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CIRC 19D INACTIVE AS OF 6/4/71

THIS IS FOLDER 2 OF 2 FOLDERS.
OTHER FOLDER IN INACTIVE FILE ALSO

The Medical Research Center
Brookhaven National Laboratory
Upton, L. I., New York

REPOSITORY Records Holding Area Bldg. 494
COLLECTION Committee - Clinical Investigations
and uses of Radioisotopes
BOX No. 4
FOLDER CIRC #19D

1179888

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: MAY 24, '71

TO: DR. G.C. COTZIAS

FROM: R.B. Aronson, Ph.D.

SUBJECT: CIRC Proposal 19D

In compliance with recent FDA and HEW notices requiring periodic reviews of clinical research projects, your CIRC proposal, number 19D is scheduled for review soon. Please indicate at the bottom of the page if this proposal should be continuing or placed on the inactive list.

This proposal was last reviewed and approved by the Committee on June 13 1966. Do you wish to make any substantive changes in your proposal? _____

Have you noticed any adverse effects during the experimental program which have not already been reported to the Department Chairman's Office? _____. Please include the nature and frequency of such effects.

Approximately how many patients have been submitted to the experimental regime since the last approval? _____

The Sponsoring Physician on this proposal is _____. Has there been a change of Sponsoring Physician or Responsible Investigators? _____

If you have obtained IND numbers from the FDA in connection with this proposal please list on a separate sheet the compounds and corresponding IND numbers, and attach.

Please attach to this sheet copies of any reports submitted to the FDA, HEW, or other Granting Agency (in connection with this proposal and the IND numbers given above), since the last CIRC approval date.

Please add any additional information which may be of use to the Committee in its deliberations. Include a copy of the Patient Consent Form now in use for this study.

CIRC PROPOSAL NUMBER 19D IS: Continuing

Inactive

Signed George C. Cotzias M.D. June 4, 1971
per B. Callister Date

Please return this completed form to Dr. R.B. Aronson as soon as possible.

1179889

BROOKHAVEN NATIONAL LABORATORY
MEMORANDUM

DATE: June 3, 1971

TO: Dr. Robert Aronson

FROM: George C. Cotzias, M.D.

SUBJECT: CIRC 19 D

Acceleration of Manganese Turnover By Feeding
Manganous Sulfate.

Our proposal CIRC 19D is presently inactive. If it will
ever become activated again it will necessitate our obtaining
an IND from the Food and Drug Administration.

George C. Cotzias / J Callister
George C. Cotzias, M.D.

GCC:im

Dictated by Dr. Cotzias but signed and mailed in his absence.

1179890

Minutes CIRC Meeting

17 May 1971

Present: J. S. Robertson, S. Cohn, H. R. Connell, R. A. Love, G. A. Price,
and N. P. Rathvon, Jr.

Absent: J. F. Klopper

The meeting was held in the Small Conference Room of the Medical Research Center.

Dr. Robertson opened the meeting at 1500.

The minutes of the 10 May 1971 meeting were approved as read.

The following communications were received by the Committee:

- 1) A memo from M. Goldhaber dated 6 May 1971, amending the 6 April memo appointing the committee.
- 2) Memos from Dr. Cohn and Dr. Cotzias concerning compliance with requests made by the committee concerning CIRC #36.
- 3) A memo from Dr. Cotzias in compliance with a request concerning CIRC #66.

In consideration of a question asked of Dr. Robertson by ~~Dr. Cronkite~~, it was agreed by the committee that there was no special need to have a member of the clergy on the Committee but that he would be welcome on the Committee if the Director of the Laboratory wishes to make such an appointment.

The Committee then took up for consideration CIRC #11 and CIRC #17.

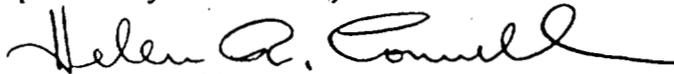
These proposals were approved subject to receipt of a statement from the principal investigator that there have been no adverse reactions to the procedures stated in the proposals since their original approval or, if there have been adverse reactions that they be described. Also, the Committee requests assurance that informed consent will be obtained.

Consideration of other CIRC proposals on the agenda for this meeting, namely, 2, 2A, 7, 19D, was postponed until such time as forms for updating the proposals for re-review are received by the Committee.

