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

DATE: 1950 Apr 24

DOC#: API013

DOCUMENT DESCRIPTION: Meeting Minutes & Attendee List - API Medical Advisory Committee

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AMERICAN PETROLEUM INSTITUTE
MEDICAL ADVISORY COMMITTEE

ELEVENTH MEETING

Minutes of Meeting
April 24, 1950
Hotel Sherman
Chicago, Illinois

MEMBERS PRESENT

Kieffer Davis - Chairman
B. B. Reeve - Vice Chairman
Marshall Clinton - Secretary

W. O. Armstrong	J. P. Holt	E. P. Luongo
V. C. Baird	(Rep. by R. E. Eckardt)	M. N. Newquist
F. F. Boys	T. J. Kelly	Chas. A. Swan
T. M. Frank	E. K. Linder	E. Richmond Ware
A. E. Hoag	James W. Long	McIver Woody

ASSOCIATES PRESENT

E. W. Adams	Allan E. Dooley	K. G. Mackenzie
R. D. Bent	R. W. Faulk	C. A. Neilson
R. C. Cole	L. M. Henderson	W. H. Price
L. O. Crockett	R. M. Landon	R. M. Shepardson
T. E. DeVilliers	H. P. Lankelma	F. M. Watkins

GUESTS

R. G. Birrell - Imperial Oil Limited
A. R. Bowles - The Texas Company
Philip Drinker - Harvard University
J. W. Hammond - Humble Oil and Refining Company
A. W. Horton - University of Cincinnati
Robert A. Kehoe - University of Cincinnati
Chas. A. Miller - The Texas Company
John J. Phair - University of Cincinnati
A. O. Seeler - Harvard University
H. G. S. van Raalte - Shell
H. R. Warrick - The Texas Company

API STAFF

D. V. Stroop

Total in Attendance - 44

MEMBERS ABSENT

Theodore E. Allen	L. E. Curtis	Robert Bell Lynn
Wm. Crookshank	D. M. English	R. C. Page
	W. R. Levis	

ASSOCIATES ABSENT

W. R. Argyle	J. B. DeLaune	D. W. Larmer
L. C. Beard, Jr.	R. S. Driver	C. R. McKay
J. S. Boylan	H. G. M. Fischer	R. B. Roaper
C. R. Brown	N. J. Gothard	H. D. Wilde
	E. W. Isom	

.....

I

MINUTES OF TENTH MEETING

Action The Minutes of the Tenth Meeting, held November 11, 1949, were approved as circularized.

II

REPORT OF SUBCOMMITTEE ON CARCINOGENICITY - DR. McIVER WOODY, CHAIRMAN

The Subcommittee on Carcinogenicity submitted progress reports (copies of which are attached hereto as Appendix A).

The Committee discussed but deferred action on this report.

III

REPORT OF SUBCOMMITTEE ON FLUORIDES - DR. A. E. HOAG, CHAIRMAN

Dr. Hoag reported progress. He submitted a report from the Kettering Laboratory (copy of which is attached hereto as Appendix B).

IV

REPORT OF SUBCOMMITTEE ON CUTTING FLUIDS - DR. B. B. REEVE, CHAIRMAN

The Subcommittee on Cutting Fluids made a report (copy of which is attached hereto as Appendix C) and recommended that this material be made available to members and associates of the API Medical Advisory Committee and on request to representatives of contributors to the Medical Research Fund and to members of Institute committees which are interested in the subject.

Action The Committee voted to make the report available in this manner.

V

REPORT OF SUBCOMMITTEE ON PERMISSIBLE CONCENTRATIONS
DR. V. C. BAIRD, CHAIRMAN

The Subcommittee on Permissible Concentrations submitted a report (Appendix D) and the progress report from Harvard University (Appendix E). As suggested in the report, the problem of petroleum products used in conjunction with economic poisons was presented by Dr. Kehoe and discussed in detail by the Committee.

Action The report of the Subcommittee was accepted and all recommendations were adopted.

VI

REPORT OF SUBCOMMITTEE ON MEDICAL POLICIES AND PRACTICES
DR. L. E. CURTIS, CHAIRMAN

In the absence of Dr. Curtis no report was made for the subcommittee.

VII

FIRST AID AND SAFETY TRAINING COURSE

Mr. Charles A. Miller presented an outline of a proposed first aid and safety training program.

Action The Committee voted that the API Medical Advisory Committee endorses in principle the establishment of an API First Aid and Safety Training program and will cooperate with the Central Committee on Accident Prevention in the establishment of such a program, and, further, that the Chairman is authorized to appoint a subcommittee to work with the Central Committee on Accident Prevention in developing the medical aspects of this program.

VIII

OCULAR EFFECTS OF CUTTING OIL ADDITIVES

Dr. B. B. Reeve presented correspondence on this subject, for the information of the committee (copies were circularized to members on April 26, 1950).

IX

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA

Action The Committee voted to defer action on the question of joining the Industrial Hygiene Foundation.

X

EXECUTIVE SESSION

Report of Subcommittee on Carcinogenicity

Action The Committee voted to accept the report of the Subcommittee on Carcinogenicity in the understanding that the report to be published would not include data on the two hydrocarbons and that prior to publication the revised manuscript would be sent to members of the Committee for review.

Report of Subcommittee on Permissible Concentrations

Action The Committee voted to authorize D. V. Stroop to arrange the details of payment of $5000 for Professor Drinker's services from July 1, 1950 to June 30, 1951.

Changes In Organization

Actions (1) The Committee accepted the resignation of Dr. Holt from the Editorial Committee and as API representative on the ASA Committee on Allowable Concentration of Toxic Dusts and Gases. The Chairman was empowered to appoint successors to these positions.

(2) The Committee voted to establish a subcommittee to study the question of eye problems peculiar to the petroleum industry.

(3) The Committee empowered the Chairman to appoint a special subcommittee to report on the advisability of accumulating information and/or carrying on investigations of petroleum solvents used in conjunction with economic poisons.

(4) The Committee voted to continue its standing subcommittees on:

(1) Medical Policies and Practices.
(2) Permissible Concentrations.

XI

TWELFTH MEETING

The Committee voted to hold its twelfth meeting at the Biltmore Hotel, Los Angeles, California, on Friday and Saturday, November 10, and 11, 1950.

NOTE: Subsequently a number of members have requested that the meeting dates should be advanced one day so that the meeting would be held on Thursday and Friday, November 9th and 10th. Members who object to this change are requested to inform D. V. Stroop immediately. In the absence of objections, arrangements will be made to hold the meeting on November 9th and 10th.

XII

ADJOURNMENT

There being no further business to be considered, the meeting was adjourned.

