PROCEDURE OF THE MEDICAL SCHOOL
AND THE UNIVERSITY
IN THE MATTER OF HUMAN EXPERIMENTATION

of lead in the air and repeating the observations throug
as may be necessary to obtain a stable curve. (Obvious
somewhat below the slightest concentration that will in

The full protocol of these related experiments
extensive for presentation here. It is anticipated that
be continued for some additional years.

Purpose of Study

The primary purpose is to explore and reveal
the metabolism of lead in the intact, healthy human orga
conditions. The practical objective is to relate the p
lead to conditions of environmental exposure to lead, a
the differentiation of safe from dangerous human exposu
respect to occupational exposure, and also in relation
ingestion under basic conditions of respiratory exposure

The present experiments are intended to provi
respect to the concentration of lead in the air which w
population of the urban centers in the United States, i
factors contribute to the dispersion of lead compounds
in the eyes of public officials is, of course, the exte
compounds discharged from the exhausts of automobiles m
the lead content of the atmosphere of streets, freeways
on the somewhat dubious assumption that other sources,
proportions.)

response. (Previous experiments have been carried out
more intensive exposure, but always below the threshold
the concentrations of lead in the tissues, body fluids,
been found in association with the mildest manifestatio
present experiments do not approach threshold levels.)

(b) Despite the lack of hazard, and in order
data, the subjects are maintained under the supervision
to the best and most exacting medical regimen) of a phy
otherwise for the experimental regimen, and has the aut
experimental exposure to lead for any medical or hygien
valid. A medical examination is carried out, weekly, a
this physician, and certain observations of the laborat
some at weekly intervals, for the purpose of a meticulo
status of the subjects, as well as for the gathering of

Previous Work Done in this Area

Two publications (reprints) which are little
methodology and the principal results, are submitted he

Method of Procuring Subjects

All but two* of the subjects engaged for these
more than a score in the past thirty years, have been o
as non-academic members of the staff of the Kettering L
that are regarded as adequate, reimbursing them complet
expense (food, special clothing, and certain medical ex

* These were members of the research staff during thei

Each subject has been selected after exhausti
to determine his physiological fitness; each subject ha
prophylactic medical and dental care that has been indi
during the preliminary period of normal or basic metabo
afterward if necessary.

Each subject has been interviewed by the prin
most thorough and informative manner, with respect to t
experiments, the potential risks involved (on the backg
experience of the investigator in industrial practice i
one subject in this entire period of time has failed to
respect, and, in this one instance, the subject became
somewhat exacting regimen after a few months, and wishe
some financial advantage was being exploited at this ti
not the primary consideration).

No written agreement or waiver has ever entei
and with all due regard for the provision of a record t
and position of the principal investigator and that of
facts be questioned and a claim made, it is our informe
on the part of the subject is worth, in law, the paper
and also that no document can substitute for or guarant
that sees, first, the service to mankind that can be re
in addition holds firmly in mind the plain duty not to
well-being of the subject in any manner that is known c

of the University is defined and limited by this arrang

however, that these legalistic considerations do not re

the direct professional responsibility of the principal

fulfillment of the most exacting ethical requirements f

safety and well-being of the subjects.

Evelyn V. Hess, M.D.
Chairman, Faculty Committee on Research
University of Cincinnati
Cincinnati General Hospital
Cincinnati, Ohio 45229

Dear Doctor Hess:

I am entirely willing to provide the information whic
I hope, that which is necessary at this time.

I wish to make it quite clear that what is under way,
"new project." It is rather the continuation of a sy
began in 1939, to examine many aspects of the behavio
The general plan was interrupted some years ago (abou
into the practical significance of lead in the ambien
what level of the concentration of finely divided (pa
to be at, or near, the maximum concentration which we
by average people in the general population.

This interruption has come to an end with the comple
(which, we believe, have produced an answer to the qu
taking up where we left off at the end of 1958, in th
dimensions of the dispersed particles of a specific c
Pb_2O_3, in the respired air, on the rate of accumulati
and the rates of increase in the concentration of lea
output of lead in the urine.

The level of exposure of a female subject is to be ma
0.15 mg. of Pb per cubic meter of air (the actual exp
under the experimental conditions to be described, ha
until January of 1971 or thereabouts, dependent upon
observations). The experiment then is to continue at
above, which is well within the limits of complete sa
time, so long as the conditions of the exposure are
week (actually here 37.5 hours, which regimen corresp
industrial exposure, what with changing clothes just
bathing and changing clothes afterward) as the latte
controlled within limits which are known to be harml
safety). In addition, this subject, in accord with
the surveillance of a physician whose sole function
that she is free of any and all illness, including a
which might be believed (or imagined by the subject
experimental factors. He can require the discontinu
at any time which is advisable, in his judgment.