The Committee recommends that the Informed Consent Form contain on it the CIRC # for the program to which it applies.

The meeting adjourned at 1645, with the next meeting date set for 24 May 1971.

Respectfully submitted,


Helen R. Connell

cc: CIRC Committee
Mr. Finn
Dr. Aronson
File

1179891

HOSPITAL OF ... MEDICAL RESEARCH CENTER,
BROOKHAVEN NATIONAL LABORATORY
Upton, New York 11973

CLINICAL INVESTIGATION AUTHORIZATION FORM

Purpose of Review: Initial Revision Continuing Addendum

Title: Acceleration of Manganese turnover by feeding manganous sulfate

CIRC# 19D

Assigned
on (date) 6/6/66

To Chairman, CIRC,

The proposal for clinical investigation identified by the above CIRC number and title is forwarded herewith for review and recommendation.

E.P. Cronkite

14 May '71

E.P. Cronkite, M.D., President of Staff Date

To President of Staff,

The Clinical Investigation and Uses of Radiosotopes Committee reviewed the above identified proposal on _____ and recommends _____ with the following modifications:

J.S. Robertson, Chairman

G.C. Cotzias, Alt. Chairman

H.R. Connell

S.H. Cohn

E.A. Popenoe, Alternate

R.A. Love

G. Price

J.F. Klopfer

N.P. Rathvon, Jr.

S.E. Duby, Alternate

A.P. Wolf, Alternate

To _____,

The above titled and numbered proposal is _____ subject to the following:

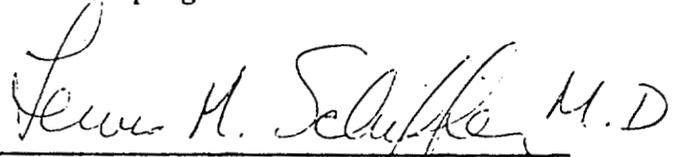
E.P. Cronkite, M.D., President of Staff

Date

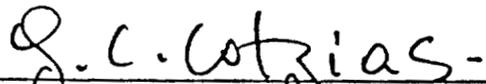
The Committee on Clinical Investigations and Use of Radioisotopes
hereby approves the program with the following title:

ACCELERATION OF MANGANESE TURNOVER BY FEEDING MANGANOUS SULFATE

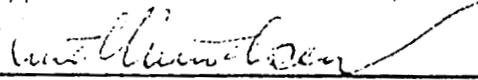
CIRC # 19-d has been assigned to this program.



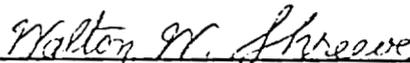
Lewis M. Schiffer, M.D., Acting Chairman



George C. Cotzias, M.D.



Knud D. Knudsen, M.D.



Walton W. Shreeve, M.D., Ph.D. (ex officio)

Date: June 13, 1966

Place: Medical Research Center
Brookhaven National Laboratory
Upton, New York

1179893

JUN 6 1966

Initial Approval:

3

FORM FOR INITIATION OR REVIEW OF CLINICAL
INVESTIGATIVE PROGRAMS

V.P. Bond, M.D.
Chairman

CIRC #19-d

(Submit original only to Department Chairman)

- A. Title of the proposal: Acceleration of manganese turnover by feeding manganous sulfate
- B. Sponsoring physician(s): G.C. Cotzias
- C. Responsible investigator(s): G.C. Cotzias and P.S. Papavasiliou
- D. Brief description of the study, including its general goals and purpose, and pertinent information on past studies: (Attach additional sheets if necessary.)

We wish to continue investigations started before this Committee was constituted. These consist of feeding manganous sulfate to patients in order to accelerate the distribution and excretion of this metal. The reasons for doing this were 1) to define homeostatic control mechanisms in man; 2) to determine possible aberrations thereof in patients with rheumatoid arthritis and related conditions; 3) in order not to miss a remotely possible therapeutic effect. Further justification for these reasons lies with the fact that untreated rheumatoid arthritics have very slow manganese turnovers, defective mucopolysaccharide synthesis while both these findings characterize manganese deficient experimental animals. Administration of prednisone accelerates the turnover of both arthritics and healthy experimental animals. Administration of manganese has not been studied fully in this context.