Marshall Clinton, M.D.
Secretary

Approved:

Kieffer Davis, M.D.
Chairman

6/23/50

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APPENDIX A

To Minutes of 11th Meeting of Medical Advisory Committee

REPORT TO THE API MEDICAL ADVISORY COMMITTEE

BY THE SUBCOMMITTEE ON CARCINOGENICITY

Dr. McIver Woody - Chairman

April 23, 1950

On behalf of the Subcommittee on Carcinogenicity, I wish to submit the following report to the Medical Advisory Committee for transmission to the Safety Committee of the Board of Directors of the American Petroleum Institute:

Dr. A. Wesley Horton reported on the progress of the experimental work at the University of Cincinnati. A report summarizing this work was sent to all members and associates of the Medical Advisory Committee on April 11. The report was accepted and approved.

Dr. Horton stated that a report on the dose-response of the two strains of mice to various concentrations of methylcholanthrene would be submitted for publication in the journal "Cancer Research" and that it would be desirable to include in that report the tumor index curves of two typical high-boiling catalytically-cracked oils.

Dr. J. J. Phair described the proposed epidemiological study in the petroleum industry and distributed an outline of the procedures which should be followed. Dr. Phair's report was accepted and approved with the understanding that the word "needed" will be used in place of "required" where it fits the context. (Dr. Phair's amended report is attached as a part of Appendix A).

An exchange of samples, which will be identified only by code numbers, is being worked out with the Institute of Petroleum in England.

It is recommended that the Medical Advisory Committee approve:

1. Publication of the report as described by Dr. Horton in his letter of April 7, 1950 to Mr. D. V. Stroop.

2. The proposed epidemiological study as described by Dr. Phair.

UNIVERSITY OF CINCINNATI
DEPARTMENT OF PREVENTIVE MEDICINE AND INDUSTRIAL HEALTH

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

CABLE ADDRESS: KETLAB. CINCINNATI
TELEPHONE: CAPITOL 1414

May 15, 1950

TO: Members of the Subcommittee
on Carcinogenicity
Medical Advisory Committee
American Petroleum Institute

FROM: John J. Phair, M.D.

I am submitting herewith a revised Progress Report for the Proposed Epidemiological Studies of the Project on Carcinogenicity at the Kettering Laboratory. It contains the modifications and revisions suggested for the report presented at the meeting of the Subcommittee on Carcinogenicity of the Medical Advisory Committee held April 23, 1950 in Chicago.

The standard clinical record and occupational history forms to be employed in gathering the information required for the Retrospective Study and the Current Registry are in preparation, and it is hoped that these can be distributed for immediate use early in June. It is planned that the code to be used in the tabulation of these data will be ready for circulation at the same time. As many personal visits as feasible will be made before the November meeting of the Subcommittee, so that a uniform handling of these records can be insured, insofar as possible, under existing conditions.

As an additional activity of the epidemiological survey, a simple questionnaire requesting certain fundamental descriptive facts about each refinery or installation of the participating companies will be sent to each Medical Director in the near future. This will be the first step in the routine assembling of necessary basic information for this study regarding the employee population involved and the control measures presently in force or as adopted.

JJP:hp

For Information Only - Not for Publication

Kettering Laboratory

University of Cincinnati

THE PROJECT ON CARCINOGENICITY

PROPOSED EPIDEMIOLOGICAL STUDIES

Progress Report

for

The Subcommittee on Carcinogenicity

of the

API Medical Advisory Committee

April 23, 1950

Revision - May 15, 1950

PRESENT STATUS

At the Subcommittee meeting held March 25, 1950, the following objectives were presented:

I. The determination of incidence and prevalence rates of retrograde, hypertrophic or neoplastic reactions in employees of the Petroleum Industry.

II. The comparison of these rates with those of the general population and other industries.

III. The evaluation of control procedures that have been accepted, employed or recommended.

IV. The recommendation, if the studies justify the action, of standardized safety and control measures.

The possible approaches to these objectives are:

I. A Retrospective or Historical Study of all available records of such cases among the employees of the Petroleum Industry.

II. A Current Registry receiving reports of such cases as they are discovered by and/or reported to the various Medical Departments.

III. A study of the Employee Health Benefit Plan records with the hope that like data can be secured from other industries.

IV. Field Surveys of retrograde or hyperkeratotic lesions on exposed skin surfaces.

V. A repetition of the studies which have pointed out an unusual hazard in the Slack Wax Process.

VI. The establishment of a Consultation Service to assist in the planning of comparable company studies. This last approach was not discussed at the Cincinnati meeting.

FUTURE PLANS

A. It is proposed to implement immediately, insofar as possible and/or feasible, with due consideration and understanding of the wide variation in company policies, medical care programs, management interest and labor relations, the first two approaches, namely, (I) the Retrospective Study and (II) the Current Registry.

I. Retrospective or Historical Study

1. Description

This approach requires the assembling of the clinical records and employment histories of proved cases of Neoplastic disease known to have occurred among employees of the cooperating Petroleum Companies, regardless of site, type of tumor, degree of exposure to various carcinogenic hazards and employment status.

The Medical Departments, under this plan, within the limits of their legal responsibilities (See Appendix, Page 1), would be expected to forward to the Survey Group of the University of Cincinnati the records of all known cases of proved or suspected Neoplastic disease which have occurred among their employees during the period covered by their immediately available files.

It would be expected that the details of the clinical records would be augmented, supplemented and/or verified, insofar as possible, by the various Medical Departments

through their relationships with their subordinate offices, private physicians, hospitals, clinics and laboratories.

To determine the degree of possible exposure to various potential carcinogens, the various Medical Departments would be expected to request that their Personnel Departments furnish, insofar as their records permit, a detailed employment history, including not only information regarding the employment of the patient in the company or industry, but also any other employment in other industries as covered by their records.

(See Appendix, Pages 2, 3, 4, 5 and 6 for the details of the information to be requested on (1) the initial report, (2) the clinical record and (3) the employment history.)

The Survey Group of the University of Cincinnati would be expected to set up the necessary clerical mechanism to receive the initial reports, to process the clinical records and employment histories and to provide interim and final summations to the Medical Advisory Committee. The tabulations and analyses would be arranged to protect the identity of the companies and/or the individual patients involved in the study through the use of a code system.

2. Objectives

The serious defect in this plan arises from the great variation in the amount and type of information available in files of the various Medical and Personnel Departments. For some companies, the need to collect this data is an entirely new concept. In others, even the provision of medical care programs for the employees is a relatively recent activity.

This approach, even with optimum conditions, information and cooperation, can only furnish a crude estimate of the prevalence of Neoplastic disease among employees of the cooperating companies who have had exposures to the older conditions and processes. The tabulations cannot be used to ascertain the potential hazards of the newer processes.

However, if a consistent pattern in the occupational histories of this group of cases was found, the presence of overlooked hazards in the older methods might be indicated. Furthermore, if an unusual distribution is reported with regard to type and site of tumor, further epidemiological studies of Neoplastic disease in employees of the Petroleum Industry might be limited to only certain types and sites.

