56
9473
11789
19823

\begin{tabular}{|c|c|c|c|c|c|}
\hline
9473  & 9442 & 9442  & 9442  & 9442  & 9442  \\
\hline
11789 & 11789 & 11789 & 11789 & 11789 & 11789 \\
\hline
19823 & 19823 & 19823 & 19823 & 19823 & 19823 \\
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Judgment rendered 4/24/1961
Total Exp. $31,025.85

\text{Expenses:
1. Hires, etc. of 3/10/1960, 1542.00
2. Premiums, 2/13/1960, 197.00
3. Premiums, 2/14/1960, 197.00
4. Premiums, 2/15/1960, 197.00
5. Premiums, 2/16/1960, 197.00
6. Premiums, 2/17/1960, 197.00
7. Premiums, 2/18/1960, 197.00
8. Premiums, 2/19/1960, 197.00
9. Premiums, 2/20/1960, 197.00
10. Premiums, 2/21/1960, 197.00
11. Premiums, 2/22/1960, 197.00
12. Premiums, 2/23/1960, 197.00
13. Premiums, 2/24/1960, 197.00
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**Authorization**

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<td>2</td>
<td>25 April 1957</td>
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<td>3</td>
<td>17 Sept 1958</td>
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<td>$179,400</td>
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</table>

**NEUROLOGIST**

4,000.00 of Title Act funded

141,592.00 + 132,592.00 = 274,184.00

4,000.00 funding negated by project

---

**Notes:**

- The total cost for each memo includes the estimated cost plus the 4% fee.
- The funding for the neurologist is listed as 4,000.00, with an additional notes indicating a negation of 4,000.00 for a project.

---

**Title:** Financial Information - 1959

---

**Page:** 54-1

---
January 13, 1982

The following data was obtained from the
comptroller's office on March 2, 1981, in connection with
the audit of the books and records of the company as of
January 31, 1981.

I hereby report the information as set forth above.

[Signature]

[Administrator]
<table>
<thead>
<tr>
<th>Description</th>
<th>Amount</th>
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<td>General</td>
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<td>January-February</td>
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<td>March 3, 1960</td>
<td>655.85</td>
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<td>Supplies</td>
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<td>Total March 1, 1960</td>
<td>2,932.17</td>
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<td>Revenue</td>
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<td>Total</td>
<td>2,932.17</td>
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Financial Report
March 1, 1960 to December 31, 1960

Received  

(Seeds)  

Stamford
MAIL DEPOSIT RECEIPT

We credit your checking account this day, as per validated amount below.

Date: 3-8-24
Amount: 6443.82

MAILING BY MAIL:

Please address deposit to the Stanford University Checking Account in care of the Stanford University Depository, 555 University Ave., Stanford, Calif. The deposit will be acknowledged and returned to you along with your next statement. The deposit is not negotiable and should be enclosed in a letter to the attention of the Depository. The Deposit Receipt is not negotiable and should be enclosed in a letter to the attention of the Depository.

[Handwritten notes and signatures]

MAIL ON THESE LINES
April 29, 1960

We are enclosing our financial statement covering the

for the period September 1, 1959 to February 29, 1960.

Sincerely yours,

Assistant Controller
Financial Statement

September 1, 1959 to February 29, 1960

Balance August 31, 1959 $15,015.00

Expenditures:

Salaries $7,475.00
Equipment 5,423.40
Supplies 2,515.67

TOTAL Expenditures 15,413.07

Balance February 29, 1960 (Deficit) $(471.07)

I have examined and approved the submitted expenditures.

Chief
TSS/Chemical Division
November 11, 1959

We are enclosing our financial statement covering
for the year ended August 31, 1959.

Sincerely yours,
Assistant Controller
Financial Statement
September 1, 1958 to August 31, 1959

Balance August 31, 1958  $10,815.09
Funds Received

Expenditures:
  - Salaries: $31,963.76
  - Fellowships: 1,000.00
  - Travel: 556.05
  - Equipment: 11,351.03
  - Supplies: 4,851.25

Total Expenditures: 49,722.09

Balance August 31, 1959  $15,015.00

I have examined and approved the submitted expenditures.

[Signature]
[Position]
[Division]
April 28, 1961

Dr. [Name] of our Clinical Staff has informed me that your office has never received a financial statement for the year 1957-58, covering expenditures on the [Department], which was at that time under the direction of the [Department].

We are enclosing a copy of that financial statement which our records show was forwarded on April 13, 1959.

If we can be of further assistance, please do not hesitate to call on us.

Sincerely yours,

[Name]
Research Supervisor
Financial Statement
September 1, 1957 to August 31, 1958

Balance August 31, 1957
Funds Received

Expenditures:
Salaries 15,484.14
Fellowships 667.00
Equipment 4,052.59
Supplies 4,589.90
Travel 4,808.18
Remodeling Animal House 9,967.00
Total Expenditures

Balance August 31, 1958

I have examined and approved the submitted expenditures.

Chief
TSS/Chemical Division

Date: 8/4/61

Net Balance:

$15,053.90
35,380.00
50,433.90

15,053.90
32,568.81

39,621.81
10,815.00
27 December 1960

Stanford University
Stanford, CA

Will you please send us a copy of the financial statement covering the period 1 September 1957 to 31 August 1958. In check through our project files we find the above account is missing.

Sincerely yours,

M. D.
Financial Statement
June 1, 1956 to August 31, 1957

Balance June 1, 1956
Funds received

Expenditures:
Salaries $7,875.82
Equipment 2,003.41
Supplies 4,241.81
Maintenance 1,214.69
Travel 167.50
Total expenditures $15,503.23

Balance August 31, 1957

Outstanding commitments:
Supplies and equipment $4,131.84
Remodeling animal house 10,000.00
Total commitments $14,131.84

Uncommitted balance August 31, 1957

I have examined and approved the submitted expenditures.

[Signature]
TSS/Chemical Division
Your research proposal on metabolism of ethanol at the [Redacted] has been approved by our Board of Directors. A check for $17,940.00 payable to [Redacted] is forwarded herewith.

The above monies are [Redacted] in support of your alcohol metabolism studies and are for a period of one year.

It is requested that a summary accounting be rendered [Redacted] which was extended until the residual balance was expended on the research in progress.

It is further understood that previous agreements relating to expenditures and summary accountings as well as the return of any unexpended funds remaining at the termination [Redacted] apply to [Redacted].
I hereby acknowledge receipt of the following checks:

Cashier's Check No. A239594, dated April 5, 1960, drawn on the amount of $17,940.00, made payable to the

Official Check of the No. G40663, dated April 6, 1960, in the amount of $717.60, payable to the
<table>
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<tr>
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</table>

EXPLANATION OF ENTRY

TOTALS

DATE PREPARED BY
DATE REVIEWED BY
CERTIFIED FOR PAYMENT OR CREDIT
DATE SIGNATURE OF CERTIFYING OFFICER
MEMORANDUM FOR: CHIEF, FINANCE DIVISION

VIA: TSD/Budget Officer

SUBJECT: Project MLULTRA, Subproject 56, Invoice 46
        Allotment 0525-1809-4202

1. Invoice 46 covering the above subproject is attached.
   Payment should be made as follows:
   [Checkmark and details scratched out]

2. Please forward the checks to Chief, TSD/Chemical Branch
   through TSD/Budget Officer by 11 April 1960.

3. This is a final invoice. However, since it is anticipated
   that additional funds will be obligated for this project, the files
   should not be closed.

