)
6. Graph showing data from painting a sample of high boiling catalytically cracked oil (Sample III, Exp. 11) N.B. We have removed the cross-hatching which this graph erroneously shows between 40 and 70 days.
7. Definition of Cancer and of Tumor Indices.
8. Cancer Index/Tumor Index data on oils with various boiling ranges.
9. Reduction of carcinogenicity of high boiling oils by dilution with non-carcinogenic oils.
10. Carcinogenicity of aromatic contrasted to paraffinic fractions of a high boiling catalytically cracked oil.
11. Carcinogenicity of crude waxes contrasted to that of their aromatic fractions.

SLIDE #7

TUMOR INDEX:

TOTAL NUMBER OF ANIMALS THAT DEVELOPED TUMORS
ORIGINAL NUMBER OF ANIMALS LESS THE NUMBER
DEAD AT 90 DAYS WITHOUT TUMORS

CANCER INDEX:

TOTAL NUMBER OF ANIMALS THAT DEVELOPED CANCER
ORIGINAL NUMBER OF ANIMALS LESS THE NUMBER
DEAD AT 90 DAY WITHOUT CANCERS

SLIDE #8

SAMPLE NO.	% DISTILLING ABOVE 700°F.	CI/TI at 250 days
217	less than 1	0/0
213	3	0/0
224	10	0/0
207	28	4/12
219	3	4/4

SAMPLE NO.	% DISTILLING ABOVE 700°F.	CI/TI at 250 days
206	74	33/67
173	78	38/57
223	78	38/77
216	45	46/71
212	78	67/87

SLIDE # 9

REDUCTION OF CARCINOGENICITY OF A HIGH BOILING
OIL BY DILUTION WITH NON-CARCINOGENIC OILS

CI/TI
at 250 days

MH 101 (45% distilling above
700°F)

27/62

BLEND CONTAINING:

127	67% MH 101
121	55% MH 101
115	29% MH 101

23/67

13/57

0/27

CI/TI
at 281 days

173 (78% Distilling above 700°F)