3. Approximate Period of Study

It is readily apparent that, due to the many diverse situations found in the industry, the variation in the degree of cooperation offered by the different companies, the time needed to secure general acceptance of a standardized report and the necessary lag that will be encountered in setting up the clerical mechanism at the University of Cincinnati, this approach will require approximately two years to complete. It would be expected that the final report including cases as they have occurred up to and including January 1, 1951 could not be submitted before 1952.

II. Current Registry

1. Description

This approach envisions the establishment of a continuing Central Registry for Neoplastic diseases to be employed by the various cooperating companies to report routinely through their Medical Departments proved or suspected cases of Neoplastic diseases which occur among their employees, regardless of site, type of tumor, degree of exposure to various carcinogenic hazards and employment status.

The Medical Departments, under this plan, within the limits of their legal responsibilities, would be expected to report currently to the Survey Group at the University of Cincinnati all cases of proved or suspected Neoplastic disease which occur among their employees.

It would be expected that, in addition to this notification, insofar as possible, a detailed clinical record would be completed by the various Medical Departments, augmented, supplemented and/or verified through their regular contacts with their subordinate offices, private physicians, hospitals, clinics and laboratories.

Furthermore, in order to ascertain the degree of possible exposure of the reported cases to various carcinogenic hazards, processes or environment in or out of the Petroleum Industry, the various Medical Departments would be expected to request that their Personnel Departments furnish, insofar as their records permit, a detailed history, including not only a

description of the job of the individual in the company and/or industry, but also all other employment covered by their records. It is hoped that this record can be augmented or supplemented, if necessary, by the Medical Departments, since, in many instances, the patient will be in direct contact with the Medical Director or his immediate subordinates.

(See Appendix, Pages 2, 3, 4, 5 and 6 for the details of the information to be requested on (1) the initial report, (2) the clinical record and (3) the employment history.)

It would be expected that the various Medical Departments, either directly or by securing the assistance of their Personnel Department, would furnish, periodically, similar employment histories for certain groups of employees in their company. The groups or samples required for this phase of the study would be selected with a direct request from the Survey Group, but only after personal consultation with the various Medical Directors and subject to the general approval of the Medical Advisory Committee.

(See Appendix, Pages 5 and 6 for the employment history as used for cases which would be sought not for all, but only a sample of the total number of employees in the company or industry.)

The Survey Group of the University of Cincinnati would be expected to set up the necessary clerical mechanism to receive the initial reports, to process the clinical records and employment histories and to provide periodic interim summations to the Medical Advisory Committee. The tabulations

and analyses would be so arranged that the identity of the companies and/or the individual patients involved would again be protected through the use of a code system.

In the attempt to calculate incidence rates for at least a fraction of the industry, it would be expected that the Survey Group would prepare the plan, subject to the approval of the Medical Advisory Committee, for selecting the needed employee groups for the population studies as previously described.

As an adjunct to the Central Registry, it would seem desirable to create a Central Pathology Service at the University of Cincinnati to whom the various cooperating Medical Departments could forward slides and/or tissues for diagnosis and a uniform classification. This particular activity would stimulate the cooperation of the physicians in the search and reporting of cases to the Central Registry. It would also establish a uniform level for acceptance of a case as one of proved Neoplastic disease. How this service can be established and financed still remains an open question.

2. Objectives

This approach would furnish, in contrast to the prevalence rates of the Retrospective Study, an approximate estimate of the incidence of Neoplastic disease among employees of the cooperating companies, since it is hoped that, for at least a portion of the industry, adequate estimates of the number of employees involved and possible exposures to various potentially carcinogenic hazards will be obtained.

It would be expected that this plan would augment, supplement and finally supplant the Historical Approach in defining far more accurately the hazard of the older processes. If successful, and since this will be a current registry providing for reports in the years to come, the analyses could be used to ascertain the hazards of the newer processes, provided that the study is maintained and supported for a sufficient period of time to take into account the long latent period commonly found with Neoplastic disease.

It is also possible that this plan, in the future, will provide comparisons of incidence rates not only between various processes, but also geographic areas, racial groups, companies, other industries and the general population.

3. Approximate Period of Study

It would be well to call attention at this point to the fact that the greatest obstacle to this approach is the dynamic almost fluid state of the technology of the Petroleum Industry. This situation will seriously interfere with any logical attempt to define accurately the degree and period of exposure, except in the very broadest of terms. It will be, likewise, the most dangerous factor in the estimation of exposed populations, since process changes bring about the frequent shifting of the employees in the refinery operations.

Also, since it is generally accepted that Neoplastic reactions require usually a relatively long and heavy exposure to even proved carcinogenic agents, and that there is, likewise, usually a very long period between exposure and

reaction, it is readily apparent that the registry must be continued and adequately maintained for a considerable period of time before it will even begin to measure the hazard of the newer processes. It is to be hoped, however, that satisfactory rates measuring the hazards of the older processes would be available much earlier.

B. It is proposed to continue the exploration and the possible implementation, as soon and insofar as possible and/or feasible, with due consideration and understanding of the wide variation in company policies, medical care programs, management interest and labor relations, of the third and fourth approaches, namely, (III) Employee Health Benefit Plan Study and (IV) the Field Survey for Retrograde or Hyperkeratotic Lesions.

The description, objectives and approximate period of study for both of these attractive and possibly feasible approaches must await further consultation, discussion and pilot trials before they can be brought to the Subcommittee and/or Medical Advisory Committee for their consideration. It is hoped that these two avenues can be explored sufficiently during the summer of 1950 to permit firm planning at the November meeting.

C. It is proposed to implement, as soon and insofar as possible and/or feasible, with due consideration and understanding of the wide variation in company policies, medical care programs, management interest and labor relations, the last two approaches, namely, (V) Repetition of the Slack Wax Studies and (VI) the Consultation Service.

It is not proposed that the Survey Group take an active part in the Slack Wax Studies, but that the observations will be repeated by individual companies. It is hoped that the Survey Group of the University of Cincinnati, through personal contact, can make certain that adequate observations are secured so this question can be thoroughly explored and evaluated. In serving as an agency to insure that the individual company protocols are valid, acceptable and comparable, it is expected that they can act as a medium of dissemination so that the various other cooperating Medical Departments will have access to this information.

It is planned, likewise, that the Survey Group of the University of Cincinnati will stand ready to assist, upon the specific request of any Medical Department, in the planning of other studies to determine particular and/or unusual hazards. It is not expected that the information so gathered would be disseminated generally unless the interested company permitted this action. The sole objective for this approach would be to insure comparability of studies and observations in case general dissemination or comparisons became desirable.

A P P E N D I X

COPY

December 20, 1949

Dr. McIver Woody
ESSO Standard Oil Co.
BUILDING

Dear Doctor Woody:

You have told me the plan is being developed to accumulate in the hands of investigators of the University of Cincinnati, who have been designated for the purpose, data with respect to operatives engaged in petroleum refining and petroleum handling who may have been determined to be suffering from or who may be suspected of suffering from cancer which may be attributed to their occupation or to contact with petroleum products. You have asked me if I see any objection from a legal standpoint to transmitting to the designated authorities at the University of Cincinnati the records of such patients.