Attachments:
   Invoice & Certifications

Distribution:
   Orig & 2 - Addressee

[Signature]
Chief
TSD/Chemical Branch

[Stamp]
I CERTIFY THAT FUNDS ARE AVAILABLE
[Details scratched out]
[Date: 11 April 1960]
INVOICE

For services

CERTIFICATIONS

(1) It is hereby certified that this is invoice #6 applying to Subproject 56 of MKULTRA, that performance is satisfactory, that services are being accomplished in accordance with mutual agreements, that a detailed agenda of the payments and receipts is filed in TSD/CD, that this bill is just and correct and that payment thereof has not yet been made.

Date:

(2) It is hereby certified that this invoice applies to Subproject 56 under MKULTRA which was duly approved and that the project is being carried out in accordance with the memorandum dated 13 April 1953 from the DCI to the DD/A, and the extension of this authority in subsequent memoranda.

Date:

Chief, TSD/Chemical Branch

Research Director
<table>
<thead>
<tr>
<th>Date</th>
<th>Remarks and References</th>
<th>Obligations Incurred</th>
<th>Obligations Liquidated</th>
<th>Unliquidated Balance</th>
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<td>23 MAR</td>
<td>N. S. Lott 56. Auth #1</td>
<td>$17,900.00</td>
<td></td>
<td>$18,657.60</td>
</tr>
<tr>
<td>1 APR</td>
<td>Borrower #6</td>
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<td></td>
</tr>
</tbody>
</table>
MEMORANDUM FOR:  COMPTROLLER

ATTENTION:  Finance Division

SUBJECT:  MKULTRA, Subproject No. 56
          Additional Authorization No. 4

Under the authority granted in the Memorandum dated
13 April 1962 from the DCI to the DD/A, and the extension of
this authority in subsequent memoranda, Subproject 56 has been
approved and $12,637,60 of the overall Project MKULTRA funds
have been obligated to cover the subproject's expenses and should
be charged to Allocation 6325-1009-1952.

APPROVED FOR OBLIGATION
OF FUNDS:

[Signature]

Research Director

Date: ____________________

Distribution:

Grig & 2 - Attached

1 - TSD/OC
2 - TSD/ACS
2 - TSD/CD

TSD/CD [redacted] (11 Mar 60)

9 March 1963

Chief
TSD/Chemical Branch

[Certification]

[Signature]

CERTIFY THAT FUNDS ARE AVAILABLE

[Allocation Number]

CHARGE TO [Allocation Number]

[Signature]
MEMORANDUM FOR: THE RECORD

SUBJECT : MKULTRA, Subproject No. 56

1. The purpose of this project is to provide funds to continue a research program at Stanford University Medical Center. This program is designed to exploit all the knowledge and facilities available in providing information of direct interest to the Agency in the area of alcohol intoxication. Specifically, basic information required to provide practical answers will be developed. A proposal for an extension of the work during the coming year has been submitted and is attached herewith.

2. Executive of the Department of Neurology at Stanford University Medical Center was the principal investigator on this project. It has been determined that the research program to be pursued under the budget proposed herewith will be pursued in a diligent and fruitful manner.

3. The funds for this project will be transferred using the as cutout in the usual manner.
4. Costs for this program for a period of one year are estimated to be $17,940.00. To this sum must be added a four per cent fee to __________ making a total amount of $18,657.60. Charges should be made against Allotment 0525-1009-4902.

5. __________ has requested __________ to submit to them a summary accounting on an annual basis of all monies received from __________ Any unexpended funds remaining at termination __________ will be returned to the __________

6. The requirement for a six months' informal accounting on the part of the principal investigator is waived.

7. Title to any permanent equipment purchased by funds granted __________ shall be retained __________ in lieu of higher overhead University rates.

8. In connection with travel under this project, it is agreed that the Agency will accept the travel documentation and accounting which conform with the practices __________

9. It is agreed that technical reports reflecting the progress of the research program shall be submitted at mutually acceptable intervals.

10. The project is unclassified after it leaves __________

APPROVED FOR OBLIGATION OF FUNDS: __________

Research Director 3/25/63

Chief TSD/Chemical Branch

Attachment: Proposal & Budget
We are desirous of continuing our research activities on measures aimed at permitting consumption of larger amounts of ethanol without an increase in overall nervous system depression. Our research to date (see technical reports) has brought us to a better understanding of the intermediary metabolism of ethanol. As previously reported, it appears that the limiting factor in the rate of disappearance of ethanol from the body is due to the relative rate of conversion of ethanol to acetaldehyde. Any measures that can increase the rate of this reaction would certainly reduce the overall effects of ethanol upon the nervous system.

Currently, we have established a coordinated clinical program of investigation with human volunteer subjects in the and affiliated

This, of course, would open up many new vistas and avenues of approach and investigation.

Therefore, it is our proposal to continue to conduct our research activities as follows:

I. The continuing program of work will be biologically and enzymologically oriented to determine the steps involved in the intermediary metabolism of alcohol.

A. A comparison of the incorporation of acetate $\text{C}^{14}$ and ethanol $\text{C}^{14}$ in fat fractions will be made to determine whether the pathway of ethanol metabolism enters the acetate stage.

B. In view of the fact that large doses of ethanol will inhibit methanol metabolism, attempts will also be made to compare the pathways of methanol vs. ethanol metabolism. The influence and effects of catalase, both in vivo and in vitro, upon methanol and/or ethanol metabolism will be investigated.

C. The role of alcohol dehydrogenase in reducing glyceraldehyde to glycerol and its relationship to the effects of fructose in increasing the rate of ethanol metabolism will also be investigated. The implications in this specific instance hold great promise towards devising an antagonist against the depressant effects of ethanol.
BUDGET

I. PERSONNEL

Professional Services

- Neurologist (M.D.) 1/4 time $-0-$
- Neurophysiologist (M.D.) 1/4 time $-0-$
- Enzymologist (Ph. D.) full time $8,600$
- Research Assistant, full time $4,200$

Subtotal $12,800$

II. Supplies (expendable)

- Chemicals, glassware, etc. $2,000$

III. Experimental Animals (small)

- University overhead 15% $800$

Total $17,940$
27 November 1959

has in a sense "left the ship without a rudder". I have been appointed Acting Executive of the Department of Neurology in his place. Urgent reorganization and unavoidable confusion within the Department has resulted in my delay in preparing the attached research proposals.

The previous year's contracts expired on September 30, 1959. It was pointed out to me that commitments for both research space and personnel had been made for an additional year subject to your final approval. There is still a residual balance of last year's contracts available to meet our current obligations. Therefore, I would appreciate your granting us an extension of last year's contracts and authorizing expenditures from the residual balance until the new contracts can be issued.