36/50

175 Non-carcinogenic oil

0/0

176 10% 173

0/4

177 20% 173

16/36

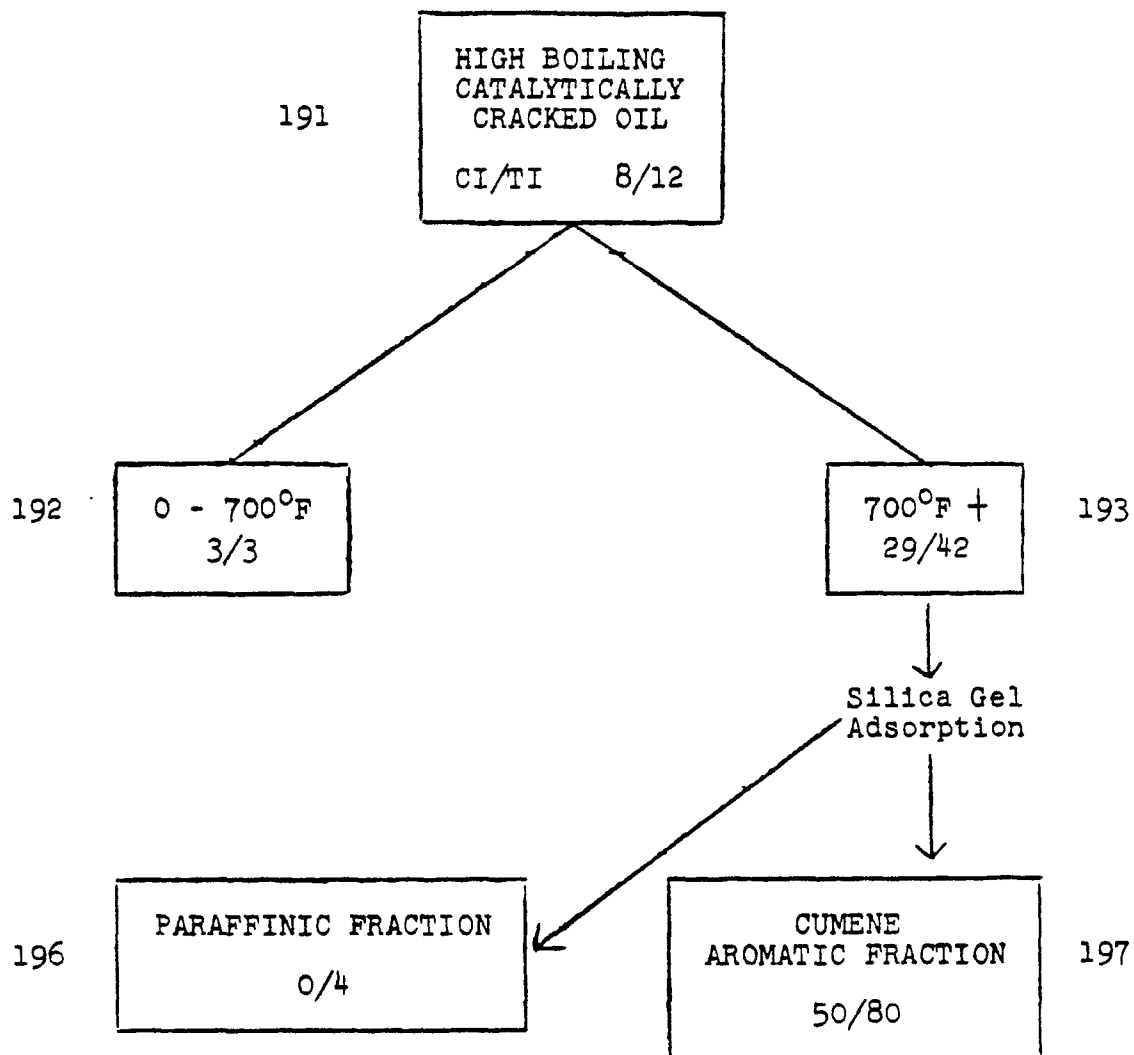
178 30% 173

3/24

179 40% 173

44/59

SLIDE # 10



CANCER INDEX
TUMOR INDEX at 250 days

SLIDE #11

CANCER INDEX
TUMOR INDEX

at 450 days

CRUDE WAX

AROMATIC EXTRACT

8/19

24/38

7/7

23/35

4/4

17/43

0/7

14/34

0/4

9/13

0/4

8/30

4/4

4/30

4/4

4/19

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

May 16, 1950

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

CABLE ADDRESS: KETLAB, CINCINNATI
TELEPHONE: CAPITOL 1414

FILE

Mr. D. V. Strop,
The American Petroleum Institute,
50 West 50th Street,
New York City 20.

Dear Mr. Strop:

I am sending you herewith, for your information, a statement of expenditures made on behalf of The American Petroleum Institute for the first quarter of 1950. If you have any questions or comments, Doctor Kehoe would appreciate your bringing them to his attention.

Very truly yours,

E. R. Fortlage
E. R. Fortlage, Secretary to
Dr. Kehoe

ef

Enc.

UNIVERSITY OF CINCINNATI
KETTERING LABORATORY
ACCOUNT OF AMERICAN PETROLEUM INSTITUTE

For the First Quarter of 1950

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

Francis Heyroth	- Supervision	75.00
John Phair	-	1375.02
Wesley Horton	- Chemical Assistance	1950.00
Frank Dutra	- Pathological Assistance	30.00
Frank Cleveland	- " "	187.14
Russell Tye	- Chemical Assistance	900.00
Ruth Pierle	- " "	1125.00
Sylvan Witherup	- " "	11.51
Harold Schlecht	- Technical Assistance	8.05
Dorothy Templeton	- " "	330.05
Karl Korpi	- " "	153.50

6145.27

SCCELLANEOUS EXPENSE

Purchase of Animals	438.88
Laboratory Supplies	272.31
Traveling Expense	842.50
Proportion of Secretarial, Library, Janitors, Wash Boys, Draftsman, Shipping Clerks, Animal Caretakers, Histo- pathological Preparation etc	2397.32
Proportion of Heat, Gas, Electricity, Steam, Telephone, Maintenance, Pensions, Annuities etc	1901.07

TOTAL 11,997.35

Balance Available for Work in 1950
at End of 4th Quarter 1949 \$34,594.15

Receipts - January 12, 1950 38,963.39
73,557.54 ✓
Expenditures - 1st Quarter 1950 11,997.35 ✓

Balance Available for Work in 1950
at End of 1st Quarter 1950 \$61,560.19 ✓

May 16, 1950

Dr. Robert A. Kehoe
University of Cincinnati
Dept. of Preventive Medicine and
Industrial Health
Cincinnati, Ohio

Dear Dr. Kehoe:

Your letter of May 9 has been received just as I am pushing off for a week of meetings in Atlantic City and Chicago.

Some time between meetings I shall study your memorandum.

Upon my return I shall give you my suggestions.

Yours very truly,

D. V. Stroop
Executive Assistant

DVS:prd

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

May 9, 1950

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

CABLE ADDRESS: KETLAB, CINCINNATI
TELEPHONE: CAPITOL 1414

Mr. David Stroop,
Director of Safety,
American Petroleum Institute,
50 West 50th Street,
New York City 20.