There has grown up a feeling, and perhaps a right, on the part of patients to have their consultations with their physicians and the physicians' records with respect to the patients treated as confidential between the physician and the patient. Even if the patient's right to have such communications and records treated as confidential is not fully established, I think our anxiety to develop cordial relations between our employees and company doctors ought to compel us to regard those communications and records as confidential. Starting from this premise, I think it is entirely proper from a legal standpoint, and feasible from the standpoint of the relations we want to preserve with our employees, for you to report cases of the kind herein mentioned, provided you keep the identity of the patient strictly confidential. I suggest that these reports may be made under a series of code numbers or under fictitious names, you preserving in your confidential files the identity of the code number or fictitious name of the patient involved. I think if this anonymous scheme is observed in making the reports you have described to me, it cannot offend the patient's legal rights. I feel equally strong it is not likely to cause any disturbance in the relationship between our employees and our company doctors.

I would think that if the designated authorities at the University of Cincinnati desire to compile and use generally in the industry or with the public any statistics with respect to data of the kind herein described, which they receive from our company and from other companies, they ought to again use code numbers so that the identity of the company whose employees are embraced in the statistics will be carefully concealed.

If the foregoing restrictions are observed, I think the confidential nature of the physician-patient relationship will be preserved, and, similarly, the confidential nature of the company records will be preserved and I do not anticipate any trouble would be involved.

Very truly yours,

ESH A

Original Signed E. S. Hall

Preliminary Notification

I. Identification Data

A. Code Number - All identifying data (Name-Address) to be retained by the Medical Director, correlated with the code number.

B. Age (Year born)

C. Sex

D. Race

II. Clinical Data

A. Type of Tumor

B. Site of Tumor

C. Date of Diagnosis

Detailed Clinical Record

(To be completed in duplicate)
(One copy to be retained by the Medical Director)

I. Identification Data

A. Code Number - All identifying data (Name-Address) to be retained in the office of the Medical Director.

B. Age (Year born)

C. Sex

D. Race

E. Marital Status

F. Employment Status

II. Clinical Data

A. Dates

1. First Symptom
2. First Visit to Physician
3. First Diagnosis
4. First Treatment or Hospitalization
5. Death

B. Clinical and Pathologic Diagnosis - List of tumors to be reported which will be placed on the reverse of record. This list is not exhaustive but comprises the great majority of terms usually used. When there is doubt concerning the malignant nature of a tumor, it should be reported.

Carcinoma
Sarcoma
Epithelioma
Endothelioma
} and any term of which one of these words is a part.

Acanthoma
Astrocytoma
Brain Tumors
Chorioma
Chloroma
Cholesteatoma
Embryoma
Ependymoma
Ganglioneuroma
Glioma
Granulosa Cell Tumor (Ovary)
Hypernephroma
Hodgkin's Disease
Leukemia
Lymphoma
Lymphosarcoma
Linitis Plastica (Stomach)
Melanoma
Meningioma
Myeloma
Medulloblastoma
Mesothelioma
Mixed Tumor
Neurocytoma
Oligodendroglioma
Pinealoma
Syncytioma
Seminoma
Sympathoblastoma
Spongioblastoma
Teratoma
Thymoma
Paget's Disease (Breast)
Wilms' Tumor (Kidney)
Ewing's Tumor (Bone)
Grawitz' Tumor (Kidney)

C. Primary Site and Stage

D. Treatment Advised and Received

E. Complications - Metastatic Sites

III. Unusual Exposure to Possible Carcinogens - Including estimates of Degree, Type and Length of Time (As elicited by the Physician) List which will be placed on the reverse of the record.

A. Physical Agents

1. Trauma
2. Radiant Heat
3. Solar Rays
4. Ultraviolet Rays
5. Radioactive Substances or Roentgen Rays

B. Inorganic Substances

1. Arsenic
2. Chromates

C. Organic Substances

1. Aromatic Amines
2. Tar or Pitch
3. Soot
4. Creosote and Anthracene Oils

Detailed Occupational Record

(To be completed in triplicate)

(One copy to be retained by the Medical Director and Personnel Department)

I. Identification Data

A. Code Number

B. Age at Commencing Work

C. Employment Status

II. Occupations and Detailed Employment Record - Listed in Chronological Order

A. Name of Companies and/or Plants

B. Products Handled by Worker

C. Job Descriptions - The Broad Classifications which will be placed on reverse of card.

1. Production

a. Riggers and Drillers
b. Others

2. Refining

a. Cracking
(1) Catalytic
(2) Thermal
(3) Others

b. Lubricant and Paraffin
(1) Crude Wax
(2) Others

c. Straight Run Distillation and Light Ends

d. Special Products

e. Maintenance
   (1) Pipe fitters and Boilermakers
   (2) Others

f. Control Laboratory

g. Others

3. Transportation
   a. Pipe Line
   b. Fuel Oil Carriers
   c. Others

4. Marketing and Executive
   a. Service Station
   b. Others

5. Others - Specify in detail

D. Periods Employed

III. Unusual Exposure to Possible Irritants - Including estimates of Degree, Type and Length of Time (As elicited by the Employment Record)

(See list - Detailed Clinical Record)

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APPENDIX B

To Minutes of 11th Meeting of Medical Advisory Committee

REPORT TO THE API MEDICAL ADVISORY COMMITTEE

BY THE SUBCOMMITTEE ON FLUORIDES

Dr. A. E. Hoag - Chairman

April 23, 1950

ANNUAL REPORT on the PROGRESS OF EXPERIMENTAL INVESTIGATION OF THE STORAGE OF ABSORBED FLUORIDES BY MAN

The observations to be described in this report were obtained by the continuation of experiments in which three human experimental subjects were engaged. Earlier phases of these experiments were discussed in the Annual Reports for 1947 and 1948.

Experimental Subjects

The human experimental subjects employed in these experiments were, 1. EB, a 43 year old colored male, 2. KW, a 39 year old white female and 3. EL, a 37 year old white male. Recent physical and roentgenographic examinations of these subjects indicated that they have continued in good health and no changes of any sort were detected.

Methods

In connection with the materials ingested and excreted by the subjects, the following procedures were followed: Samples of solid food, milk, fruit juices, soups, et cetera, representing duplicates of all materials eaten during each day, were collected by each subject in a chemically clean glass jar, and duplicates of liquids (water, coffee and other beverages) containing little or no suspended material were collected in chemically clean glass jugs. The total daily urinary output was collected by the subjects in clean glass jugs and all feces were collected in clean glass jars.

The separate samples of mixed foods collected by the subjects were homogenized in a Waring-type blender and portions for each subject were analyzed on a daily basis. Samples of liquids were also analyzed on a daily basis and each sample of feces was analyzed separately.

The individual sample was ashed, the fluorides separated from the ash by a perchloric acid distillation, and the distillate titrated by the thorium nitrate backtitration procedure commonly employed.