Due to the consolidation of the departments and the continuance of our original activities in the Division, I am herewith enclosing two separate research proposals for your perusal. Within our present activities, we have established a coordinated clinical program of investigation that is research oriented.

Your previous support of medical research has been greatly appreciated. We hope we will be able to justify your continuing support and continue to perform in a manner and fashion established.

Very truly yours,

Acting Executive
Division of Neurology
MEMORANDUM FOR: THE RECORD

SUBJECT: Extension of

Subproject #56, expiring 30 September 1959, is extended without additional funds for a period not to exceed eight months or until the balance as of August 31, 1959 is expended.

Chief
TSD/Chemical Branch
RECEIPT

I hereby acknowledge receipt of the following two checks:

Cashier's Check No. A202870, dated October 2, 1958, drawn on the [redacted], in the amount of $53,922, made payable to the [redacted].

Official Check No. 209-345465, dated September 30, 1958, in the amount of $2,156.88, payable to [redacted].

Date: Oct 1958
22 September 1953

NOTIFICATION FOR: CHIEF, PHYSICAL DIVISION
VIA: CH/Insplt/Office
SUBJECT: A/5 Project 16, Invoices 15, Assistance请提供正确的符号或清晰的图片。
CERTIFICATIONS

(1) It is hereby certified that this is Invoice No. 5 applying to Subproject 56 of MURRA, that performance is satisfactory, that services are being accomplished in accordance with mutual agreements, that a detailed agenda of the payments and receipts is on file in TES/CD, that this bill is just and correct and that payment thereof has not yet been made.

Chief, TES/Chemical Division

Date:

(2) It is hereby certified that this invoice applies to Subproject 56 of MURRA which was duly approved, and that the project is being carried out in accordance with the memorandum dated 13 April 1953 from the DSI to the DSA, and the extension of this authority in subsequent memoranda.

Research Director

Date:
MEMORANDUM FOR: THE RECORD

SUBJECT: MKULTRA Subproject No. 56

1. The purpose of this project is to provide funds to continue the research program conducted by Stanford U. School of Medicine. This program is designed to exploit all the knowledge and facilities available to its director in providing answers to specific questions of direct interest to the Agency in the area of alcohol intoxication. In addition, those areas of basic knowledge required to provide these practical answers will be developed.

2. has submitted the attached progress report and a proposal for an extension of the work during the coming year. It should be noted that three publications based on the material covered in the short progress report are presently in press. Included as a part of this project is a proposal from who is working in laboratory . work will make available a much better indicator of alcoholic intoxication than is now available. Presumably it will make possible an absolute measure of physiological impairment due to alcohol which will in turn materially aid in the final phases of the general work.
3. The funds for this project will be transferred using the
    cutout in the usual manner.

4. Costs for this program for a period of one year beginning
    August 31, 1958 are estimated to be $53,922.00 to which must be added
    a four percent (4\%) fee to the

5. Stanford U. has requested
    to submit to the Agency a summary accounting on an annual
    basis of all monies received from Stanford U. Also, it has been requested
    that any unexpended funds be returned at the close of the fiscal year.

6. The requirement for a six months' informal accounting on
    the part of the principal investigator is waived.

7. Title to any permanent equipment purchased by funds granted
    shall be retained by Stanford U. in lieu of higher overhead rates.

8. In connection with travel under this project, it is agreed
    that the Agency will accept the travel documentation and accounting which
    conform with the practices of Stanford U.

9. It is agreed that technical reports reflecting the progress
    of the research program shall be submitted at mutually acceptable intervals.
10. [Blank] is cleared through TOP SECRET and is aware of the true purposes of the program. He has also agreed to comply with the requirements of the Memorandum of Agreement.

APPROVED FOR OBELICATION OF FUNDS:

Research Director

Date: 1944

Attachment: Progress Report and Proposal

Distribution: Original only.

Chief
TSS/Chemical Division

Approved by: [Blank]
by authority of: [Blank]
date: June 1977

E2 IMPEMT: DOD

DEPARTMENT OF DEFENSE
OFFICE OF THE SECRETARY OF DEFENSE
DAF ALL

[Handwritten note: 'TOP SECRET']
Research on Antagonists to the Depressant Effect of Ethyl Alcohol

As an informal interim progress report, the following research for this year has been completed and is in preparation for publication.

1. Tri-iodothyronine
   The prominence attributed to the use of tri-iodothyronine as an agent for rapid "sobering up" has not been substantiated in our laboratories. The dosage of tri-iodothyronine used experimentally in our dogs were astronomical in relation to the usual therapeutic dose in man. Amazingly, the dogs tolerated the high dosage quite well and manifested only a rise in body temperature and increased panting. The effect of tri-iodothyronine on the rate of alcohol oxidation was negligible and certainly not more than that normally caused by the increase in body temperature.

2. Pyridoxine
   The effectiveness of pyridoxine or vitamin B6 is essentially the same as that of tri-iodothyronine. It is difficult to account for the reputation recently gained by both pyridoxine and tri-iodothyronine in the press without the support of critical experimental data.
   Perhaps this can be accounted for by the fact that the effect of a rising concentration of alcohol in the blood does not have a linear relationship to nervous system depression, but rather a logarithmic one. Therefore, there is a critical concentration below which the individual may appear relatively sober and above which, by a very small margin, a few milligrams/100cc, a considerable demonstrable degree of intoxication is present. Therefore, any agent, with or without any appreciable effects on the rate of alcohol metabolism and/or concentration, given at this critical level, may give a spurious impression of being an excellent alcohol antagonist.
3. Alcohol metabolism in mice

The effects of glucose, fructose, pyruvate, alanine, glycine, glutamine, glutamic acid and aspartic acid on the rate of ethanol metabolism in vivo were studied in mice with equivocal results. Data obtained were extremely variable from mouse to mouse, as well as from week to week, in spite of the large number of animals used. There is strong indication that the mouse may possess metabolic pathways for ethanol that are unique to that specie.

4. Alcohol metabolism in dogs

Various compounds studied showed a definite effect in promoting an increase in the rate of alcohol metabolism. Glycine showed an increase of 25-50%; alanine 25-60%; and fructose, which gave an increase of about 25%. Glucose, pyruvate, tri-iodothyronine and pyridoxine showed no increase. In the case of acetate, the converse, a slowing of alcohol metabolism seemed to result.

5. In vitro studies on rat and mouse liver slices

Experiments with liver slices showed that liver from a fasting animal metabolizes alcohol about one half as rapidly as that from normal animals.

Steps were initiated to determine where the block in alcohol metabolism by liver slices from fasting rats may occur. The most likely starting place seemed to be the first step in oxidation, the conversion of alcohol to acetaldehyde. Since the necessary coenzyme of the enzyme mediating this step is diphosphopyridine nucleotide, or DPN, the first experiments were designed to determine whether the coenzyme is deficient in the livers of fasting animals. Our experimental measurements showed that DPN was not deficient in the livers of fasting animals.