Dear Mr. Stroop:

I am sending you herewith several copies of a memorandum I have prepared for submission to the sponsors of the experimental work of the Laboratory. I believe this will be self-explanatory, but I have considered it desirable to append a note to it, in explanation of its length, which seems a bit long. It is my firm conviction that there is nothing which this Laboratory can do for industry, and specifically for the petroleum industry, which would be more useful in the long run than to spend some of our efforts in training medical men to appreciate the general problems of industrial health. This is a service that industry needs, and I am sure that it can afford to pay a nominal cost for the benefits to be achieved. Therefore, I have gone to some length to explain our program and our ideas in connection with it.

I realize that this may be a very poor time to suggest more extensive expenditures. On the other hand, I think this should be presented for consideration. It might have been wise to do it at the formal meeting of the Medical Advisory Committee, but, quite frankly, I did not want to cloud the issues under consideration by bringing forward a proposal of this type. I leave it entirely to your discretion the manner and the time of presenting this. In my feeling, if it were approved in principle, we would be in position to handle the situation fairly well this year, since our cost for the current year will probably be relatively small. I shall appreciate hearing from you at your convenience concerning this matter.

Sincerely yours,

Robert A. Kehoe
Robert A. Kehoe, M. D.

RAK ef

Enc.

The
Institute Of Industrial
Health

of the

University Of Cincinnati

UNIVERSITY OF CINCINNATI
THE GRADUATE SCHOOL OF ARTS AND SCIENCES
INSTITUTE OF INDUSTRIAL HEALTH

KETTERING LABORATORY OF APPLIED PHYSIOLOGY
COLLEGE OF MEDICINE - EDEN AVENUE
CINCINNATI 19, OHIO

CABLE ADDRESS: KETLAB, CINCINNATI
TELEPHONE UNIVERSITY 2665

MEMORANDUM

TO RESPONSIBLE EXECUTIVES OF ALL INDUSTRIAL ORGANIZATIONS
INVOLVED IN THE EXPERIMENTAL PROGRAM OF THE KETTERING
LABORATORY, COLLEGE OF MEDICINE, UNIVERSITY OF CINCINNATI

The developments of recent years in the field of industrial health and, specifically, the evolution and growth of the activities of this Laboratory in this field, have posed a number of problems that are of considerable importance to this Medical College and University and are, likewise, matters of concern to industry. It is necessary to formulate certain policies and plans in order to deal with these problems on some more or less permanent basis, and it is the purpose of this memorandum to obtain an expression of opinion from representatives of industry relative to such plans.

The work which led to the creation of the Kettering Laboratory began in the Department of Physiology in the Medical College in 1925, when the study of a single toxicologic and hygienic problem was undertaken for, and at the expense of, one industrial organization. While this work was expanding beyond the space and facilities available in the laboratories of the Medical College, additional industrial organizations became interested in our engaging in other investigations. There being no source of funds in the University by which to provide facilities for such work, a group of three industrial organizations provided funds to build and equip a laboratory, which was completed late in 1930, and was named the Kettering Laboratory, in honor of the distinguished industrialist, scientist and inventor, Charles Franklin Kettering, whose

work, with his associate Midgley and others, had created the industrial commodity (antiknock material containing tetraethyl lead as the primary ingredient) out of which our first industrial investigation grew.

The significance of the foregoing comments is that American industry, with particular reference to the chemical industry, was on the way to its present dominant position in international production and commerce, creating, as it developed, the special industrial hazards which it had no proper means of appreciating or controlling. Historically, the same thing had happened in Germany, and it was inevitable that medical attention should be brought to bear on these problems by some means. The facilities available in the United States were very scanty and wholly inadequate, and, by sheer accident, we were drawn into this type of work at a comparatively early time. The Laboratory, therefore, has developed, with something of a lag, in response to the needs of the situation, and since no other means was available, these developments, in the University, were financed by industry exclusively. From its small beginning, the Laboratory has expanded its equipment and personnel to fit the work that it has been able to accept, and with the completion, equipping and staffing of a new wing in July of 1949, which more than doubled the available space, its physical facilities accommodate a staff of more than one hundred persons, and its annual budget comes to about \$400,000.00 per year.

This growth and development has not been merely quantitative but qualitative as well, in that experience with the problems of industry has contributed to the shaping of policies, methods of procedure and functions. It became apparent at an early date that the experimental work had to be applied in the industrial environ-

ment, and that much of it would have to be done with the practical problems of industry clearly in mind. This resulted in frequent consultations with industrial people, in a variety of direct professional services to industry, and in the acquisition of direct familiarity with the industrial organizations, plants, and personnel involved. This experience demonstrated, among other things, that trained personnel for the work of industrial health were not available. Therefore, nothing was more clear than that a University medical center such as this had the duty of making provision for professional training. For the most part, the facilities required for such training were available in the Colleges of this University, but a great deal of planning and organizing was necessary to put them to work. By July of 1947 plans had been crystallized for this purpose, the Institute of Industrial Health had been organized in the Graduate School of Arts and Sciences of the University, and two graduate physicians had been enrolled for a course of three years of study and training as candidates for the degree of Doctor of Industrial Medicine.