For an experiment in which an experimental subject was to inhale low concentrations of hydrogen fluoride in air, an inhalation chamber approximately 160 cm X 190 cm X 190 cm, volume approximately 6000 L, was assembled. Panels in the chamber were covered with a transparent vinyl-type plastic sheeting. All other exposed surfaces of the interior were coated with a water-emulsion vinyl-type plastic paint.

A small cylinder of anhydrous HF was connected to a copper tube (1/4 inch in diameter) 6 feet of which was coiled to be immersed in heated oil where the HF was to be warmed to 45°C prior to its introduction into a small steel tank. This tank, approximately 6 inches in diameter and 7 inches in height, was immersed in the same oil bath as was used for the coiled copper tubing. This tank was also filled with oil and the oil displaced each time a charge, 1 to 2 L, of HF was introduced into the tank. A side arm attached to the bottom of the tank allowed oil to be pumped into the tank at a measured rate and thus displace the HF at a measured rate. During this phase of the operation the HF escaped through a small monel orifice into a brass tube (3/4 inch in diameter) through which nitrogen was passed at the rate of 5 L per minute. The HF was thereby swept along and into a sheet iron pipe (6 inches in diameter) where it was mixed with air blown into the pipe at the rate of 295 L per minute. The interior of this mixing pipe and of the pipe (4 inches in diameter) connecting it to the inhalation chamber was coated with paraffin.

The gaseous mixture was circulated inside the inhalation chamber by means of small circulating fan operated on a table in front of and blowing away from the experimental subject. A glass sampling tube, coated with paraffin, extended into the chamber to a point just in front of the subject and samples of air for analysis were withdrawn by suction through a small impinger tube and through a small bubble tower. A solution of NaOH, 0.03 N, was used in the sampling towers to absorb the HF. The fluoride content of the liquid was determined by the usual titration procedures without preliminary ashing or distillation.

Results

Subject EB

Throughout 1949 this human experimental subject continued the ingestion of fluoride (as NaF) added to his diet at the rate of 12 mg per day. This experiment has been in progress

since June 28, 1948, and is expected to continue until July or August, 1950.

During all of 1949 a part of the fluoride ingested by EB was not recovered in the urine and feces and in this respect the results were similar to those covering the initial weeks of the experiment and described previously. This constituted a state of positive balance, referred to as storage of fluoride, and was found to vary from season to season. The variation was such as to suggest that the changes in the temperature of this geographical area paralleled the changes in the rate of storage. The total weekly amount of fluoride stored and the mean temperature for each week were tabulated and these values grouped into periods of 4 weeks, or roughly, into months. Analysis of the variance between months for the interval June 28, 1948, through January 15, 1950, and intervals for 4 smaller intervals, 16 weeks each, within that period were recorded in Table 1 along with 4 still shorter intervals. These shorter intervals, 9 weeks each, were grouped into periods of 3 weeks and comparisons of the variance was made between these periods. The weeks considered in groups of four mentioned first above were labeled 4A through 4E in Table 1 and those in groups of 3 weeks were labeled 3A through 3D.

The long interval, 4A, and the shorter intervals, 4B, 4C, and 4E, all showed variances sufficiently large that their significance (in terms of the possibility that the variance was due to chance alone) fell in the range 0.05% to 2%. However, removal of that part of the variance which was due to the influence of temperature reduced both the size of adjusted variance between months and the significance of the variance ratio.

Two relatively short intervals (3A and 3B) were selected from the warmer months of 1948 and 1949 so that the mean temperatures were fairly high, reasonably constant and as similar as possible in respect to variation of the recorded temperatures. In a similar fashion, periods 3C and 3D were chosen in relation to the colder months of each of two winter seasons. Only the variance for 3A was significantly greater than the variance for the other periods. However, the variance ratios, after they were adjusted for the removal of the effects due to temperature, indicated that there was no significant variance between periods inside the 9 week intervals themselves. On this basis, it seemed safe to consider the average storage for 3A and 3B to be characteristic of the results obtained when the influence of temperature on the apparent rate of storage was at its maximum. For similar reasons 3C and 3D were taken to represent the storage under conditions of the minimum influence of temperature. The differences between the rates of apparent storage observed during warm

weather and the rate during a colder season (3C) suggest that as much as 18 mg each week (or 2.5 mg each day) may have been lost through the skin. In that case, the true storage rate may never have exceeded 4.5 mg each week.

From January 10, 1949, through January 15, 1950, the average fecal elimination of fluoride by EB was 6.7 mg each week. This was very similar to the value, 6.1 mg, observed in the early weeks of the experiment and reported previously.

Changes that have occurred in the urinary excretion of fluoride in the last year have not been large enough to seem significant except in relation to the changes in rates of storage referred to above. The average for the 52 weeks of 1949 was 57.7 mg each week and 7.1 mg per liter.

Subject KW

Excretion which exceeded in amount the fluoride intake by human experimental subject KW during the first weeks of 1949 was a reflection of the experiments previously carried out (described in the Annual Report for 1948). During a large part of 1948 this subject ingested fluoride, as $NaBF_4$, so that there existed a state of positive balance, referred to in these reports as storage of fluoride. The storage rate was small, 6 to 9%, and the actual amount stored during the course of some 34 weeks of observations totaled approximately 250 mg of fluoride ion. Immediately after the cessation of fluoborate ingestion (December 20, 1948), the urinary fluoride excretion (0.96, 0.89, and 0.56 mg/day were the averages for the 1st, 2nd, and 3rd weeks respectively) fell to near normal levels. This period (control) of observations when no extra dietary fluoride was being ingested has been separated into three periods, January 4 through February 19, February 20 through March 28, and March 29 through May 2, 1949. The amounts by which the excretion of fluoride exceeded the intake by KW during these intervals are recorded in Table 2.

During the first of these three intervals (January 2 through February 19), the mean daily output exceeded the mean daily intake (see Table 2), the difference of those means being 0.94 ± 0.023 mg. The probable error for this difference, $\pm$ 0.023, was so large as to suggest that the apparent excess excretion of fluoride was just a chance finding and did not, therefore, represent any genuine spillage (state of negative balance) by KW. However, the mean for the daily differences themselves during this same period (see column 6, Table 2) did show stability and statistical significance. This suggests that spillage did occur up to and including February 19 and perhaps during the interval February 20 through March 27.

The amount by which the fluoride output of KW exceeded the intake diminished progressively during the entire

control period and KW was considered to have reached a state of fluoride balance during the interval March 28 through May 2.

Beginning May 3 and continuing through March 13, 1950, fluoride ion, as NaF, was added to the dietary intake of KW at the rate of 3 mg each day. The period of elevated fluoride intake has been broken into 6 shorter intervals and the mean daily difference between the intake and output of fluoride during each of these intervals was recorded in Table 2. The amounts stored were also recorded in this table. The total amount stored was approximately 200 milligrams, an amount about equal to the storage that might have occurred during the experiment referred to above which ended December 20, 1948.

