The Medical Research Center

Brookhaven National Laboratory

Upton, L. I., New York

725537

BROOKHAVEN NATIONAL LABORATORY

R

MEMORANDUM

REPOSITORY Records Holding Area, Bldg 494

COLLECTION Committee-Clinical Investigations and Uses of Radioisotopes

BOX No. 4

FOLDER CIRC #15D

DATE: May 25, 1971

TO: DR. ATKINS

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

SUBJECT: CIRC Proposal 15D

In compliance with recent FDA and HEW notices requiring periodic reviews of clinical research projects, your CIRC proposal, number 15D 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 MAR. 5 1969. 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 diliberations. Include a copy of the Patient Consent Form now in use for this study.

CIRC PROPOSAL NUMBER 15D IS: Continuing ☐

Inactive ☒

Signed Harold L. Atkins March 5, 1969
Date

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

1179699

COMMITTEE ON CLINICAL INVESTIGATIONS

AND USE OF RADIOISOTOPES

Minutes
February 27, 1969

The following Committee members were in attendance: Drs. Rai, Borg, Johnson and Dahl, Acting Chairman.

The Committee reviewed and unanimously approved of:

CIRC #40 entitled "Use of ^{85}Sr in ionic state for bone scanning " submitted by Dr. J. S. Robertson.

CIRC #41 entitled "Use of ^{75}Se selenomethionine for pancrease and parathyroid scanning and for determination of biological half-life and tissue distribution" submitted by Dr. Robertson.

The Committee reviewed CIRC #15-d entitled "Modification of tissue distribution of ^{99m}Tc-sulfur colloid by gelatin". The Committee deferred approval until Dr. Atkins submitted an addendum. The addendum dated February 28, 1969 was received from Dr. Atkins and re-submitted to the individual Committee members for their approval.

The Committee again reviewed CIRC #36. It was decided that a complete copy of all pertinent material concerning this CIRC be given to the Committee. Several questions have been referred to Dr. Stanton Cohn for answers. When this is complete we will schedule another meeting of the Committee.

1179700

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: Feb. 28, 1969

TO: CIRC

FROM: H. L. Atkins HLA

SUBJECT: Addendum to #15d

The gelatin used is U.S.P. gelatin in powdered form. It is dissolved in sterile, pyrogen-free physiological saline and filtered through a 0.3 μ Millipore filter prior to administration.

1179701

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: February 27, 1969

TO: Dr. E. P. Cronkite

FROM: Clinical Investigation and Uses of Radioisotopes Comm., L. K. Dahl, Acting Chairman

SUBJECT: Meeting of February 27, 1969

The Committee approves of CIRC #40 and #41.

The Committee deferred approval of CIRC #15d until Dr. Atkins submits an addendum which will be attached to this CIRC and resubmitted to the Committee members individually.

A complete copy of all pertinent material concerning CIRC #36 is to be given to the Committee members. Several questions have been referred to Dr. Stanton Cohn for answers. When this is complete we will schedule another meeting of the Committee.

CC: Dr. H. L. Atkins
Dr. S. Cohn

1179702

CIRC # 15d

DATE:

EPC

E. P. Cronkite, M. D.
Chairman

FORM FOR INITIATION OR REVIEW OF CLINICAL

INVESTIGATIVE PROGRAMS

(Submit original only to Department Chairman)

A. Title of the proposal: Modification of tissue distribution of ^{99m}Tc-sulfur colloid by gelatin

B. Sponsoring physician(s): H. L. Atkins, J. S. Robertson

C. Responsible investigator(s): H. L. Atkins, W. Hauser

D. Brief description of the study, including its general goals and purpose, and pertinent information on past studies: (Attach additional sheets if necessary.)

We have performed studies with ^{99m}Tc-sulfur colloid in mice which indicate that by pre-injection of gelatin, less liver deposition and greater marrow uptake is obtained (see enclosure). Previous studies have indicated that gelatin is an important factor in rate of colloid disappearance from the blood stream (1,2,3). It appears to affect only gelatin-stabilized colloids. At certain dose levels (10 mg/kg body weight and above) the delay in disappearance of gelatin-stabilized colloidal gold can be used as a measure of immune response capabilities of the body (4).

Gelatin has been previously used in a 6% solution as a plasma expander (5). It is weakly antigenic and, in fact, the antigenicity may be a factor in its use

(Cont. on next page)

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

The purpose is to use the tests clinically in human beings, particularly those undergoing ECIB and thoracic duct cannulation for leukemia and renal transplants.

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.):

We would like to study all patients referred for bone marrow scans. We know of no special restrictions.