While these developments were in progress in this University, somewhat similar activities began and progressed elsewhere, in response to the continually growing requirements of American industry in these respects. Other centers of research or professional training, or both, have been established or are being established and developed. This Laboratory, however, which is the administrative and academic center of the Institute of Industrial Health in the Graduate School, and which, recently, was consolidated with the Department of Preventive Medicine to become the Department of Preventive Medicine and Industrial Health in the College of

Medicine, has the unique character of being a university enterprise created and financed wholly by industry to serve industry. It embodies the willingness on the part of an important segment of American industry to invest appreciable sums of money in the solution of industrial problems by an organization that is responsible to the public. The presumption, based on the growth of the Laboratory, is that this has been a good investment. Because of this presumption, and in keeping with the good will that has developed out of years of direct and frank relationships with industrial management, certain changes in fiscal and operating policies are proposed for consideration, which, if generally acceptable, will be incorporated in future formal agreements between the Laboratory and its sponsors.

The educational program of the Laboratory has created some expense, and the means of dealing with this expense is a problem which it seems necessary and desirable to present to the industrial organizations involved independently and jointly in the financial support of the experimental work. One point must be made clear in this regard. There are no funds available to us at present from public or private sources, other than those earmarked for the prosecution of experimental work agreed upon between the University and industrial organizations. Nor can the University of Cincinnati, which is a municipal institution, provide funds for the support of any part of the experimental or educational program of this Laboratory, it being caught, as are most American universities, on the two vicious horns of the dilemma of diminishing private gifts of all kinds and returns on endowment funds, on the one hand, and the increasing cost of all

of its activities, on the other. The result of this is the necessity of turning to industry for the entire support of the activities believed to be necessary. Since everyone who wants money turns either to government or to industry for it, this has a familiar sound. There is a difference, however, we believe, in that the entire productive effort of this enterprise is designed to benefit industry, in an area of great industrial need and weakness. Moreover, present trends in industrial legislation and practice, with reference to health and welfare, employee relations, and community comfort and health (with specific stress on stream and atmospheric pollution), are such that the present lack of adequately trained personnel in the field of industrial health is a serious and growing threat to American industry. If our experience of the past twenty years is to be trusted, the urgent need for competent industrial physicians will have to be met in the near future. Moreover, industrial management is more aware of this, we believe, than is the medical profession, in general, including those responsible for the training of physicians, and therefore we can expect to obtain understanding and support from industrial management in this matter before it will be forthcoming elsewhere.

With these matters in mind, we have considered the cost of our educational program carefully, and have decided to propose to the sponsors of our work that we be authorized to add to the cost of all experimental work an overhead charge of 10 per cent for educational purposes. This figure has been arrived at on the basis of previous cost accounting and estimates which extend somewhat into the future. Appended hereto, is a bulletin in which the program of graduate education is outlined, together with a

schedule of fellowship stipends offered to graduate physicians who are accepted for training. (The stipends are offered as a means of reducing the economic hurdle for physicians who may wish to extend their training beyond the already prolonged period required, thereby encouraging able but impecunious applicants. It is also evident that some inducement must be offered to potential candidates, in view of the almost overwhelming tendency of graduate physicians to enter into other fields of professional practice.) Our intention is to accept four students per year for training if satisfactory applicants are available. Present facilities in the Laboratory, and in the University generally, will not justify our accepting a larger number at this time. This would mean that we would have eight fellows (in two classes) in the school per year, since the third year group would be in residencies in industrial establishments for which they will be compensated by the industry in which they are working. (Arrangements have been made to take care of a certain number of trained men in these residencies, and additional arrangements can be made as required.) Under these conditions, the cost of all of the fellowship stipends will not exceed \$22,800.00 per year, and will usually be somewhat less than this sum. Various plans are under way to obtain funds for this purpose from other academic and professional sources, and to the extent that these succeed, the funds obtained will be applied against this cost, but it seems necessary in lieu of such sources to secure the financial structure of this educational program through funds made available by the supporters of the general work of the Laboratory.