Attention was next directed to the enzyme itself, alcohol dehydrogenase. Livers were assayed for total content of alcohol dehydrogenase and it was determined that fasting animals had a higher concentration of the enzyme.

Since the equilibrium constant for alcohol dehydrogenase is far to the left in favor of alcohol, it would appear that if the concentration of acetaldehyde rises, the rate of alcohol oxidation would be slowed. Therefore, semicarbazide, which couples with acetaldehyde, was added to the incubating medium. Our data shows that the addition of semicarbazide did not change the rate of oxidation. Moreover, the addition of either acetaldehyde or acetate did not change the relationship. Thus it would seem that the accumulation of acetaldehyde did not influence the rate of alcohol metabolism.
The possibility that the rate of oxidation and reduction of DPN may have a direct relationship to the rate of alcohol metabolism was investigated. The reduced DPN molecule (DPNH) must be reoxidized to DPN before it is available to oxidize another molecule of ethanol. Three compounds capable of reoxidizing any DPNH which might accumulate were tested: methylene blue which acts as a short circuit between the flavin system and oxygen; ferricyanide which directly links DPNH and oxygen; and pyruvate, which in the process of being enzymatically reduced to lactate oxidizes DPNH. Experiments show that pyruvate increased the rate of metabolism in both the fed and fasting animal livers. Methylene blue and ferricyanide raised the rate in the fasted animal livers, but not in the fed.

From the promising leads above, investigation of the actual state of oxidation and reduction of the DPN in liver was undertaken and is now in progress.

5. Radioactive alcohol and acetate

The deposition of radioactive carbon in the tissues of mice fed radioactive alcohol or radioactive acetate indicate that the metabolic pathways for both alcohol and acetate were very similar.
August 22, 1958

Gentlemen:

We are desirous of continuing our work further on measures aimed at permitting consumption of larger amounts of ethanol without an increase in nervous system depression. Considerable progress has been made in our research program since September 1, 1957.

The attached progress report summarizes our research completed to date. In the past year, we have made tremendous strides towards a better understanding of the intermediary metabolism of ethanol. It appears that the limiting factor in the rate of disappearance of ethanol from the body is due to the rate of conversion of ethanol to acetaldehyde. Any measures that can increase the rate of this reaction would reduce the overall effects of ethanol on nervous system depression.

Moreover, we are now in the position of being able to conduct clinical experiments with human volunteer subjects. This, of course, opens up many new avenues of approach and investigation.

Provided we are able to obtain a supplemental for the coming year, we can conduct a series of experiments to determine whether or not tranquilizers exert a synergistic and/or supplemental effect or action upon the usual rate and degree of alcohol intoxication.

Stanford
Therefore, it is our proposal to continue to conduct our next year's investigation along the following lines:

1. Expedite the removal of alcohol from the blood stream through selective metabolic pathways.

   Preliminary studies indicate that glycine, alanine and fructose will increase the rate of alcohol metabolism. We plan to determine whether or not these effects are statistically significant.

   We also intend to continue studies on the intermediary metabolism of alcohol. Experiments have been formulated to determine the effects of lactate on the speed of alcohol metabolism; the effects of pyruvate on the DPN/DPNH ratio and the use of another enzyme system, such as the oxalo-acetate-malate one, to reoxidize the DPN coenzyme so necessary to convert alcohol to acetaldehyde.

   The use of radioactive alcohol will be continued in the study of intermediary metabolism pathways. After ingestion of radioactive alcohol, various tissues and fractions, including the water soluble fraction, phospholipids, non-saponifiable fraction and fatty acids will be isolated and their specific activities determined.

2. Determine the effectiveness of various types of fat and fat products in delaying the absorption of alcohol from the gastrointestinal tract.

   Preliminary work demonstrated that fat will delay the absorption of alcohol from the gastrointestinal tract. We intend to initiate clinical studies on the various types of fat in this respect. Expressed fats and oils, theobroma, butter, suet, lanolin, kaolin and gastric mucin will be investigated.

   The effects of wine buffers on the rate of absorption will also be investigated clinically.
3. Determine the effectiveness of sympathomimetic drugs in delaying the absorption of alcohol from the gastrointestinal tract.

Since the absorption of alcohol from the gastrointestinal tract is related to the emptying time of the stomach, the effectiveness of various sympathomimetic drugs, such as nalline, Bonamine, ephedrine and others, will be investigated.

The following is the proposed yearly budget:

I Professional services
   Neurologist (MD) half time
   Fellow, neurophysiologist (MD) 2/3 time
   Enzymologist (PhD) full time

II Technical services
   Technician, laboratory
   Secretary
   Laboratory, animal keeper

III Clinical subjects

IV Equipment and apparatus

V Supplies, expendable (radioactive alcohol, etc)

VI Large animals (incl upkeep)

VII Travel (alcohol meetings)

Sub total

University overhead 14%

Total
The research proposal and budget for [redacted] and his added research activities are attached. His proposed research would certainly yield invaluable data specially suited for your purposes.

We are extremely grateful for your generosity in supporting us and were it not for the extraordinary opportunity of having [redacted] with us, we would most certainly not request a supplemental [redacted]. At this time, however, we feel that this opportunity should be exploited to the fullest.

Your immediate attention and consideration would be greatly appreciated.

Sincerely yours,

Professor of Medicine
( Neurology )
PROPOSAL

To determine whether or not tranquilizers exert a synergistic and/or supplemental action upon the usual rate and degree of alcohol intoxication.

INTRODUCTION

The present day definitions of anxiety and stress remain in dispute. However, anxiety can be considered essentially a human function because it is associated with the capacity for delayed reaction, self reflection of motivation and the capacity for projection of the individual into the future. The concept of stress revolves around the arousal of anxieties. In general, anxiety may be aroused by any condition which threatens the integrity of the organism. Therefore, any stimulus may, in principle, arouse an anxiety response because of the particular meaning of threat it may have for that particular individual. However, we can distinguish a class of stimuli which will invariably produce disturbances in most individuals. The term "stress" can be applied to this class of conditions.

Acute stresses and anxieties with in our social patterns of behavior necessitates the use of tranquilizers on the part of many persons to adequately meet and cope with these problems. Often times people will partake of "a few tranquilizers" prior to going out for an evening of social drinking and partying. How does the combination of tranquilizers and alcohol affect the motor skills, sensory processes and critical judgements which are not normally affected by either tranquilizers or alcohol taken separately?

Therefore, the following course of investigation is proposed:

1. Design and test methods involving clinical subjects which will discriminate between normal, tranquilized, alcoholic, and tranquilized-alcoholic states; and for particular and specific states or effects which can eventually be related to overt behavioral responses of a sort which entail some possibility of practical exploitation.

2. Validate the above methods and effects in normal humans and relate them to alterations in mood and behavior in as objective a fashion as possible.