1179703

D. Brief description of the study .... (Cont.)

as a colloid stabilizer (6,7). Although antibodies have been detected, no reactions have been recorded. We have never encountered an allergic reaction with our gelatin-stabilized colloid of ^{99m}Tc despite multiple injections in many patients.

We would like to inject 10 mgm/kg of a 2.5% solution in normal saline (about 30 ml) intravenously one-half hour prior to injection of our usual dosage of ^{99m}Tc-sulfur colloid for marrow scanning. Disappearance curves from the blood and liver accumulation curves will be obtained by external counting. Ratios of activity in liver, spleen and over the sacrum will be determined at 1 hour. The results will be compared with studies done in the same patients without gelatin.

Should results warrant, we would then study patients before, during and after treatment with ECIB to determine effect on immune response.

References

1. Kampschmidt, R. F., et al. Factors in the suspending media which alter the carbon clearance rate. J. Reticuloend. Soc. 3: 214-222, 1966.

2. Filkins, J. P. and Di Luzio, N. R. Mechanism of gelatin inhibition of reticuloendothelial function. Proc. Soc. Exptl. Biol. Med. 122: 177-180, 1966.

3. Benacerraf, B. et al. Physiology of phagocytosis of particles by the R.E.S. in physiopathology of the R.E.S. A symposium. Blackwell Scientific Publ., 1957, pp 52-79.

4. Wagner, H. N., Jr., and Iio, M. Studies of the reticuloendothelial system (R.E.S.) III. Blockade of the R.E.S. in man. J. Clin. Invest. 43: 1525-1532, 1964.

5. Merck Index, 7th ed., page 474.

6. Maurer, P. H. I. Antigenicity of oxypolygelatin and gelatin in man. J. Exptl. Med. 100: 497-513, 1954.

7. Murray, I. M. The mechanism of blockade of the reticuloendothelial system. J. Exptl. Med. 117: 139-147, 1963.

1179704

G. 1. Are drugs not in the U. S. Pharmacopoeia (USP) or the NNR being used or contemplated for use? Yes 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 X

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 X

4. Is external or internal radiation other than accepted diagnostic or therapeutic procedures to be administered? Yes ____ No X

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 X

6. Are any radioisotopes to be administered to human beings? Yes X No ____

a. If yes, are the radioisotopes to be used solely within the limits of procedures, specifically described in the USP? Yes ____ No X

Describe the radioisotopic preparation(s): ^{99m}Tc-sulfur colloid

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 X No ____

Note the project number: 15

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.

J. S. Robertson
Sponsoring Physician

1179705

1/15/69 Summary of data to date

Dose mg/gm	Liver	Spleen	Femur
.0002	86.3±1.6	1.24±0.41	0.50±0.11
.0008 (Sample [illegible])	87.3±0.4	1.89±0.16	0.45±0.05
.0008 0.1 mg/gm gelatin pre Rx	81.4±1.1	2.43±0.24	0.54±0.03
.0008 0.2 mg/gm gelatin pre Rx	76.6±3.8	2.29±0.28	0.58±0.06
.005	84.2±2.4	1.89±0.42	0.50±0.09
.004 + 0.02 ml 1/2 L before	78.3±1.9	2.04±0.17	0.71±0.10
.01	79.1±1.6	1.94±0.32	0.57±0.09
.012	80.7±1.7	1.80±0.18	0.61±0.10
.016	74.3±2.5	1.89±0.26	0.75±0.15
.020	72.1±1.9	1.84±0.19	0.85±0.08

H_2S colloid

Dose	Liver	Spleen	Femur
.0008 0.2 ml N.S pre Rx	87.6±1.3	1.78±0.13	0.47±0.06

Thiosulfate

Dose	Liver	Spleen	Femur
.0067	89.4±1.37	1.61±0.47	0.41±0.12
.01	90.3±3.0	2.55±0.45	0.29±0.08
.0067 + 0.09 mg/gm gel pre Rx	88.4±1.1	1.61±0.28	0.35±0.07
.0067 + .0067 H_2S colloid pre Rx	89.6±0.5	1.37±0.45	0.34±0.07
.0067 + 0.09 mg/gm gel. mixed	89.1±1.1	1.65±0.26	0.34±0.07
.004 + 0.012 ml colloid H_2S 1/2 L before	90.7±0.9	4.42±0.83	0.24±0.05