About two years (perhaps only 18 months) will be req
after which the particle size will be reduced to abo
(average size within a small range), a new subject w

concentration of a chromate or chromite in the resp
implication of these compounds (perhaps only one, b
to differentiate between the several compounds) in
pulmonary malignancies.

I should point out to you that, because of the plac
the framework of the original project, and because
all aspects of this matter, from the viewpoint of r
that any approval from any source was required for
formal report of our procedure has been made, there
your information. This statement does not mean tha
ourselves to be lacking in any way in our willingne
the Public Health Service, the University of Cincin
representatives of its faculty. We shall comply, f
I would hope, however, that this does not mean that
continuation (into exposure) of an experiment which
May of 1970. It is worthwhile, I think, to bear in
physiological experiments of this type, and the app
their performance, were developed by ourselves many
were thought of in the Public Health Service or by
the specific subject involved in this case, is suc
ethically, among our colleagues, in the nature of t
defensively, as a matter of opposition to the prese
but rather to clarify the issue of professional and
the long run, human experimentation, whether for th
must be considered by an appropriate authority in t
of the vital requirements of the precautions to be
that there be adequate knowledge on which to assess
experiment to be undertaken. As a senior member of
status), I find it necessary to abide fully by the
their due consideration of the issues involved in a

* I have given you something of the plans which I
communicated to my present associates). It is appa
full of years and cannot be expected to direct this
to develop, and I believe I have achieved, a degree
gram of experimentation, so that it can be expected
longer available to look after it. This means, I t
phases of the program to be carried out and that th
within the Medical Center as to how best to maintai
within the faculty with the work program, and also,
as to what information should be supplied by the La
Medical College. It is not possible to learn many
mineral metabolism in man (or for that matter, the
than minerals) without investigating the behavior o

the laboratory, if they are to be sufficiently preci
can be expected to be engaged in many activities of

Some means will have to be developed to spare the pr
expenditure of undue effort and time in reporting an
institution. It is also necessary, I think, to keep
within this institution. Not only will there be wor
Health Service has no responsibility, as in the pres
no sponsoring role to play. There is no good reason
University of Cincinnati, for example, experimental
the U.S.A., should require governmental consent to b
land should so specify. It is wrong, I believe, to
established in that direction. I think, therefore,
it would be well if you (and perhaps others) were to
of situation and plan to meet them, rather than to f
not designed to deal with matters of this type.

Yours s

Robert
Profess
Occupat

RAK:wb

KE 0012372

I wanted to talk to you briefly to let you know tha
with other people in the Laboratory, which will ext

The one is sponsored by Ethyl Corporation, and an a
been made, to be drawn on at the end of the year (o
we choose, so as to leave no sums due as of Decembe
entire $25,000, I am sure, this year, and the work
pace in 1970. Dr. Pfitzer is initiating the work,
Coroner's cases will be taken for analysis as they
stream of samples from other sources. Dr. Stanley
It seems likely that the cost can be assessed again
of the number of samples which are analysed during
with you about the means of accounting for our cost
vacation in August and get back to my desk on Augus
instance, is available, but is to be paid in on a bi
advice and consent. I trust that this will be suff
can, of course, discuss it, if you wish, with Dr. F
take it up with Dr. Suskind, later, in view of the
arrival. Not that I was sidestepping Dr. Foulkes,
complicating matters.

The other project has to do with the continuation o
directing, in which Mr. Cholak, Mr. Schafer, Mr. Pa
Dr. Lerner are co-investigators with the technical
I have discussed the prospect for the future with t
sponsors - Dr. Jerry Cole, of Lead Industries Assoc
Corporation, E.I. du Pont de Nemours, and The Assoc
The specific part of this project which has been un
past eight years, is in effect a side issue of the
of the work began in 1939, and was interrupted by t
level of lead in the general atmosphere which is co
This problem has been explored since 1960, and has
very near the solution.

It is planned now to return to the point in the ori
departed in 1960, and to resume the investigation f
annual rate of expenditure of $75,000. I have made
the consideration of the group of Sponsors, and thi
anticipation of approval) between now and the end o

I would suppose that the funds from this source hav
in advance, but I am not sure that this is the case
prepared to request, unless it is fully understood
procedure, or unless you wish me to make a differen
my assumption that you will consult Dr. Suskind on
for doing so.

Sincerely

Robert A.

FROM: Robert A. Kehoe, M.D.

