

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

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API
HISTORY
OF THE
SUBCOMMITTEE
ON
CARCINOGENICITY

1953-1954

API 05529

Hueper
to 05561

Copy from D. V. Stroop for Information of Members and Associates
of the Medical Advisory Committee

1-19-53

ESSO LABORATORIES
Standard Oil Development Company

Medical Research Division

P. O. Box 51
Linden, N. J.

January 15, 1953

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

Dear Mr. Stroop:

I am attaching a reprint of an article recently
written by Dr. Hueper. I think that this article should be
brought to the attention of all of the members and associates
of the Medical Advisory Committee of the API.

Very truly yours,

/s/ R. E. Eckardt

R. E. ECKARDT, M. D.

REE:ilk

Encl. - Environmental Cancers:
A Review by Dr. W. C. Hueper
Reprinted from CANCER RESEARCH
Vol. 12, No. 10, pp. 691-97, October 1952.

API 05554

epi

AMERICAN PETROLEUM INSTITUTE

50 WEST 50TH STREET
NEW YORK 20, N. Y.

February 2, 1953

Mr. T. J. Sullivan
Chairman, Study Committee
API Division of Refining
c/o Gulf Oil Corporation
Gulf Building
Pittsburgh 30, Pennsylvania

Dear Sir:

As requested in your letter of November 19, the views of the Medical Advisory Committee membership on the report and recommendations of the Working Group are transmitted for your consideration, as follows:

1. That portion of the report, as well as the first recommendation, dealing with the epidemiological phase of the Kettering project constitutes encouraging support to recommendations which have been considered and advocated repeatedly by the committee. The members need and welcome the assistance of refining executives in the compilation of adequate standardized records for the petroleum industry.
2. The balance of the report and the recommendation for an investigation of the epidemiology of cancer in other industries lack definition necessary for a critical review; however, in principle, the members deem it unwise for the American Petroleum Institute to initiate such a project. It seems unnecessary to recite the many difficult problems incidental to such an undertaking.

For your information, the members of the Subcommittee on Carcinogenicity of the Medical Advisory Committee, by letter ballot in September 1952, expressed considerable doubt as to the wisdom of extending to employees of customers the epidemiological studies of cancer by the Kettering Laboratory under the sponsorship of the American Petroleum Institute.

On behalf of members of the Medical Advisory Committee, I express my sincere appreciation for the interest shown by members of the Study Committee and its Working Group in this subject.

Very truly yours,

E. Kern Linder

E. Kern Linder, M. D.
Chairman, Medical
Advisory Committee

cc: To Members
Medical Advisory Committee

API 05564

*high carcinogenicity
refinery mat'ls*

discernible but it was not anticipated that any such trends would be discernible prior to at least 5 years experience. It is hoped that the support which the General Committee, Division of Refining has given to the epidemiological study will stimulate renewed reporting of the cases with sufficient medical and occupational histories to permit some early correlations to be made about 1956.

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observations of
H. Lab (P. 6)*

Summary

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

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

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

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

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

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

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

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*Payer review
at API*

Ministry

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

January 26, 1954

TO: The Members of the Medical Advisory Committee

I am attaching a copy of a manuscript of a paper which Dr. A. Wesley Horton wishes to submit to the Journal of Analytical Chemistry in the near future. This paper was presented to the RPA Committee at its meeting in Cincinnati on January 21, 1954. Certain minor modifications were made at that time, and these modifications have been incorporated into the attached manuscript, the revised copy having been received in my office on January 25, 1954. It was the unanimous agreement of those of the RPA Committee present in Cincinnati (Dr. L. C. Beard and Dr. C. H. Hine were absent) that this manuscript was acceptable for publication.

I would greatly appreciate it if each of you would review this manuscript in detail and transmit any criticisms or suggestions which you may have concerning it to Mr. Stroop within the next 20 days*. At the end of that time, if no major objections to the publication of this manuscript have been received from any of you, it is the plan to transmit it to the Health Committee of the Board for their approval. As you know, the total time for clearance of this manuscript is 60 days, at the end of which time Kettering Laboratory can submit this paper for publication, so that anything you can do to expedite comments would be greatly appreciated.