The above methodology will involve the use of a Nystagmograph, electroencephalograph (Lead II), Breathalyzer, Polygraph, and Drive-U-Meter. Biochemical methods include enzymatic and biochemical determinations of alcohol levels in blood, urine, and saliva. It is envisioned that at the end of a ninety days study, some definitive answers, substantiated by objective data, will be obtained.
BUDGET

The following is the proposed ninety days budget:*  

I. Professional services  
   a. Neurophysiologist (MD)  
      (Full time)  
      $2400  
   b. Neurophysiologist (MD)  
      (Half time)  
   c. Neurologist (MD)  
      (Half time)  
      1050  

II. Technical services  
   a. Technician, Bio Chemical  
      1200  
   b. Technician, Neurophysiological  
      1050  
   c. Electroencephalographer  
      1200  
   d. Secretary  

III. Subjects, Clinical  
     1500  

IV. Supplies, Expendable  

V. Equipment and Apparatus  
   300  
   900  
   8400  

VI.  

Sub total  

University  

Overhead (14%)  

Total  

8400  

1176  

9576  

This budget has since been extended to one year without change in funds.
17 September 1958

MEMORANDUM FOR: CONTROLLER

DEPARTMENT: Finance Division

SUBJECT: MLTIDM, Subproject 56, Additional Authorization No. 3

Under the authority granted in the memorandum dated 13 April 1953, both the BCI to the DD/A and the extension of this authority in subsequent memoranda, Subproject 56 was previously approved. Thereby, the need authority on additional use of $22,673.33 has been authorized to cover the subproject's expenses (thereby bringing to a total of $35,673.33 funds obligated during FY 53), to be charged to Allotment 3-1902-15-462.

CHIEF
TSF/Chemical Division

ATTACHED FOR RELEASE OF FUND:

Research Director

Date:

Distribution: Orig 3 2 - Addressed

1 - TSF/CC
1 - TSF/FMIB
1 - TSF/CD
2 - TSF/CD
22 September 1958

MEMORALUM FOR:  CHIEF, FINANCE DIVISION

VIA:  TES/Budget Officer

SUBJECT:  IGUMPA, Subproject 56, Invoice #5, Allotment 9-2562-75-502

1. Invoice No. 5 is attached covering the above subproject. Payment should be made as follows:

   Cashier's check in the amount of $53,922.00, drawn on a
   
   Cashier's check in the amount of $2,156.00, drawn on a

   Each check should be made payable to [REDACTED]

2. The checks should be forwarded to Chief, TES/Chemical Division, through TES/Budget Officer, no later than Monday, 6 October 1958.

3. This invoice represents the total amount currently authorized under Subproject 56. However, since it is anticipated that additional funds will be obligated for this project, the files should not be closed.

CHECK PAY 9/6/58 36-21-4
AMOUNT OF CHECK 56-21-4
RECEIVED 9/6/58

[Redacted]

CHECK PAY 9/6/58 36-21-4
AMOUNT OF CHECK 56-21-4
RECEIVED 9/6/58

[Redacted]

Chief
TES/Chemical Division

Attachments:
Invoice and Certifications

Distribution:
013 & 2 – Attention
RECEIPT

I hereby acknowledge receipt of the following two checks:

Cashier's Check No. A193344, dated May 1, 1958, drawn on the

of $26,220.00, made payable to

Cashier's Check No. 65624, dated April 30, 1958, in the
amount of $1,048.80, drawn on the

payable to

Date: 5/8/58
21 April 1958

MEMORANDUM FOR: CHIEF, FINANCE DIVISION

VIA: TSE/Budget Officer

SUBJECT: MULCH, Subproject 56, Invoice #4, Allotment 7-2304-10-001

1. Invoice No. 4 is attached covering the above subproject. Payment should be made as follows:

Cashier's check in the amount of $20,320.00, drawn on a
Cashier's check in the amount of $1,040.00, drawn on a

Each check should be made payable to the

2. The checks should be forwarded to Chief, TSE/Chemical Division, through TSE/Budget Officer, no later than Monday, 19 May 1956.

3. This invoice represents the total amount currently authorized under subproject 56. However, since it is anticipated that additional funds will be obligated for this project, the file should not be closed.

Attachments:
Invoice and Certifications
Distribution:
Grig & 2 - All source
1 - TSE/MD
2 - TSE/BM
2 - TSE/CD

[Signature]
Chief
TSE/Chemical Division

[Stamp]
(1) It is hereby certified that this is Invoice No. 4 applying to Subproject 56 of FMHRA, that performance is satisfactory, that services are being accomplished in accordance with mutual agreements, that a detailed record of the payments and receipts is on file in CM/06, that this bill is just and correct and that payment thereof has not yet been made.

[Signature]

Date:

(2) It is hereby certified that this invoice applies to Subproject 56 of FMHRA which was duly approved, and that the project is being carried out in accordance with the memorandum dated 13 April 1953 from the D1 to the DE/A, and the extension of this authority in subsequent memorandums.

[Signature]

Date:
I hereby acknowledge receipt of the following two checks:

Cashier’s check No. A176790, dated August 23, 1957, drawn on the in the amount of $13,110.00

Treasurers Check No. 68094, dated August 23, 1957, drawn on the in the amount of $524.40.

DATE: 28 Aug 57
MEMORANDUM FOR: CHIEF, FINANCE DIVISION

VIA: TSS, Budget Officer

SUBJECT: MKULTRA, Subproject 56, Invoice #3
Allotment 7-2502-10-001

1. Invoice #3 covering the above subproject is attached. Other invoices will follow. It is requested that payment be made as follows:

Cashier's check in the amount of $12,110.00, drawn on a

Cashier's check in the amount of $524.40, drawn on a

Each check should be made payable to the

2. The checks should be forwarded to Chief, TSS/Chemical Division, through TSS, Budget Officer, no later than Tuesday, 20 August 1957.

Acting chief TSS/Chemical Division

Attachments:
Invoice and Certifications

Distribution:
Orig & 2 - Addresses
1 - Comptroller

1 - TSS/FASB
2 - TSS/CD
INVOICE

For services

$13,634.40

CERTIFICATIONS

(1) It is hereby certified that this is Invoice No. 3 applying to Subproject #56 of MKULTRA, that performance is satisfactory, that services are being accomplished in accordance with mutual agreements, that a detailed agenda of the payments and receipts is on file in T55/CD, that this bill is just and correct and that payment thereof has not yet been made.

[Signature]
Acting Chief, T55/Chemical Division

Date:

(2) It is hereby certified that this invoice applies to Subproject #56 of MKULTRA which was duly approved, and that the project is being carried out in accordance with the memorandum dated 13 April 1953 from the DCI to the DD/A, and the extension of this authority in subsequent memoranda.