Such administration seems innocuous on the following grounds: 1) Prior to the institution of your Committee we have given manganous sulfate monohydrate orally in doses of 2 gm/day for as long as 19 months (Cotzias, G.C., Miller, S.T. and Edwards, J., J. Lab. Clin. Med. 67: 836, 1966). 2) Others have given manganous glycerophosphate to arthritics (Vop. Reum. (Russian) 5:57, 1965 (no author).

- E. Reasons why the investigation(s) are to be performed on human subjects.

Animals do not get rheumatoid arthritis.

- F. Type of patient in which the study is to be done (including approximate number of subjects, if known; special restrictions or requirements; method of obtaining consent; etc.):

A few patients with subacute, non-pallindromic rheumatoid arthritis will be chosen among those who need cortisone analogues but might be developing intolerance or side effects. These will be given manganous sulfate by mouth in amounts similar to those used earlier on non-arthritics.

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- G. 1. Are drugs not in the U. S. Pharmacopocia (USP) or the NNR being used or contemplated for use? Yes x x No
2. Is an unusual use of a drug(s) accepted by the USP or NNR contemplated? (An example would be the use of an accepted drug in dosages far exceeding the recommended limits or for purposes distinctly different from the usual indications cited.) Yes No xx
3. Are any biological products to be administered that do not bear on their containers or labels notation of approval by the Biological Control Division of the National Institutes of Health? Yes No xx
4. Is external or internal radiation other than accepted diagnostic or therapeutic procedures to be administered? Yes xx No
5. Are any (other) unusual procedures being performed or proposed which in your judgment may entail a special hazard - particularly a hazard above and beyond any imposed by accepted diagnostic and therapeutic measures for that patient? Yes No xx
6. Are any radioisotopes to be administered to human beings? Yes xx No
- a. If yes, are the radioisotopes to be used solely within the limits of procedures, specifically described in the USP? Yes No xx
- Describe the radioisotopic preparation(s):
- b. Or are the radioisotopes to be used only in accordance with a project previously approved by the former Radioisotope Committee of this Department? Yes xx No
- Note the project number: H-49 and Circ 19

IF ANY OF QUESTIONS 1 THROUGH 5 ARE ANSWERED AFFIRMATIVELY, a detailed analysis of the potential hazards must be appended, including pertinent bibliographic citations and other relevant information.

IF QUESTION 6 IS ANSWERED AFFIRMATIVELY, a completed supplementary form for Radioisotope Administration to Human Beings must be appended. However, this form need not be filed provided that question 6a or 6b is also answered affirmatively. A separate form must be submitted for each radioisotopic species to be administered.

George C. Wolfson
Sponsoring Physician

Committee on Clinical Investigations and
Uses of Radioisotopes

Approval recommended ✓ Date 6/17/64

Disapproval Date

V. P. Bond

V. P. Bond, M. D.
Chairman, Medical Department

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6/25/63.
mlk

Page 2
May 26, 1966

or to patients with lupus (Redleaf, P.D., Arthritis and Rheumatism, 2:112, 1958), in amounts of about 900 mg/day. 3) 150 Chilean miners seem vigorous and healthy in spite of large tissue burdens of manganese (Mena, I., Marin, O., Fuenzelida, S. and Cotzias, G.C. submitted to Neurology).

1179896

The Committee on Clinical Investigations and Use of Radioisotopes
hereby approves the program with the following title:

ACCELERATION OF MANGANESE TURNOVER BY FEEDING MANGANOUS SULFATE

CIRC # 19-d has been assigned to this program.

Lewis M. Schiffer M.D.

Lewis M. Schiffer, M.D., Acting Chairman

G. C. Cotzias

George C. Cotzias, M.D.

Knud D. Knudsen

Knud D. Knudsen, M.D.

Walton W. Shreeve

Walton W. Shreeve, M.D., Ph.D. (ex officio)

Date: June 13, 1966

Place: Medical Research Center
Brookhaven National Laboratory
Upton, New York

1179897



JUN 6 1965

Initial Approval:

3

V.P. Bond, M.D.
Chairman

CIRC #19-d

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George C. Lotzian
Sponsoring Physician

Committee on Clinical Investigations and Uses of Radioisotopes

Approval recommended ✓ Date 6/17/64

Disapproval Date

V. P. Bond

V. P. Bond, M. D.
Chairman, Medical Department

1179899

Page 2

May 26, 1966

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