Very truly yours,

/s/ R. E. Eckardt

R. E. ECKARDT, M. D.

REE:ilk
Attachment

* Note by D. V. Stroop

As we have been delayed in transmitting this letter until February 3, we shall defer reference to Medical and Health Committee of the Board until March 1. Three copies of manuscript are enclosed for each committee member. None is being sent to any technical advisor.

DVS

Copy From D. V. Stroop For Information of Members of Medical Advisory
Committee and Subcommittee on Carcinogenicity May 6, 1954

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

May 4, 1954

paper review

TO: Members of the Subcommittee on Carcinogenicity

Gentlemen:

I am attaching a copy of a manuscript forwarded to me by Dr. Horton entitled "Carcinogenesis of the Skin: I. Basic Methods Employed in Testing Complex Hydrocarbon Type Tars and Oils, and the Development of a Quantitative Scale to Express Their Relative Potencies to Mice". This paper has been written by Dr. Horton and his associate, Dorothy T. Denman. It is his plan, I believe, to submit this paper to Cancer Research for publication, although he has not yet indicated to me just to which journal he plans to submit it for publication.

Dr. Horton has indicated that any date in May except the period May 11-20 would be all right for a meeting of the Subcommittee. After having reviewed the manuscript, I believe a meeting of the Subcommittee with Dr. Horton would be advisable, and would suggest that this meeting be held after each of you has had ample time to review the manuscript both personally and possibly with some of your technical people, so that at the time of the meeting with Dr. Horton we will be in a position to express all suggestions to him. With this in mind I tentatively propose the dates of Friday and Saturday, May 21 and 22, or Thursday and Friday, May 27 and 28 for a meeting with the Kettering group to discuss this manuscript. I would appreciate it if each of you would let me know as soon as possible which of these two dates would be satisfactory so that final arrangements can be made with the Kettering group. As soon as your wishes are in, I shall send you definite notice of the meeting dates.

Sincerely yours,

/s/ R. E. Eckardt

R. E. ECKARDT, M. D.

REE:ilk

cc: Members of the Medical Advisory Committee
Dr. A. Wesley Horton

API 05770

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

MEDICAL RESEARCH DIVISION

ROBERT E. ECKARDT PH.D. M.D.
DIRECTOR
WILLIAM W. GERARDE PH.D. M.D.
HEAD TOXICOLOGIST

INDUSTRIAL HYGIENE SECTION

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

July 13, 1954

Studies "sold"
as preventive
of govt reg.
of oil industry
Eckardt

Dr. George M. Saunders
Security-Vacuum Oil Co., Inc.
26 Broadway
New York 4, New York

Dear Dr. Saunders:

I am attaching the report of the Subcommittee on Carcinogenicity to the Medical Advisory Committee of the API. This report summarizes briefly the work which has thus far been done, the expenditures thus far made, the anticipated future work to be done under the auspices of this Subcommittee, and the proposed budget for the period July 1, 1955-June 30, 1956. You will note that the Subcommittee suggests that funds in the amount of \$65,000 be solicited for the continuation of the work of the Bettering Laboratory during the period July 1, 1955-June 30, 1956. This represents a reduction of approximately \$7,250 in the amount already budgeted for the interval July 1, 1955-June 30, 1956.

It has been suggested by one of the Subcommittee members that this report should contain a statement which would describe the benefits which this study would accomplish for the oil industry. It is my belief that the benefits to be expected by the oil industry are contained in the brief outline of future work. However, if in your opinion this would not suffice, then I believe the following statement might be added to this report immediately following the section on future work and immediately preceding the estimated budget for July 1, 1955-June 30, 1956.

"It is anticipated that this work will benefit the petroleum industry by providing basic information which will permit the petroleum industry to control its own potential carcinogenic hazards without governmental regulation."

As Chairman of the Subcommittee on Carcinogenicity, I respectfully submit this report of the Subcommittee.

Very truly yours,

R. E. ECKARDT, M. D.

REE:ilk
Attachment

cc: Messrs. J. J. Phair
A. J. Norton
R. A. Kehoe
D. V. Streep ✓

API 05888

Epi

- 4 -

2. Epidemiology

It was early recognized by the Subcommittee on Carcinogenicity that the chemical and biological work outlined above would give only a partial answer. It was expected that the epidemiological work would develop information on the following two questions.