The cost of the instruction of graduate students, as the work of the Faculty of the Institute of Industrial Health is

presently organized, varies a little from year to year. Much of this cost applied automatically against the budget of the Laboratory for experimental purposes, in that the time spent in instruction by members of the staff of the Laboratory is paid for by salaries authorized for experimental work. (Other members of the Faculty, in other Departments of the University, receive no additional compensation for services rendered in the Graduate School.) However, the time so expended by members of our staff has been recorded and made a charge against the educational program for the past two years. It came to about \$10,000.00 in 1947-48 and to about \$13,000.00 in 1948-49. Other items of expense included the cost of instruction given by non-university personnel, the traveling expense of visiting instructors (lecturers), the cost of miscellaneous supplies, stationery, printing, books and equipment, and a reasonable share of overhead expense for light, heat, janitor service and the like. The total expense, exclusive of fellowship stipends, was \$20,000.00 in round numbers in the academic year 1947-48, and \$21,000.00 in 1948-49. This cost can be expected to increase to some extent as cost accounting of any and all expense attributable to such professional training is more rigidly scrutinized and recorded. Moreover, the further development of the professional curriculum will involve some additional cost, since not all of the Departments of the University are staffed adequately for the purposes of consultation and instruction. To the extent that the Laboratory needs and can make adequate use of consultants in a number of fields in which demands are made on us by industry, we shall undertake to augment the resources of these Departments. For example, consulting services and surveys in the field of Industrial Relations, with

specific reference to job appraisal and fitness, employee morale and production, and other aspects of the human equation in industry, merit much more attention, study and research than they have had at the hands of professional people. The work of the Harvard School of Business Administration is a notable example of what can be done by competent people in this field of study.

On the whole, it is estimated that the cost of our program of graduate training, including provision for fellowship funds not otherwise available, will rarely exceed \$40,000.00 in any one year, and that an overhead charge of not more than 10 per cent of our experimental budget (\$395,434.40 in 1950) to this purpose, would secure the educational program indefinitely. Actually the cost to be applied directly to the cost of any experimental project would not come to 10 per cent, but would be nearer to 5 per cent. It is not our intention to accumulate any special educational fund, but to distribute the cost of graduate instruction annually in such manner as to balance receipts and expenditures yearly.

Finally, it is our belief that an integrated program of medical and hygienic services to industry, of investigative work and of graduate instruction in the field of industrial health, is all of one piece; that these are related and complementary functions, and that the separation of the one from the other in terms of function or expense is disadvantageous and unrealistic. Therefore, we take pleasure in offering this combination of functions to industry, as a proper service of this University to industry and to the community, at the actual cost that is required by a University organization to supply such services. We invite the present sponsors of the work of the Laboratory to participate in

9.

this program, and request a response to this proposal, with the intention, if there is general concurrence in the proposal, of modifying all agreements with subsequent sponsors, to include this expense.

Signed:

Robert A. Kehoe
Robert A. Kehoe, M. D., Director
The Kettering Laboratory and
The Institute of Industrial Health

March 15, 1950

May 25, 1950

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

Dear Doctor Kehoe:

The memorandum transmitted with your letter of May 9th has been considered most thoughtfully.

We feel so favorably disposed that we suggest the inclusion of some suitable wording in our letter of agreement for the coming year. If you agree, it will enable us to submit a specific proposition to the Medical Advisory Committee immediately for acceptance prior to July 1, 1950.

For your consideration a rough draft of what I have in mind is enclosed for your consideration.

If you concur in this approach, please let me know and I'll circularize copies of the draft to members of the Medical Advisory Committee for acceptance or comment.

Very truly yours,

DVS:d
Enclosure
cc: Dr. McIver Woody

P.S. If there has been any change in your estimated figure for the 1950-51 budget, please give me the total to be used in the letter of agreement.

DVS

ROUGH DRAFT

26
June 30, 1970

Board of Directors
University of Cincinnati
Cincinnati 19, Ohio

Gentlemen:

This communication is authority to continue work on investigation of the toxicity and mode of action of certain petroleum products for the year ending June 30, 1971, according to the terms of the agreement dated January 8, 1966, and on the basis of a maximum budget for operating expenses of \$100,000, with the understanding that a portion, not to exceed 10 per cent, of this amount shall be expendable in support of the University's program of graduate training. *of \$8,000 or more*

Upon receipt of your approval of the continuation and expansion of the project with this conditional maximum budget we shall pay you the sum of \$50,000, the balance of \$50,000, less the unexpended balance as of June 30, 1970, to be paid on January 1, 1971.

It is understood that any balance remaining in the fund on June 30, 1971 will be returned to the American Petroleum Institute, and that no excess over the amount of the budget is to be obligated or spent without written authorization.

Very truly yours,

AMERICAN PETROLEUM INSTITUTE

By _____
President

By _____
Secretary

Accepted and Approved

UNIVERSITY OF CINCINNATI
Through its Board of Directors

By _____

By _____

which is conditioned upon a minimum unexpended balance of \$8,000 remaining in the fund at the University of Cincinnati as of June 30, 1970

(Kough Draft)

AMERICAN PETROLEUM INSTITUTE

50 WEST 50TH STREET

NEW YORK 20, N. Y.