[Signature]
Research Director

Date:
<table>
<thead>
<tr>
<th>Date</th>
<th>Purchases and Payments</th>
<th>Omissions Received</th>
<th>Omissions Liquidated</th>
<th>Current and Expired</th>
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<tbody>
<tr>
<td>26/02</td>
<td>Building 1</td>
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</tr>
<tr>
<td>18/03</td>
<td>Service 2</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>24/03</td>
<td>Goods</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1 May 1957

MEMORANDUM TO: CONTROLLER
ATTENTION: Finance Division
SUBJECT: MITLPAW, Subproject 98, Additional Authorization No. 1

Under the authority granted in the memorandum dated 13 April 1957, from the SCI to the DO/A and the extension of this authority in subsequent memoranda, Subproject 98 was previously approved. Under the same authority an additional sum of $40,903.20 has been authorized to cover the subproject's expenses (thereby bringing to a total of $40,903.20 funds obligated during FY 57) to be charged to Account 7-2392-10-001.

SIDNEY GOTTLEIB
Chief, TSS/Chemical Division

Research Director

Date: MAY 31

Distribution:
- 1 - TSS/OC
- 1 - TSS/FASD
- 1 - TSS/IRB
- 2 - TSS/CD

TSS/OC (1 May 57)
MEMORANDUM FOR: THE RECORD

SUBJECT: MKULTRA Subproject No. 56

1. The purpose of this project is to provide funds to continue the research program conducted at [Redacted] in order to provide answers to specific questions of direct interest to the Agency in the area of alcohol intoxication. In addition, those areas of basic knowledge required to provide these practical answers will be developed.

It should be noted that although the attached proposal describes the facilities which will be used in the study, the program itself was deliberately described in general terms in order to comply with its unclassified status.

2. Attached is the research proposal submitted by [Redacted] requesting a renewal of the project for another year. According to his interim progress report, considerable progress has been accomplished; in a relatively short period of time, to wit: additional laboratory facilities have been equipped and placed into functional state, additional personnel have been recruited and specially trained, and substantive research completed to date and now in progress.

3. In view of the above, it is desired to describe more specifically the various phases of the general program to be initiated or continued as an extension of research activities now in progress.

(a) Expedite the removal of alcohol from the blood stream by selective metabolic pathways that will allow the alcohol to be stored rather than completely metabolized. Studies will be conducted on a number of agents claimed to expedite alcohol metabolism (alanine, pyruvate, fructose, alcohol dehydrogenase).

(b) Determine the effectiveness of foodstuffs in delaying the absorption of alcohol from the gastrointestinal tract. Investigations will be conducted on the effects of various fats on the absorption rate of alcohol. The effects of gastric mucin, kaolin and wine buffers will also be determined.

(c) Determine the effectiveness of sympathomimetic drugs in...
delaying the absorption of alcohol from the gastrointestinal tract. The effectiveness of various sympathomimetic drugs on the emptying time of the stomach will be investigated on larger animals. (Amphetamine, Nalline, Bonamine)

3. The funds for this project will be transferred using the cutout in the usual manner.

4. Costs for this program for a period of one year beginning August 31, 1957 are estimated to be $39,530.00 to which must be added a four percent (4%) fee to the University ($1,573.20), making the total amount $40,903.20. Charges should be made against Allotment 7-2302-10-001.

5. has requested to submit to them a summary accounting on an annual basis of all monies received from Also, it has been requested that any unexpended funds be returned at the close of the grant year.

6. The requirement for a six months' informal accounting on the part of the principal investigator is waived.

7. Title to any permanent equipment purchased by shall be retained by University in lieu of higher overhead rates.

8. In connection with travel under this project, it is agreed that the Agency will accept the travel documentation and accounting which conform with the practices of University.

9. It is agreed that technical reports reflecting the progress of the research program shall be submitted at mutually acceptable intervals.

10. is cleared through TOP SECRET and is aware of the true purposes of the program. He has also agreed to
comply with the requirements of the Memorandum of Agreement.

Chief, Branch II
TSS/Chemical Division

APPROVED FOR OBLIGATION OF FUNDS:

Research Director

Date: 8-57

Approved:

Research proposal

Distribution: Original only
Gentlemen:

We are desirous of continuing our work further on measures aimed at permitting consumption of larger amounts of ethyl alcohol without an increase in nervous system depression. Considerable progress has been made in our research program since 1 September 1956.

Our laboratories have been equipped and placed into functioning condition since the last visit of your representative. The suite of three rooms in the Nurses’ Residence has been converted into a Biochemistry Laboratory and an Enzymology Laboratory for and an office and machine shop for myself. The Enzymology Laboratory is set up for in vitro work with tissues and enzymes. In addition, a Neurophysiology Laboratory, named for our osistant to the Animal Surgical Operating Theatre, on the fifth floor of the Medical School Building, has been allotted to the Department of Neurology under me. As a nucleus for expansion, the Neurophysiology Laboratory is already equipped with an 8 channel Grass Model 3 EEG and a Meditron EMG.

As an informal interim progress report, the following research for this year has been completed or is very near completion.

A. The deposition of carbon derived from the ingestion of radioactive alcohol has been published under joint authorship with and in the
A paper on the EEG in acute alcohol intoxication has been
submited for publication to the Quarterly Journal of Studies
on Alcohol.

We have completed a paper on the effects of premedication
with nicotinamide on the speed of alcohol metabolism.

The comparison of the depoition of radioactive carbon in
the tissues after continued feeding of alcohol and acetate is
being completed by

The dehydrogenase method of alcohol determination has been
standardized by , whereas continues to refine the dichromate method. With these two micro
techniques developed to a satisfactory stage, in vivo studies
on mice can be conducted.

It is our proposal to continue to conduct our next year's in-
vestigations along the following lines:

(1) Expedite the removal of alcohol from the blood stream by
selective metabolic pathways that will allow the alcohol to be stored
rather than completely metabolized.

We plan to study the effects of a number of agents that are
claimed to expedite alcohol metabolism (alanine, pyruvate, fructose,
alcohol dehydrogenase). Preliminary studies indicate that the nutri-
tional state of the animal is very important and if this is maintained
at an optimal state, none of the agents show any striking, if indeed
statistically significant effects.

(2) Determine the effectiveness of foodstuffs in delaying the
absorption of alcohol from the gastrointestinal tract.

Preliminary work demonstrated that neither carbohydrate
nor protein can be expected to delay the absorption of alcohol. How-
ever, fat was found to be effective in an inconsistent way.

We intend to continue studies on the effects of various types
of fats on the absorption rate of alcohol. (Expressed oils, olive,
peanut, theobroma; soft animal fats, butter, suet, lanolin.) The
effects of gastric mucin and kaolin will also be investigated in this
respect.
Determine the effectiveness of sympathomimetic drugs in delaying the absorption of alcohol from the gastrointestinal tract.

With the addition of the Neurophysiology Laboratory, we plan to re-enter the field of working with larger animals (dogs, cats), and testing synergism and antagonism between alcohol and other drugs.

Since we are convinced that the effectiveness of fat in delaying the absorption of alcohol from the gastrointestinal tract is related to the slowing of the emptying time of the stomach, it is desired to investigate the effectiveness of other measures which might have the same effect. The sympathomimetic drugs suggest themselves as likely candidates in this respect. (Amphetamine, Nalline, Bonamine, Ephedrine.)