- a. Does work in the petroleum industry or at any specific job within the petroleum industry subject the worker to an increased risk of developing cancer?
- b. Have newer refining processes, such as catalytic cracking, or increased severity of thermal cracking introduced any new risks of developing cancer to any segment of the petroleum workers? It is in general these newer processes which have been shown to produce materials which have a high degree of carcinogenicity to mice.

A central registry for the reporting of cancer cases occurring in the petroleum industry represented by the participating companies of the API was established at the Kettering Laboratory under the direction of Dr. Phair. In addition to reporting such cases, it was deemed essential that a complete occupational history for each case also be reported so that correlations with occupation could be made.

In the course of setting up this registry, it soon became apparent to Dr. Phair that the medical departments and medical records of some petroleum companies were inadequate to permit accurate reporting of cancer cases. Initially, therefore, Dr. Phair's major effort was in assisting medical directors, or refinery managers where medical directors were unavailable, in organizing their departments and/or records so that good case reports and occupational histories would be received in his office. Therefore, it has only been in the past year or two that an approach to effective reporting of all types of cancer cases and occupational histories has been achieved. Despite incomplete uniformity of reporting and participation, over 1,300 cancer cases have been reported to Dr. Phair from 15 companies, and are in the process of statistical analysis. It is believed that worthwhile statistical analysis of these cases will require maintenance of this registry for a minimum of 6 years. In the interim, Dr. Phair continues to act in an advisory capacity to the petroleum companies and their medical directors for the collection and reporting of these cases.

API 05892

members
conc. S.C.

- 7 -

Salaries

\$14,000

Miscellaneous Exp.

Animals	\$ 1,250
Supplies	5,000
Travel	4,000
Overhead	10,750

21,000

\$65,000

Composition of Subcommittee

R. E. Eckardt, M. D., Chairman
Standard Oil Development Company

E. W. Adams
Standard Oil Company (Indiana)

L. C. Beard, Jr.
Secony-Vacuum Oil Company, Inc.

Allan E. Dooley
The Texas Company

F. D. Gassaway, M. D.
Gulf Oil Corporation

L. M. Henderson
The Pure Oil Company

27
C. H. Hine, M. D.
Shell Development Company

E. K. Linder, M. D.
The Atlantic Refining Company

R. C. Mithoff
California Research Corporation

M. N. Newquist, M. D.
The Texas Company

API 05895

*wording of
publication
to stress only
Carc. "to mice"*

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

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

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

July 16, 1954

Dr. Leo Wade
Esso Standard Oil Company
15 West 51st Street
New York 19, New York

Dear Dr. Wade:

Your comments concerning the first paragraph of Dr. Horton's and Miss Dorman's paper on "Carcinogenesis of the Skin I." has created a considerable amount of comment and discussion. There is apparently also some concern about how your comments can be resolved with the Kettering Laboratory.

One suggestion is that the last sentence of this paragraph have the phrase "to mice" added on the end of it. If this change would overcome the objections which you have to this paragraph, I am sure that the Kettering Laboratory would be amenable to this minor change.

If the above change does not satisfy the objections which you have to this paragraph, it would be my suggestion that you rewrite the first paragraph as you would wish to see it worded, and that you submit this rewriting to Dr. Saunders with a carbon copy to Dr. Kehoe (Dr. Horton) to see if the Kettering Laboratory would be agreeable to rewriting the first paragraph as you would wish it rewritten. In the event that the Kettering Laboratory would not agree to your rewrite, it would then appear to me that when this paper is forwarded to the Committee of the Board prior to publication, we could also recommend, as the Medical Advisory Committee, that your rewrite would be preferable to the one that the Kettering Laboratory proposes. The Board Committee would then be in a position to suggest either that the Kettering Laboratory wording or that your wording would be more preferable to them. Naturally, the Kettering Laboratory would be in a position not to concur with the recommendations of the Board Committee, but knowing Dr. Kehoe and others at the Kettering Laboratory, I believe that they would give considerable thought to this if they decided to publish their own wording instead of that preferred by the Board Committee and would undoubtedly have very strong reasons for adhering to their own wording.