Subject EL

Throughout 1949 the excretion of fluoride by human experimental subject EL exceeded the dietary intake of fluoride; there was no other fluoride ingested by EL during this time. The spillage resulted from fluorides stored during an experiment carried out during 1948 (April 14 through December 21) in which fluoride, as $NaBF_4$, was ingested. During that period of time approximately 400 mg of fluoride were not recovered and were assumed to have been stored in the osseous tissues. During January, February and March, 1949, the elimination of fluoride by EL was 2.2 times greater than the amount that was ingested. Samples collected during May, 1949, showed that the output of fluoride exceeded the intake by 1.5 times.

Resumption of collection of samples began August 17 and the mean results of their analysis are shown in Table 3. The output of fluoride by EL exceeded the intake by approximately 0.3 mg each day during all four of the intervals of time shown in Table 3. It had been hoped that a state of fluoride balance would be reached before the start of an experiment in which this subject would inhale low concentrations of hydrogen fluoride in air. However, it seemed evident that no significant decrease in the spillage of fluoride had occurred between May 1949 and February 1950. Since there was no reason to anticipate any sudden decrease in spillage within the next few weeks, the next experiment was started without waiting for EL to return to a state of exact fluoride balance.

It was found to be very difficult to maintain a specific concentration of HF in air inside the inhalation chamber. When an average concentration of 2.5 ppm (as HF) had been reproduced several times without anyone in the chamber, a series of observations were begun on February 27, 1950. The presence of EL in the chamber added to the difficulties in producing a uniform concentration of HF. The average concentration for 9 days was 1.5 ppm and the average for the several days varied from 0.96 to 1.84 ppm.

At the start of a series of test runs, EL spent an average of 4 hours a day in the inhalation chamber. Although there was evidence of an immediate increase in urinary fluoride excretion, the data were still too meager to warrant their being included in this report.

Discussion

A different statistical treatment of our observations, the availability of data covering longer periods of observation, and directing attention more toward storage values than toward rates of urinary fluoride excretion have helped to clarify the question of losses of fluoride through the skin. By using the methods of analysis of variance, the effect due to temperature, acting as a co-variant by increasing or decreasing losses of fluoride through the skin, was established. Although the linear regression for this relationship has not yet been computed, the correlation between an increase in the recorded temperatures and an increase in the amount of the positive fluoride balance was apparent in the statistical results. Existence of correlation between these two variants can be deduced from the following: (1) In the hottest weather when the average recorded temperatures were consistently high, the extent of the positive balance of EB was relatively large while the variability was not very striking (3A, 3B, and 4D of Table 1), (2) when colder weather prevailed and average recorded temperatures were consistently low (3C and 3D) the variance of the fluoride balance values was similarly unstriking but the extent of positive balance had fallen to less than 1/4 of the highest level, (3) the variance for the balance values was most marked during those intervening months that included marked variations in the temperature. The amount of the positive balance seemed to increase if the temperatures were increasing and seemed to decrease if the temperatures were decreasing. From these observations it seemed reasonably certain that losses of fluoride by EB through his skin increased or decreased as the ambient temperatures increased or decreased.

In our Annual Report for 1947 the attempt was made to establish a relationship between changes in recorded temperatures and any associated increase or decrease in loss of fluoride through the skin. Since the previous efforts were directed toward the values for urinary fluoride excretion, it seems evident that the small, but perhaps significant variations in the amount of the positive balance occurred but were missed when comparisons were made involving much larger quantities such as those found in the urine. Because of the relatively recent application of the analysis of variance to our data, the earlier (1947 and 1948) observations have not yet been rechecked to see if either the recently adopted statistical approach or the more thorough examination of weekly or, wherever possible, daily balance values will yield additional useful information.

The fact that we now have data covering much greater periods of time than in any of our previous experiments may be the most important new factor in our series of observations. It seems likely that intervals shorter than 16 weeks fail to reveal the effects due to temperature; for example, data for the last 9 weeks of period 4B were examined to see if a more pronounced variability due to changing weather conditions could be detected. Limiting the interval to those weeks showing the most pronounced variations in temperature but at the same time shortening the interval being considered seemed rather to make less certain and less apparent the effect due to temperature. This was important in terms of the attempt made and failure to detect the influence due to changes in temperature (data for the interval August 16, 1948, through October 24, 1948 were used) which were described in our Annual Report for 1948. However, an interval of 16 weeks, June 28 through October 17, 1948, taken from this same series of observations has shown a pronounced effect due to temperature. Re-examination of other data collected during previous experiments may be profitable.

It has been assumed that at the time when the loss of fluoride through the skin was at its maximum the extent of the positive balance was approximately 23 mg each week. If it is also assumed that when the recorded temperatures were consistently low no significant loss of fluoride through the skin and that 5 mg (3C in Table 1) represented the maximum weekly rate of retention of fluoride in the tissues of EB then the difference, 18 mg, would represent the maximum weekly loss of fluoride through the skin. That quantity would amount to roughly 20% of the fluoride absorbed by EB. One question that arises from such considerations is, why wasn't a loss of this magnitude detected when these subjects were ingesting fluoride at a level, 126 mg each week, as $NaBF_4$? The borates are known to penetrate the skin quite readily and the fact that the fluoride ion goes through the skin has been established for at least one of our subjects as well as those included in the investigations described by McClure (McClure, F. J. and coworkers: Balances of Fluorine Ingested from Various Sources in Food and Water by Five Young Men. J. Ind. Hyg. and Toxicol., 24: 199, 1948).

The very most recent trend in the urinary excretion of EB though not described among the results in the preceding section, deserves a brief word. On some days the amount of fluoride recovered in the urine has equaled or slightly exceeded the fluoride intake. This suggests that the rate of deposition of fluoride in the bones may have been decreasing or may have reached a state of equilibrium so that mobilization of fluoride keeps up with the deposition. Another related matter that may be relevant concerns the variance ratios for periods 4B, 4C,

and 4E all of which show a reduction in variability of the data when the effects due to temperature are removed. Even though all three periods included months wherein there was great variability among the recorded temperatures, there was a progressive increase in the variance remaining after the effect due to temperature was removed. Both of the above observations indicate that perhaps some other variable was exerting a progressively stronger influence on the results; a decreasing rate of deposition of fluoride in the bones of EB might be just such a variable.

Additional data must be obtained before a more extensive discussion of this possibility is undertaken.

Subject KW

The experiment in which each day KW was ingesting 3 mg of fluoride as NaF had continued for a sufficiently long time and the extradietary ingestion was terminated March 13, 1950. The end of that period of ingestion was chosen so that the estimated amount of fluoride stored in the tissues (without making any allowance for possible losses through the skin) would be very nearly the same as the amount of fluoride assumed to have been stored by KW when fluoride, as $NaBF_4$, had been ingested during a preceding experiment which ended December 20, 1948. A negative fluoride balance or spillage of fluoride had occurred (see Table 2) in the months following the experiment last mentioned above and it was deemed advisable to stop the administration of the NaF at a point which would make the two experiments similar in respect to the amounts of fluoride that had been stored in the tissues of KW. The object was to discover whether additional and perhaps more definite evidence of spillage could then be obtained. Since the amount of fluoride ingested had been so small, evidence of spillage would indicate that storage had occurred. Should that prove to be the case then one can say that deposition in the tissues may occur at levels of fluoride intake that are quite low indeed.