In order to utilize to advantage the increased laboratory space now available to me, I plan to increase my research staff and also, my own active participation. The following is the proposed yearly budget:

<table>
<thead>
<tr>
<th>Description</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurologist (M.D.) half time</td>
<td>$4,000.00</td>
</tr>
<tr>
<td>Fellow, neurophysiologist (Ph.D.)</td>
<td>$7,600.00</td>
</tr>
<tr>
<td>Enzymologist (Ph.D.)</td>
<td>$8,000.00</td>
</tr>
<tr>
<td>Technician, Laboratory</td>
<td>$4,000.00</td>
</tr>
<tr>
<td>Laboratory, animal keeper</td>
<td>$2,000.00</td>
</tr>
<tr>
<td>Equipment &amp; apparatus</td>
<td>$3,500.00</td>
</tr>
<tr>
<td>Supplies (chemicals, radioactive</td>
<td>$3,000.00</td>
</tr>
<tr>
<td>alcohol, etc.)</td>
<td></td>
</tr>
<tr>
<td>Large animals (upkeep, etc.)</td>
<td>$1,500.00</td>
</tr>
<tr>
<td>Travel</td>
<td>$1,000.00</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$34,500.00</strong></td>
</tr>
<tr>
<td><strong>Overhead 14%</strong></td>
<td><strong>$4,830.00</strong></td>
</tr>
<tr>
<td><strong>University</strong></td>
<td><strong>$39,330.00</strong></td>
</tr>
</tbody>
</table>

Total $34,500.00

S F O R C E S A N D M E T H O D S I N V O L V E D
It is our hope that with our assembled research team, more definitive results will be obtained in the very near future.

Very truly yours,

Professor of Medicine
(Neurology)
RECEIPT

Receipt of $3,628.76 from the [redacted] representing a return to the Agency of surplus funds under contract RD-37 from

Date: 6/4/56
Receipt is hereby acknowledged of the sum of $2,360.40 in cash.

Date: C

Receipt is hereby acknowledged of the sum of $2,360.40 in cash.

Date: C
RECEIPT

Receipt of $10,440.63 from the representing a return to the Agency of surplus funds under contract HD-37 from

Date: 5/4/56
I hereby acknowledge receipt of the following two checks:

Cashier's check No. DM 35652, dated April 16, 1956, drawn on
in the amount of $310.67.

Official Check No. C 3258, dated April 16, 1956, drawn on
in the amount of $10,190.48.

Date: 21 May 56
1. Invoice 2 for the above subproject is attached. Payment should be made as follows:


e) Check in the amount of $10.07, drawn on a bank, payable to the

f) Check in the amount of $10,120.48, drawn on a bank, payable to the

Cash in the amount of $10,070.19, in denominations of one hundred, fifty, and twenty dollar bills.

2. Both checks and the cash should be forwarded to Chief, TEC/Chemical Division, through TEC/Budget Officer, no later than 30 April 1956.

3. This is a final invoice. A total of $32,616.00 was obligated during FY 56 under this subproject. However, since the work is not yet completed, the files on subproject 56 should not be closed.

LIEUT. COL. BILL
Chief
TEC/Chemical Division

Attachments:
Invoice & Certification

Distribution:
Grig & 9 - Assistant
1 - Controller

Drafted: 12/30/55
9 April 1956

SUBJECT: MODERN Subproject 56, Invoice 2
ALLOWANCE 4-24-56-001

1. Invoice 2 for the above subproject is attached. Payment should be made as follows:

Cashier's check in the amount of $210.67, drawn on a payable to the

Cashier's check in the amount of $20,076.19, in denomination of
one hundred, fifty, and twenty dollar bills.

2. Both checks and the cash should be forwarded to Chief, 965/Chemical Division, through FIA/Budget officer, no later than 20 April 1956.

3. This is a final invoice. A total of $21,076.19 was obligated during FIA 56 under this subproject. However, since the work is not yet completed, the invoice on subproject 56 should not be closed.

C. M. DILLINGHAM
Chief
965/Chemical Division

Attachments:
Invoice & Certifications

Distribution:
CRI 2 - Advance

MODERN 4-24-56-001

[Signature]

[Stamp: CERTIFIED]

[Stamp: RECEIVED]

[Stamp: APPROVED]

[Stamp: DISBURSED]
(1) It is hereby certified that this is Invoice 2 applying to KUSETTA Subproject 56, that performance is satisfactory, that the services are being accomplished in accordance with mutual agreements, that a detailed agenda of the payments and receipts is on file in TSS/CD, that this bill is just and correct and that payment thereof has not yet been made.

Sidney Gottlieb  
Chief, TSS/Chemical Division

Date: June 13, 1956

(2) It is hereby certified that this invoice applies to KUSETTA Subproject 56, which was duly approved, and that the project is being carried out in accordance with the memorandum dated 13 April 1953, from the IC to the DE/A, and the extension of this authority in subsequent memoranda.

[Signature]
Research Director
I hereby acknowledge receipt of the following checks:

1. Cashier's Check #147037
   in the amount of $3,732.00;

2. Cashier's Check #253563
   in the amount of $405.33;

both checks payable to

Date       25 May 76
6 April 1956

RECIPIENT FOR: CHIEF, FINANCIAL DIVISION
VIA: TSS/Budget Officer
SUBJECT: HABLA Subproject 57, Invoice 1, Allotment 6-2502-30-001

1. Invoice 1 covering the above subproject is attached. Other invoices will follow later. It is requested that payment be made in the following manner:

   Cashier's check for $3,732.63, drawn on ____________
   Cashier's check for $405.33, drawn on ____________
   Cash in the amount of $6,400.45, in denominations of one hundred, fifty, and twenty dollar bills.

2. The cash and both checks should be forwarded to Chief, TSS/Chemical Division, through TSS/Budget Officer, no later than 20 April 1956.

DISTRIBUTION:

Attachments:
Invoice & Certifications

Orig & 2 - Address (w/attachments)
   1 - Controller

129/38 (5 April 1956)

CHECK/ENDORSED AMOUNT OF $6,400.45 RECEIVED. 24/4/56

CHIEF
TSS/Chemical Division

CHECK/ENDORSED AMOUNT OF $6,400.45 RECEIVED. 24/4/56
(1) It is hereby certified that this is Invoice 1 applying to Subproject 56 of KDHRA, that performance is satisfactory, that the services are being accomplished in accordance with mutual agreements, that a detailed agenda of the payments and receipts is on file in TBS/CD, that this bill is just and correct and that payment thereof has not yet been made.

Chief, TBS/Chemical Division

Date:

(2) It is hereby certified that this invoice applies to Subproject 56 under KDHRA which was duly approved and that the project is being carried out in accordance with the memorandum dated 13 April 1953 from the DSI to the ED/A, and the extension of this authority in subsequent memoranda.

Research Director

Date:
1 March 1956

SUBJECT: CERTIFICATION

ADDA : Finance Division

Under the authority granted in the recommendation dated 13 April 1955 from the D.A to the DVA, and the assumption of the authority in subsequent memoranda, it has been requested that the full amount of the overall budget of the project number 56 be allocated to cover the expenditures estimated. This estimate of funds should be charged to Account C-4012-10-001.