I attempted to discuss this with you on the telephone today, but since you were out of your office I thought it could be handled by mail, since I am going on my vacation starting on the 17th and will be out of the office for two weeks. I would be happy to discuss this further if you feel it necessary after I return from my vacation and if it has not already been settled in the meantime.

Sincerely yours,

RKE:ilk

R. E. ECKARDT, M. D.

API 05899

cc: Dr. G. M. Saunders ✓

*✓ employee
relations
problems "
faced at
Esso*

July 6, 1954

Dr. George Saunders, Chairman
Medical Advisory Committee
American Petroleum Institute
50 West 50th Street
New York, New York

Dear Doctor Saunders:

Dr. Eckardt sent us a copy of his letter to Mr. Stroop concerning the proposed publication by Mr. Horton and Miss Denham regarding carcinogenesis of the skin. Most of the suggestions we have made have been properly recognized. We are still of the opinion that the opening paragraph is misleading and not in strict keeping with the facts of the situation. Until such time as a definite clinical correlation has been established between exposure to high boiling aromatic fractions and the occurrence of skin cancer, I believe these animal data are only suggestive.

It is my understanding that Mr. Horton objects to any revision of this paragraph. If one could be sure that the manuscript will stay in strictly professional channels, his objections are well taken. From past experience, however, I feel reasonably sure that this assumption cannot be relied upon to protect us from unjustified employee relations problems. ||

Very truly yours,

LEO WADE, M. D.

DW:jak
cc: Dr. R. E. Eckardt
Mr. William Naden
Mr. D. V. Stroop

THE REPORT OF THE SUBCOMMITTEE ON CARCINOGENICITY
TO THE MEDICAL ADVISORY COMMITTEE OF THE API

The Subcommittee on Carcinogenicity of the API Medical Advisory Committee, one of the first subcommittees created, was established early in 1945. It was formed after it became known that certain petroleum oils and fractions had been demonstrated to possess fluorescence similar to certain known carcinogens, and, when painted on mice, produced tumors and cancers.

Negotiations were then begun between this Subcommittee and Dr. Kehoe of the Kettering Laboratory which culminated, early in 1946, in an agreement between the API and the University of Cincinnati, under which the Kettering Laboratory of Applied Physiology would "investigate the toxicity and mode of action of certain petroleum products."

The investigation began with the testing of 8 oils supplied by three participating companies, in addition to negative controls of water and white oil and positive controls of methylcholanthrene. Of the 8 oils tested, only 2 produced skin tumors in mice. One of these was an unflashed thermal residue, the other a clarified oil. These investigations were carried out at a cost of \$6,000, and were reported in detail to the Subcommittee by the Kettering Laboratory on November 5, 1948.

However, when the results were becoming apparent early in 1948, the Medical Advisory Committee, on the advice of the Subcommittee on Carcinogenicity, forwarded to the members of the Safety Committee of the Board of Directors of the API a resolution dated April 5, 1948. This resolution called upon the Executive Committee of the Board of Directors "to establish a comprehensive research project for the development of fundamental facts, analytical techniques and related information pertaining to cancer-causing compounds which may occur in petroleum or be produced therefrom." This resolution called for the solicitation of contributions to a special research fund in the amount of \$110,000 for the first year, of which \$50,000 would be a non-recurring capital expenditure for construction of extraordinary experimental facilities at the Kettering Laboratory. This resolution was presumably approved by the Executive Committee and on July 1, 1948 a check in the amount of \$65,000 was sent to the Kettering Laboratory, \$40,000 of this amount as a grant for animal quarters.

With the expansion of this research project in 1948, A. W. Horton, Ph. D. was added to the staff of the Kettering Laboratory to supervise the chemical and biological work on petroleum and petroleum fractions, and the services of J. J. Phair, M. D., Professor of Preventive Medicine, University of Cincinnati, College of Medicine, were made available to the staff to develop and supervise an epidemiological survey of the incidence of cancer in the petroleum industry. From this point on, the research project can be divided into two phases, namely (1) the chemical and biological work, and (2) the epidemiology.