June 30, 1950
~~1949~~

Board of Directors
University of Cincinnati
Cincinnati 9, Ohio

Gentlemen:

This communication is authority to continue work and to ^{on} expand the scope of investigation of the toxicity and mode of action of certain petroleum products for the year ending June 30, 1950 ¹⁹⁵¹ according to the terms of the agreement dated January 8, 1946 and on the basis of a maximum budget for operating expenses of \$98,825 which is conditioned upon an unexpended balance of \$7,878 or more remaining in the fund at the University of Cincinnati as of June 30, 1949. ^{with this} ^{understanding that a portion not to exceed 10% of the amount shall be expendable for support of the University's programs of graduate training}

Upon receipt of your approval of the continuation and expansion of the project with this conditional maximum budget we shall pay you the sum of \$49,413, the balance of \$49,412, less the unexpended balance of \$7,878 or more, to be paid on January 1, 1950.

¹⁹⁵¹
It is understood that any balance remaining in the fund on June 30, 1950 will be returned to the American Petroleum Institute, and that no excess over the amount of the budget is to be obligated or spent without written authorization.

Very truly yours,

AMERICAN PETROLEUM INSTITUTE

By *W. Lloyd F.* President
By *W. J. Kough* Secretary

Accepted and Approved

UNIVERSITY OF CINCINNATI
Through its Board of Directors

By *W. J. Kough* Chairman
By *W. J. Kough* Clerk

AMERICAN PETROLEUM INSTITUTE

30 WEST 50TH STREET

NEW YORK 20, N. Y.

June 14, 1950

To Members
Medical Advisory Committee

Subject: University of Cincinnati
Kettering Laboratory

Gentlemen:

For your consideration we enclose a copy of a letter dated May 9 and memorandum dated March 15 both from Dr. Robert A. Kehoe who outlines a need for increasing the University's overhead charges against research projects carried on at Kettering Laboratory. You will note that his proposed program of graduate training is expected to increase the total overhead percentage by more than 5% but less than 10%.

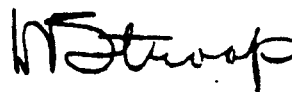
As recommended in November 1949, the carcinogenicity budget for 1950-51 is \$92,000. With the additional overhead, Dr. Kehoe estimates the maximum total budget should be increased to \$100,000 to cover the next 12 months.

We believe the unexpended balance of current funds at Kettering Laboratory on June 30, 1950 will be at least \$8,000; Therefore, our payment of new money should not exceed the \$92,000 which is now available and on deposit at the Institute.

In view of these facts and with the possibility that you may favor acceptance of Dr. Kehoe's recommendation, we enclose a rough draft of a modified letter of agreement for your consideration.

Your comments, either favorable or unfavorable, should be mailed to me at the earliest possible date because the agreement should be submitted to Dr. Kehoe not later than June 26. If no objections are received on or before that date we shall assume you have none to submit.

Yours very truly,



D. V. Stroop

DVS:fn
Enc.

C O P Y

C O P Y

C O P Y

UNIVERSITY OF CINCINNATI
Department of Preventive Medicine and Industrial Health

May 9, 1950

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

Cable Address: Ketlab, Cincinnati
Telephone: Capitol 1414

Mr. David Stroop,
Director of Safety,
American Petroleum Institute,
50 West 50th Street,
New York City 20.

Dear Mr. Stroop:

I am sending you herewith several copies of a memorandum I have prepared for submission to the sponsors of the experimental work of the Laboratory. I believe this will be self-explanatory, but I have considered it desirable to append a note to it, in explanation of its length, which seems a bit long. It is my firm conviction that there is nothing which this Laboratory can do for industry, and specifically for the petroleum industry, which would be more useful in the long run than to spend some of our efforts in training medical men to appreciate the general problems of industrial health. This is a service that industry needs, and I am sure that it can afford to pay a nominal cost for the benefits to be achieved. Therefore, I have gone to some length to explain our program and our ideas in connection with it.

I realize that this may be a very poor time to suggest more extensive expenditures. On the other hand, I think this should be presented for consideration. It might have been wise to do it at the formal meeting of the Medical Advisory Committee, but, quite frankly, I did not want to cloud the issues under consideration by bringing forward a proposal of this type. I leave entirely to your discretion the manner and the time of presenting this. In my feeling, if it were approved in principle, we would be in position to handle the situation fairly well this year, since our cost for the current year will probably be relatively small. I shall appreciate hearing from you at your convenience concerning this matter.

Sincerely yours,

/S/ Robert A. Kehoe
Robert A. Kehoe, M. D.

RAK ef

Enc.

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

RC
FILE

July 31, 1950

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

CABLE ADDRESS: KETLAB, CINCINNATI
TELEPHONE: CAMTOL 1414

Mr. D. W. Stroop,
The American Petroleum Institute,
50 West 50th Street,
New York City 20.