DATE: February 14, 1968

SUBJECT: Investigations Involving Human Subjects

In response to your memo of December 21, 1967, the mat
the Research Committee of the Medical Faculty, is forw

I have not taken the trouble to reproduce the copies o
in my files, but have sent the entire sheaf of informa
correspondence, in order that your Committee might be
transpired. It may be that you will wish to have cert
information in your files. If so, and if you will ret
provide what you require. I include the correspondenc
the opportunities afforded for misunderstanding which
situation. I do not believe, however, that these exch
place in your permanent file. You may not agree with
that you and the other members of your Committee will
decision on the matter. In any case, I shall do my be
wishes, to the extent, if you choose, and as I suggest
Committee and discussing some aspects of this matter.

The issue here, I may say, is not a matter of form or
investigators against unethical action, or accusations
the genuine protection of human beings against any typ
whether through ignorance or intention.

Sincer

Robert

wp

N13350.03

RE 0012374

Letter from Dean Grulee, dated April 4, 1966.

Dr. Kehoe's reply to Dean Grulee, dated April 6, 1966.

Letter from Dean Grulee to Dr. Edward A. Gall, dated A

Report to the Clinical Research Committee on the INVES
OF LEAD IN THE HUMAN SUBJECT (First Version)

Report to the Clinical Research Committee on the INVES
OF LEAD IN THE HUMAN SUBJECT (Dated June 7, 1966).

Letter to Dean Grulee and the Members of the Research

DATE: December 21, 1967

SUBJECT: Investigations Involving Human Su

The Committee on Ethics of Human
has reviewed the material you sent ~~to me~~ or
The Committee would appreciate having this
with a copy of the information, including pr
to the Faculty Committee on Research as wel
to it.

To facilitate the review of proje
members of the Committee will be assigned t
liaison between principal investigators and
Dr. Carl Smith will be the representative f
Please feel free to talk with him or, if yo
any other member of the Committee, about an
may have.

Thanks very much.

Sid

Sidney I

SL:rms

Answered January 12
Proposed meeting in future

N13350.04

KE 0012376

University of Cincinnati

Dear Bud:

I do not understand fully just what it is that the Resea
from the indications in your letter of April 4th, in rel
on, "Investigation of the Metabolism of Lead in the Huma
my best, however, to provide additional information, in
fill the bill. Perhaps, I expect the Committee to under
more cautious in these matters than most people would be
all knowledge and skill that I may have, in avoiding any
It is not easy to say more than just this, in connection

First, with reference to the means by which the subjects
staff that, conditional upon his being found acceptable, physi
by the physicians who act for me (or for any other princ
be involved later), the subject is offered employment, a
his employment are clearly defined in the business offic
conditions with respect to potential risk are explained
The principal investigator has been responsible for the
of safety that are now operative in the best circles of
the lead trades, these having been worked out over the p
clinical and physiological observations of the employees
It has been found that no person is poisoned by lead unl
of lead which result in a specific degree of elevation o
lead or the concentration of lead in his blood. The qua
establishing these criteria have been viewed critically
are now agreed upon in knowledgeable professional circle
they are entirely sound. They are based on the most rig
regarding as signs of lead intoxication such biochemical
with the porphyrin metabolism which cannot be explained
say within our own household, that these standards have
Kettering Laboratory, and that they are applied there mo
than they are anywhere else.) The experimental program
field is explained in detail to the potential subject, a
protection of the Laboratory against the slightest dange
vulnerable to illness from the absorption of lead. Inas
the investigation of the intake and output of lead day b
all times for the principal investigator and the respons
the Clinical Division of the Laboratory) to follow the p
the rate of absorption and excretion of lead, while he i
and laboratory investigation of the hygienic status of t
There is no more informative regimen of medical supervis
followed here.

Second, with respect to the toxicity of the lead to whic
the dosage from day to day is never in or near the range

intoxication may occasionally be expected to occur. In as conducted since 1939, have refined and verified the c if they could ever have been (in the earlier periods of as proceeding into regions of risk, they can no longer b

Incidentally, it is not quite true that "no other measur physician," for the purpose of determining the status of in the original memo. Paragraph (b), page 3, points out maintained under the supervision (in a manner comparable exacting medical regimen) of a physician etc. etc." I r the Research Committee may not know just what such a reg of the Clinical Staff of the Kettering Laboratory have s hardly necessary to set down the details of such a regim adequacy, but it has been done, and the record can be su

Finally, it is recognized that in the carrying out of hu fields, a certain amount of real risk is involved. This in dealing with most medical problems that require elucid however, that in the field of occupational medicine, the have been productive of disease are often carried out by to subject workmen to unknown risks for the sake of the community. It is not necessary, therefore, as a rule, t blindly. One can easily, therefore, take the point of v risk whatever in investigating the parameters of human p

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RAK:wp