1179706

P values

H_2S colloid

Femora

.0008 ml/gm vs 0.0002 ml/gm — P < 0.20, > 0.10

.0008 ml/gm vs. 0.005 ml/gm — P < 0.25, > 0.20

.0008 ml/gm vs .0.1 mg/gm gelatin — P < 0.025, > 0.02 *

.0008 ml/gm vs 0.2 mg/gm gelatin — P < 0.005 *

.005 ml/gm vs 0.01 ml/gm — P < 0.25, > 0.20

.005 ml/gm vs 0.012 ml/gm — P < 0.20, > 0.10

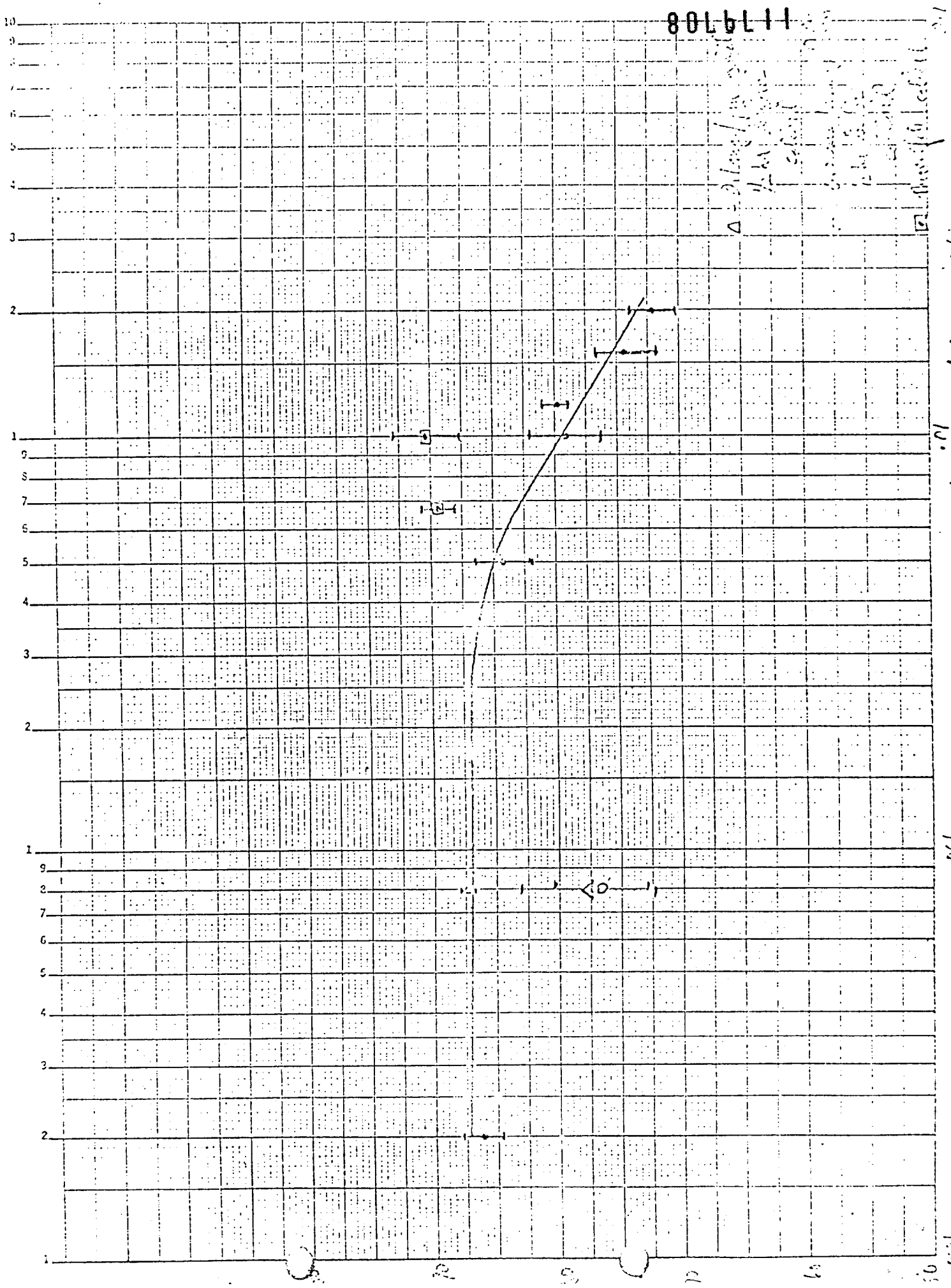
.005 ml/gm vs. 0.016 ml/gm — P < 0.005, > 0.001 *

.0008 ml/gm vs 0.02 ml/gm — P < 0.001 *

Liver 0.0008 vs .005 — P < 0.02, > 0.01 *

0.0008 vs 0.01 — P << 0.001 *

1179707


1179108
KEUFFEL & ESSER CO.

1179709

119710