Dear Mr. Stroop:

I am sending you herewith, for your information, a statement of expenditures made on behalf of American Petroleum Institute for the second quarter of 1950. If you have any questions or comments, Doctor Kehoe would appreciate your bringing them to his attention.

Very truly yours,

E. R. Fortlage

E. R. Fortlage, Secretary to
Dr. Kehoe

ef

Enc.

Note for file:
This was shown
to Dr. Woody

API 05006

UNIVERSITY OF CINCINNATI
KETTERING LABORATORY
ACCOUNT OF AMERICAN PETROLEUM INSTITUTE

For the Second Quarter of 1950

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

Robert A. Kehoe	- Supervision	200.00
Francis Heyroth	- Toxicological Assistance	50.00
John Phair	-	1375.02
Wesley Horton	- Chemical Assistance	1560.00
Frank Dutra	- Pathological Assistance	3.00
Frank Cleveland	- " "	21.15
Russell Tye	- Technical Assistance	900.00
Ruth Pierle	- " "	1125.00
Sylvan Witherup	-	-
Harold Schlecht	- " "	32.32
Dorothy Templeton	- " "	387.67
Karl Korpi	- " "	240.12
Charles Walker	- " "	151.00
Waldo Younker	- " "	356.35
Karl Krautle	- " "	61.54

6463.17

MISCELLANEOUS EXPENSE

Purchase of Animals	366.80
Laboratory Supplies	6115.81
Traveling Expense	1666.47
Proportion of Secretarial, Library, Janitors, Wash Boys, Draftsman, Shipping Clerks, Animal Caretakers, Histo- pathological Preparation etc	3836.43
Proportion of Heat, Gas, Electricity, Steam, Telephone, Maintenance, Pensions, Annuities, Educational Expense etc	2176.63

TOTAL 20,625.31

Balance Available for Work in 1950 at End of 1st Quarter of 1950	\$61,560.19
Expenditures 2nd Quarter 1950	<u>20,625.31</u>
Balance Available for Work in 1950 at End of Second Quarter of 1950	\$40,934.88

MEMORANDUM

November 10, 1949

SUBJECT: RECEIPTS, EXPENDITURES AND ALLOCATIONS -- API MEDICAL RESEARCH FUNDContributions Received

1945	\$28,900.00	
1947	27,800.00	
1948	98,300.00	
1949	<u>64,340.00</u>	
TOTAL		\$219,340.00

Expenditures Made Prior to November 10, 1949

<u>Harvard University</u>		
Toxicological Reviews	\$37,000.00	
Cutting Oil Study	<u>2,500.00</u>	
		39,500.00
<u>University of Cincinnati</u>		
Carcinogenicity	120,413.00	
Fluorine Study	<u>5,000.00</u>	
		125,413.00
<u>Miscellaneous</u>		
Books for Committee Use		<u>57.77</u>
TOTAL EXPENDITURES		<u>164,970.77</u>
BALANCE ON DEPOSIT		<u>54,369.23</u>

Payments Required to Continue Current Projects Unitl 6-30-50

<u>Harvard University</u>		
Toxicological Reviews (3-14-50 to 6-30-50)		3,000.00
<u>University of Cincinnati</u>		
Carcinogenicity	38,963.39	
Fluorine Study (11-28-49 to 6-30-50)	<u>1,500.00</u>	
		<u>40,463.39</u>
TOTAL PAYMENTS TO 6-30-50		<u>43,463.39</u>
BALANCE AVAILABLE 7-1-50		<u>10,905.84</u>

Tentative Budget for Year Ending 6-30-51

<u>Harvard University</u>		
Toxicological Reviews	10,000.00	
<u>University of Cincinnati</u>		
Carcinogenicity	92,000.00	
Fluorine Study	<u>2,500.00</u>	
		<u>94,500.00</u>
TOTAL TENTATIVE BUDGET		<u>104,500.00</u>
CONTRIBUTIONS NEEDED TO FINANCE TENTATIVE BUDGET		<u>93,594.16</u>

NOTE: If 1949 contributors should give 150% of the 1949 contributions the total for 1950 would amount to \$96,510.

24/

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

November 2, 1950

THE KETTERING LABORATORY
COLLEGE OF MEDICINE—EDEN AVENUE
CINCINNATI 10, OHIO

CABLE ADDRESS: KETLAB, CINCINNATI
TELEPHONE: CAPITOL 1414

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

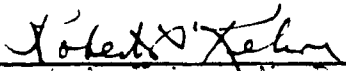
Dear Mr. Stroop:

In accordance with the request in your letter of October 6 to Doctor Horton and duly transmitted to me, I have written a summary report for the purpose suggested. It is somewhat over 500 words, but I feel that I have trimmed it to the bone.