During the first weeks of the control period following the ingestion of NaF, the output of fluoride by KW (not recorded in the section in which the results were presented) was 2 times the amount of fluoride found in duplicate samples of the dietary intake. However, further discussion of these observations can best be undertaken at some later time.

Subject EL

The metabolic state of this experimental subject was such that fluoride output continued throughout 1949 to exceed the fluoride ingested in the food and drink. No other experiment involving EL was started during this time.

A great deal of time and effort was involved in setting up facilities to produce a controlled concentration of HF in the range 2 to 10 ppm in the atmosphere. Most all of the manufactured devices readily available for measuring small volumes of gas would not function at all, or at least not for long, if HF were passed through them. The equipment thus far designed specifically for HF was not usable in the low range, 1 to 10 ml per minute, that was deemed necessary for our purposes. The apparatus and its arrangement, described in the section on results, have not been particularly satisfactory and it may still be necessary to find better and perhaps entirely different means to create reproducible concentrations of HF in the range that is desired.

In order to test the operation of the equipment and the reproducibility of the concentrations of HF in air achieved through its use, some preliminary inhalations were started. Even at a very low concentration the HF was absorbed from the atmosphere to an amazing extent by the interior of the inhalation chamber as well as by the clothing of EL during the hours he spent in the inhalation chamber.

Urine collected by EL during the first twelve hours of the experiment, 4 hours of which were spent in an atmosphere containing HF to the extent 1.8 ppm, was found to have a fluoride concentration of 3.4 mg per L (the control level had been 0.97 mg per L) and a total fluoride content of 1.62 mg. Subsequent urinary excretion values should be very interesting when the concentration of HF in the atmosphere can be reproduced with regularity.

Summary

1. Continuation of an experiment in which EB has ingested fluoride each day to the extent of 12 mg, as NaF, has made it possible to accumulate data covering intervals of time of sufficient length to permit identification of trends and relationships that were previously vague or not evident at all.

2. Loss of fluoride through the skin by EB has been found to occur and was shown to have definite statistical significance. The extent of the loss may have been 20% of the absorbed fluorides at the times when such losses were at the maximum.

3. Some of the fluoride ingested by EB was probably deposited in his tissues, but the rate of deposition may have been diminishing.

4. The statistical methods used to reveal these trends could well be used to recheck data obtained from EB in earlier experiments and to re-examine the data obtained from KW and from EL.

5. An experiment in which KW had ingested fluoride each day to the extent of 3mg, as NaF, was terminated with the purpose of observing whether or not spillage occurs and, thus, to obtain additional proof as to whether storage did or did not occur in her tissues.

6. A start has been made in which EL has inhaled HF present in air to the average extent of 1.5 ppm. After the first inhalation of 4 hours duration, there was a rapid rise to 3.4 mg/L in the fluoride concentration in the urine.

TABLE 1
FLUORIDE BALANCE
ANALYSIS OF VARIANCE OF DATA OBTAINED FROM HUMAN EXPERIMENTAL SUBJECT EB

No.	Period Date	Average Positive Balance mg/wk	Variances Between Months with Effects Due to Temperature Included	Removed	Probability Level (%) and Variance Ratios Effects Due to Temperature %	Included	%	Removed
4A	6/28/48 1/15/50*	16.25	369.1	138.1	0.05	10.5	0.5	4.1
4B	6/28/48 10/17/48	23.63	355.0	65.7	2.0	4.1	20.0	1.1
4C	1/10/49 5/1/49	10.85	244.1	86.7	0.05	10.8	1.0	7.6
4D	5/2/49 8/21/49	23.23	14.9	14.7	20.0	1.7	20.0	1.9
4E	8/22/49 12/18/49**	10.36	276.5	221.4	0.5	7.5	1.0	6.4
3A	7/12/48 9/12/48	21.42	291.2	265.3	5.0	5.2	6.0	4.2
3B	5/2/49 7/3/49	23.19	5.8	6.2	20.0	1.3	20.0	1.3
3C	1/10/49 3/13/49	4.66	1.5	1.9	20.0	6.7	20.0	5.4
3D	12/19/49 2/19/50	2.95	24.5	24.4	20.0	1.5	20.0	1.3

* Data not complete for interval 10/18/49 through 1/9/50 and, therefore, not included in these calculations.

** One week (10/31 - 11/6/49) omitted; its inclusion would not have changed the trend of the results but would have caused undue distortion.

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TABLE 2

FLUORIDE BALANCE

DATA OBTAINED FROM HUMAN EXPERIMENTAL SUBJECT KW DURING 1949

(AND FIRST 8 WEEKS IN 1950)

Date 1949	No. Weeks	Extra-dietary F	Total Intake	Total Output	Fluoride Balance		Total Storage
		mg/day	mg/day	mg/day	Status	mg/day	mg
1/4-2/19	7	None	0.34 ±0.017	0.44 ±0.015	neg.	0.088 ±0.016	-
2/20-3/27	5	None	-	-	neg.	0.075 ±0.019	-
3/28-5/2	5	None	0.34 ±0.017	0.39 ±0.009		0.058 ±0.018	-
5/3-5/30*	4	3.0 (as NaF)	-	-	pos.	1.07 ±0.069	30.0
6/7-7/18	6	Same	-	-	pos.	0.86 ±0.065	36.1
7/19-9/12	8	Same	-	-	pos.	0.77 ±0.033	43.3
9/13-11/7	8	Same	-	-	pos.	0.68 ±0.053	38.1
11/8-1/2	8	Same	-	-	pos.	0.72 ±0,039	40.3
1950 1/3-2/27	8	Same	3.45**	3.07 ±0.053	pos.	0.38 ±0.053	21.3
							209.1

* From May 30 through June 6 no samples were collected but the ingestion of F, 3.0 mg/day, was continued without interruption.

** The mean daily dietary intake of fluoride was 0.45 ±0.013 mg/day.

TABLE 3

FLUORIDE BALANCE

DATA OBTAINED FROM HUMAN EXPERIMENTAL SUBJECT EL DURING 1949

Date 1949	No. Weeks	Urine		Feces	Total Output	Total Intake	Negative Balance
		mg/L	mg/day	mg/day	mg/day	mg/day	mg/day
8/17-10/11	8	-	-	-	0.94 ±0.014	0.64 ±0.018	-0.30 ±0.023
10/12-12/13*	7	-	-	-	1.04 ±0.023	0.74 ±0.024	-0.30 ±0.033
12/14-2/7/50	8	0.89 ±0.016	0.81 ±0.016	0.109 ±0.006	0.89 ±0.016	0.64 ±0.02	-0.25 ±0.026
2/8-2/26	3	0.97 ±0.026	0.82 ±0.023	0.092 ±0.008	0.92 ±0.029	0.60 ±0.04	-0.32 ±0.05

* No samples collected 11/4/49 through 11/14/49

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APPENDIX C

To Minutes of 11th Meeting of Medical Advisory Committee

REPORT TO THE API MEDICAL ADVISORY COMMITTEE

BY THE SUBCOMMITTEE ON CUTTING FLUIDS

Dr. B. B. Reeve - Chairman

April 23, 1950

1. Both the members and associate members of the API Medical Advisory Committee should have by this time received the revised copies of "The Cutting Oil Dermatoses" prepared at the Harvard School of Industrial Hygiene by Mr. Kriete.