Research Director

Distribution:
1. DSS/CC
2. DSS/KE
2. DSS/CD

TED/37 (A P.O. 56)

[Signature]

[Signature]
MEMORANDUM FOR: THE RECORD

SUBJECT: MKULTRA, Subproject 56

1. The purpose of Subproject 56 is to continue work on alcohol research by scientists at the University of California, San Francisco, CA. The scope of the research program will be to pursue studies on determining the effectiveness of foodstuffs in delaying absorption of alcohol from the gastrointestinal tract; determining the effectiveness of various sympathomimetic drugs in delaying the absorption of alcohol from the gastrointestinal tract; expediting the removal of alcohol from the blood stream by selective metabolic pathways that will allow the alcohol to be stored rather than completely metabolized, and developing a simple and reliable test of tolerance to alcohol for use in the selection of personnel and prediction of behavior.

2. The cost of this program is estimated to be $30,400.00 for a period of one year. To this sum must be added $1,216.00 representing a four percent service charge to University Hospital. Therefore, the total cost will not exceed $31,616.00. Charges should be made against Account 6-2502-10-001.

3. [Redacted] has requested to submit to them a summary accounting of monies received. Also, they requested the return of any unexpended funds received by them in lieu of higher overhead rates. University

4. It was mutually agreed that documentation and accounting for travel expenses which are reimbursable shall conform with the accepted practices of that institution.
7. The party agreed to comply with the requirements of the memorandum of agreement.

Approval:

Research Director

Date: March 3, 1977
Gentlemen:

We are desirous of continuing our work on measures aimed at permitting consumption of larger amounts of ethyl alcohol without increase in nervous system depression. Progress in the past year has been slow; this may be attributed largely to the necessity of my devoting a larger share of my time to development of a growing Neurological Service in the Medical School. As a result of this effort, has now secured support from which have made a residency training program in neurology possible, with increased personal to put it into effect. Accordingly, I will be able to again devote a reasonable amount of personal time to research in alcohol, and want to take this opportunity to apply for continuing support.

It is our proposal to conduct our investigations along the following lines:

(1) Determine the effectiveness of foodstuffs in delaying absorption of alcohol from the gastrointestinal tract.

Preliminary work relative to determining the effect of various foodstuffs in slowing the absorption of alcohol has been of more promise, in that, as set forth in the preliminary report forwarded to you previously, the ingestion of reasonable amounts of fats or oils previous to the taking of alcohol has been demonstrated to lower significantly the peak value of blood alcohol concentration. We believe that further work along this line is indicated, to determine the optimal timing of the fat ingestion, and the degree of uniformity of the effect in different individuals.
(2) Determine the effectiveness of sympathomimetic drugs in delaying the absorption of alcohol from the gastrointestinal tract.

Since we are convinced that the effectiveness of fat in this regard is related to slowing of the emptying time of the stomach, it is desired to investigate the effectiveness of other measures which might have the same effect. The sympathomimetic drugs suggest themselves as likely candidates; indeed amphetamine was shown to have such an effect. Although such measures cannot be expected to delay indefinitely the absorption of alcohol into the blood, they may be sufficiently effective to delay absorption until the stomach can be emptied by induced vomiting by some individuals with some facility in this maneuver. Of course, the ideal substance would be a compound that would combine with the alcohol in a form that would be unabsorbable, and it is possible that some such compound not in itself unduly toxic might be found.

(3) Expedite the removal of alcohol from the blood stream by selective metabolic pathways that will allow the alcohol to be stored rather than completely metabolized.

Another point of attack on the problem is the search for measures that will expedite the elimination of absorbed alcohol from the body. The amount eliminated in the urine, breath, and sweat is not of sufficient magnitude to be of practical importance even if doubled, and obviously a greater increase than this in volume of any of these channels would not be practically acceptable for the purpose in which we are interested. Increased combustion of alcohol, especially if coupled with slowed absorption, might be highly effective. If the normal pathway of complete combustion to carbon dioxide and water alone is considered, one is limited theoretically by the fact that the ordinary rate of combustion supplies about half the caloric output needed for the body metabolism of a sedentary man, and thus any considerable increase would produce an excess of heat. Even so, it is probable that the difference of rate of alcohol metabolism brought about by a diet that will favor the burning of protein rather than fat will be of sufficient magnitude to allow
alcohol to be absorbed at double the rate without an increase in the slope of the blood alcohol curve. Even more effective would be measures aimed at promoting storage of the alcohol by utilizing alternative metabolic pathways, so that combustion would not be complete, but that the acetate formed from the alcohol might be converted to glycogen or fat. Work of others with tracer techniques using radioactive carbon incorporated in alcohol seems to show that a small proportion of the alcohol takes this pathway. It is our desire to explore this possibility more fully with long-term feeding experiments in rats and mice.

We have demonstrated (and indeed it is common knowledge) that individuals vary greatly in their resistance to the depressant effect of alcohol. Indeed it is because of this difference in tolerance that the whole study is necessary. Would it not be profitable to develop a simple and reliable test of tolerance to alcohol which would be of value in the selection of personnel whose mission and job might entail the necessity of consuming considerable quantities of alcohol? The techniques which we have developed over the years in this type of research should be valuable in this connection.

It is our proposal, then, to explore further the effectiveness of foodstuffs and drugs in delaying absorption of alcohol from the gastrointestinal tract; to investigate by the use of alcohol incorporating radioactive carbon the possibility of expediting the removal of alcohol from the blood by favoring metabolic pathways that will allow it to be stored rather than completely burned; and finally to develop a simple and reliable test of tolerance to alcohol for possible use in the selection of personnel.
The experience in this type of research we have already gained over a period of some 25 years in similar investigations. We also have the facilities for determination of blood alcohol concentration, and apparatus for testing the degree of nervous system depression produced by alcohol. My own active participation in the work is reasonably assured by the addition of personnel to the Medical School faculty to take over the bulk of the routine teaching and administrative detail of the Division of Neurology. It will be necessary to secure additional technical assistance, and if possible a research Fellow trained in neurophysiological techniques to assume the burden of the actual testing of subjects. Funds will also be required for reimbursement of subjects for this rather unpleasant and arduous research, and their retention in the hospital under observation during the period that they are intoxicated.

The following is the proposed yearly budget:

- Neurologist (MD) 9,000
- Fellow, neurophysiology (PhD) 6,000
- Technician, chemical 3,600
- Clerk-secretary 3,000
- Laboratory-animal keeper 1,800
- Equipment & Apparatus (Glassware, etc.) 1,000
- Supplies (Chemicals, radioactive carbon, alcohol, etc.) 3,000
- Subjects' fees (incl. hospitalization) 3,000

TOTAL $30,400

Although it is hoped that definitive results might be obtained in a year's time, it would be highly desirable in assembling such a team to plan for at least a two-year period.

Very truly yours,

Professor of Medicine (Neurology)
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