Fifty copies of this are being sent to you by parcel post, and are expected to arrive by the time the fifty copies of the report proper reaches you by Railway Express. I shall take additional copies with me for distribution to members of the Medical Advisory Committee and their technical advisors at the time of the meeting. It may be that they will wish to incorporate this as an abstract, so to speak, in the larger report.

Best regards,

Sincerely yours,


Robert A. Kehoe, M. D.

RAK:ef

Summary Report of Progress
In The Appraisal Of The Potential Carcinogenic Properties of
American Petroleum Products

Introduction

The history of cancer of the skin among persons whose work has involved intimate and prolonged contact with aromatic coal tars and oil shale, derived mainly from British experience, together with the less familiar record of scrotal cancer in the United States and elsewhere among men long exposed to contact with waxy gas oils and slack wax, has provided a background which has justified and brought forth much productive investigation and promoted an alertness, within the industry, to this occupational hazard. Out of such background came the recent recognition of the possibility and, later, the fact, that specific carcinogenic substances could be concentrated or actually produced in certain materials subjected to certain modern technologic operations. With this recognition came the responsibility to appraise the potential hazard to petroleum workers and consumers from this source, and to find means of obviating any actual risk that might be found to exist. This responsibility has been assumed by the petroleum industry, through the A.P.I. Medical Advisory Committee, and a comprehensive investigation has been instigated under their sponsorship. The staff of the Kettering Laboratory has welcomed the request of the Medical Advisory Committee that it undertake such an investigation, and has taken a pardonable pride in this manifestation of confidence in the efforts of the Laboratory

in the field of industrial health. The work was undertaken in the assurance that the whole-hearted help of the industry would be forthcoming, and this assurance has been fully justified.

Scope of Investigation

The plan of the investigation was laid out along four general lines; (a) a complete survey of refinery processes and materials which might have carcinogenic characteristics, in order to facilitate the selection of appropriate samples for biological testing; (b) the development and application of biological methods for measuring and expressing the relative carcinogenic potencies of the samples selected; (c) the investigation of chemical means for identifying and determining carcinogenic materials in the samples; and (d) an epidemiological program for obtaining present and future information on the actual occurrence, if any, of occupational cancer in the petroleum industry, and on the factors which may influence the occurrence of such disease. By means of these four approaches one might hope to assemble the facts in such a manner as to portray the breadth and significance of the potential hazard, to simplify and give precision to methods for defining and localizing the hazard, to formulate the measures for its adequate control, to provide early and effective diagnosis and therapy for any disease that might develop out of past or existing conditions, and ultimately to prevent the occurrence of disease of this type.

Initiation and Progress of Program of Investigation

Early in 1949 the survey of the technological background of the industry was initiated by the Laboratory, with the advice and assistance of many well informed persons within the industry. Since that time, the gathering and analytical study of samples has been facilitated by invaluable technical help from the industry, through which the biological testing has been greatly simplified and greatly reduced in cost over that originally anticipated. The methods developed and employed for the biological and chemical examination of the samples have yielded highly gratifying results, and steady progress is being made in the accumulation of necessary and apparently reliable data.

It is of the greatest importance that the methods of procedure and the manner of expressing the biological results be coordinated with those of British investigators working in the same field of endeavor. By such means the volume of data will be expanded automatically and inexpensively, while the checks on methods and judgments which stem from such scientific collaboration should prove to be valuable.

During 1950, the epidemiological aspects of the program have undergone cautious development. This highly important part of the program presents difficulties which derive in no small part from lack of uniformity in the methods and records of medical examinations in the various units of the industry. The composite difficulties affect the scope and type of the epidemiological work, as well as the ultimate reliability

of the data. The complexities of the problem are being resolved as rapidly as possible and in a spirit of good will and cooperation. Some data are available, and it is expected that an orderly flow of information will be forthcoming during 1951. The ultimate scope of the epidemiological work will be determined on the basis of what seems feasible and capable of providing useful information.

The Future of the Investigation

The investigation as planned and developed is on the way to achieving the intended purposes. The program should be maintained substantially in its present form, with such modification or extension as may be indicated by subsequent experience.

The cost of the further prosecution of the work along current lines can be estimated with reasonable precision, the only important variable being the scope of the epidemiological work. The cost of the latter will depend upon the time and personnel which can be employed profitably in gathering and studying epidemiological data, and in maintaining such contact with the medical personnel of the industry as may be required to yield satisfactory information. The next budget, effective as of July, 1951, will hardly be less than \$85,000.00 or more than \$100,000.00. This total sum is arrived at without taking account of work of this type which may be accepted under the financial sponsorship of individual units of the petroleum industry. The extent of such work, which would reduce the expenditures made on behalf of the American Petroleum Institute,

5.

cannot be estimated at this time.

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

By:

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

October 31, 1950