The Subcommittee recommends the acceptance of this Review, with commendations to Mr. Kriete, subject to modifications of paragraph 4, page 2, which now reads:

> "There are, basically, two approaches to this subject: first, measures to minimize contact between workers and cutting fluids which, in those plants on which information is available, have proved very effective (11); and second, the identification and the elimination of the etiologic factor in the cutting oils. It is with the latter that this review is largely concerned."

to read as follows:

> "There are, basically, two approaches to this subject both dealing with prevention: first, minimizing contact between workers and cutting fluids by means of personal hygiene, protective equipment and other plant control measures which in those plants on which information is available, have proved very effective (11); and second, the identification and the elimination, if feasible, of the etiologic factor in cutting oils. It is with the latter that this review is largely concerned."

The Subcommittee recommends further that this review be made available to members and associates of the API Medical Advisory Committee and, on request, to representatives of contributors to Medical Research Fund and to members of Institute Committees which are interested in the subject.

2. Copies of Cutting Oil Dermatoses by Dr. Harry Shapiro of the Medical Unit of the Division of Industrial Hygiene and Safety, of the New York State Department of Labor, were received. It is recommended that Subcommittee members write the New York Division of Industrial Hygiene as individuals extending thanks and offering constructive criticism.

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APPENDIX D

To Minutes of 11th Meeting of Medical Advisory Committee

REPORT TO THE API MEDICAL ADVISORY COMMITTEE

BY SUBCOMMITTEE ON PERMISSIBLE CONCENTRATIONS

Dr. V. C. Baird - Chairman

April 23, 1950

Your subcommittee reiterates its recommendations for publication by the Institute of 9 Toxicological Reviews which have been previously edited and accepted by the Medical Advisory Committee as follows:

1. Acetic Acid
2. Acetone
3. Beta-Naphthol
4. Butyl Acetate
5. Carbon Monoxide
6. Cyclohexane
7. Hydrogen Fluoride
8. Methylcyclohexane
9. Phosphoric Acids

In addition, your subcommittee submits for acceptance and reference to the Editorial Subcommittee for early publication, ten additional Toxicological Reviews as follows:

1. Ammonium Molbydate
2. Ammonium Nitrate
3. Amyl Acetate
4. Ditertiary Butyl Para Cresol
5. Hydroquinone
6. Maleic Anhydride
7. Mesitylene
8. Phenyl Naphthylamines
9. Silica
10. U.O.P. #5

And finally, there are still in preparation twelve reviews which may be completed before the project expires on June 30. These include the following:

1. Arsine
2. Butadiene
3. Copper Naphthanate
4. D.D.T.
5. Methyl Alcohol
6. Naphthalene

7. Nickel Carbonyl
8. Propyl Alcohol
9. Pyridine
10. Solvent Naphtha
11. Trichlorethylene
12. Triethanolamine

In concluding the Toxicological Review Project, the subcommittee desires to record the fact that no course of action is now open for the Medical Advisory Committee to follow in reviewing and revising the Toxicological Reviews as was originally planned.

The literature review on thermal burns has been completed and is recommended for information of committee members and others upon request. It is recommended that the preface of the review should include a note to the effect that:

> "The following information is presented only for information and is not intended as recommendation for therapy of burns."

It is recommended that all members and associates of the Medical Advisory Committee should express their appreciation of the valuable work done at Harvard University for the American Petroleum Institute by the adoption of a resolution as follows:

> WHEREAS, The work of the Harvard group in the preparation of the Toxicological Reviews will be terminated on June 30, 1950; and
>
> WHEREAS, These reviews represent a significant contribution to our knowledge and information,
>
> NOW, THEREFORE, BE IT RESOLVED: that all members and associates of the Medical Advisory Committee express and record their gratitude and appreciation to the Harvard group, and, in particular, to Marshall Clinton, M.D. and A. O. Seeler, M.D., for this contribution.

Your subcommittee also recommends that the Institute should have representations on any ASA sectional committee which may be formed to consider the formulation of an American Standard Code on Industrial Hygiene.

Your attention is called to a hearing in progress under the auspices of the Pure Food and Drug Administration and the Department of Agriculture on matters relating to economic poisons. You may wish to invite Dr. Kehoe to outline the scope and progress of the hearings.

In conclusion, you are advised that the Subcommittee on Permissible Concentrations has almost completed its work assignments and should be able to report completions at the 12th meeting of the Medical Advisory Committee in Los Angeles, in November.

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APPENDIX E

To Minutes of 11th Meeting of Medical Advisory Committee

REPORT TO THE API MEDICAL ADVISORY COMMITTEE

BY THE SUBCOMMITTEE ON PERMISSIBLE CONCENTRATIONS

PROGRESS REPORT

American Petroleum Institute Project
at Harvard School of Public Health

April 23, 1950

Toxicological Reviews

During the past five months tentative drafts of toxicological reviews on copper naphthenate, triethanolamine and pyridine have been prepared and distributed to the committee for their comments. Tentative drafts of reviews on solvent naphtha, alkyl nitrates, acetylene and methyl alcohol have been written and stencils are being prepared. Tentative reviews on nickel carbonyl and thermal burns have been revised and distributed for comments. Mr. Bertrand C. Kriete has made certain revisions in his review, entitled "Cutting Oil Dermatoses," that were suggested by the Subcommittee on Cutting Fluids, and a stencil of the revised review is being cut.

Silica Catalyst Problem

A. Animal Experiments

The guinea pig experiment referred to in previous reports has been concluded. Groups of guinea pigs were given intraperitoneal injections of finely ground quartz, fresh silica-alumina catalyst, spent silica-alumina catalyst, and a finely ground silicate, respectively. On gross examination fourteen months after injection only the animals given the quartz showed any fibrosis. The pathologist has not submitted his report on the microscopic appearance of the tissues as yet.

B. Survey of Neighborhood Exposure to Catalyst Dust

No further information has been submitted on dust concentrations in the neighborhood of refineries using silica-alumina catalyst.

Proposed Future Work

Since this project will end on July 1, 1950, we cannot undertake new reviews but will devote the remaining time to the completion of reviews on trichlorethylene and carbon disulfide which have been begun and to the revision of tentative drafts as comments from the Committee become available.