

10 February 1975

*P*

Present: H.R. Connell, R.A. Love, E.A. Popenoe, N.P. Rathvon, Jr., U. Reincke

Absent: G.C. Cotzias, R. Doremus, L.D. Hamilton, G.A. Price

The meeting was held in the Small Conference Room of the Medical Research Center. Mr. Rathvon presided and opened the meeting at 1400.

The minutes of the previous meeting 6 January 1975, were accepted as distributed.

First discussed were actions taken by the Committee at not regularly convened meetings:

- 1) CIRC 36 Addendum for a special variance for a 15 year old boy was approved 22 January 1975.
- 2) CIRC 122 titled "Study on patients with Chronic Lymphocytic Leukemia" was approved 15 January 1975.

As regards CIRC 122 it was noted that in paragraph C of the supplementary information on radionuclide administration (continuation on page 7) <sup>3</sup>HcDR should be replaced with <sup>3</sup>H-Cytidine.

Next, the following proposals were approved for recertification:

CIRC 26 Rev. 3/30/71, CIRC's 62, 108, 110 and 112.

The approval of CIRC 112 was on the understanding that all reasonable efforts will be taken to exclude pregnant females.

Communications received and noted:

- 1) from H.L. Atkins, 1/13/75 responding to questions raised during the review for recertification of CIRC 56. The explanations were found acceptable.
- 2) from S.H. Cohn, 1/16/75 requesting that Dr. A. Martino be an authorized participant in CIRC's 10A and 36A.
- 3) from S.H. Cohn, 1/16/75 requesting that approval be given to Dr. Aloia to see patients at NCMC on CIRC 36G and indicating that approval of the study has been requested from the NCMC CIRC.
- 4) from I. Zanzi, 1/21/75 responding to the Committee's request for additional information on CIRC 96 Rev. 3/19/74. The memorandum was found acceptable.

Further communications received were memoranda stating the following to be inactive:

CIRC's 36C  
36F  
111  
15F Rev.  
27 and 27A

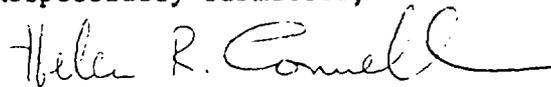
REPOSITORY Records Holding Area Bldg. 494  
COLLECTION Committee - Clinical Investigations and use of Radioisotopes  
BOX No. 4  
Investigational Consent #71.  
FOLDER CIRC # 27 & 27A

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

Before <sup>adjourning</sup> [redacted] a question was raised as to whether the CIRC should be involved in follow-up actions on programs it has approved. After discussion it was decided that no action should be taken by the CIRC but that perhaps the Medical Care Evaluation Committee might be asked to look into some matters in this regard on behalf of the Committee.

The meeting was adjourned at 1450.

Respectfully submitted,



Helen R. Connell

HRC/ck

1180137

CIRC STATUS MEMO

CIRC No. 27 & 27A

Title: Evaluation of Lung Scanning with <sup>99m</sup>Tc-macroaggregated human serum albumin

To: Dr. Atkins

Date: 12/20/74

Please indicate below whether this proposal is continuing or inactive. If continuing, complete the entire form, and 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), since the last CIRC approval date. Also please add any additional information which may be of use to the Committee in its deliberations. If inactive, merely sign and return this form.

If this form is not returned by ~~12/31/74~~ <sup>Jan 20, 1974 PEP</sup>, approval of the proposal will automatically be discontinued.

See attached recap sheet

*R B Aronson*

*Dec 24, '74*

R.B. Aronson, Ph.D., Associate Chairman

Date

To R.B. Aronson,

CIRC PROPOSAL NUMBER 27 & 27A IS:

Continuing

Inactive

Proposed substantive changes are attached The material is now commercially available and approved by FDA.  
Adverse effects that have been first noted since the last approval include:

Since the last approval \_\_\_\_\_ patients have been submitted to the experimental regimen.

The Sponsoring Physician as of this date is \_\_\_\_\_

The following changes in Investigators should be noted: \_\_\_\_\_

The following IND #'s have been obtained for specific compounds used in this proposal:

Compound \_\_\_\_\_ IND# \_\_\_\_\_ Compound \_\_\_\_\_ IND# \_\_\_\_\_

The investigational consent form(s) used in this project are numbered \_\_\_\_\_ and copies are attached. Patients involved in this study are referrals from or also studied at the following institution(s)

Attach statement from institution(s) indicating the review committee approval is current.

Signed *Harold L. Atkins* 01-06-75  
Principal Investigator Date

Signed *Harold L. Atkins* 01-06-75  
Sponsoring Physician Date

1180138

WCAP as of 12/23/74

CIRC 27 & 27A

CIRC

Initial 27 : "Scanning of Lungs" 6/6/66  
CIRC 6/20/66

Initial CIRC

27A : "Evaluation of Lung Scanning with <sup>99m</sup>Tc-Albumin Macroaggregates" 10/5/66

CIRC 27 & 27 A: "Evaluation of Lung Scanning with <sup>99m</sup>Tc-Macroaggregated Human Serum  
Combined Albumin"

	CIRC	DEPT
Recertification	11/8/71	11/9/71
	12/13/72	12/19/72
	1/14/74	1/16/74

Spon. Phys: H. L. Atkins  
Prin. Invest: H. L. Atkins  
Others: J. S. Robertson

CONSENT ~~40~~  
71 12/19/72

IND 299 (99mTc) Last Annual Report 3/11/74

Question Is there any problem in changing the # to 27 Rev. 9/29/71 in order to simplify listing? This has been handled as 27 and 27A combined since 9/29/71.

1180139

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

CIRC No. 27 & 27A

CLINICAL INVESTIGATION AUTHORIZATION FORM

TITLE: Evaluation of Lung Scanning with <sup>99m</sup>Tc-macroaggregated human serum albumin

PURPOSE OF REVIEW:

- INITIAL
- ADDENDUM
- REVISION
- RECERTIFICATION
- REACTIVATION

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 2 Jan '74  
E.P. CRONKITE, M.D., Chairman, Medical Department Date

TO CHAIRMAN, MEDICAL DEPARTMENT:

THE CIRC REVIEWED THE ABOVE IDENTIFIED PROPOSAL ON Jan. 14, 1974 AND RECOMMENDS recertification WITH THE FOLLOWING MODIFICATIONS:

- None -

Edwin A. Popenoe  
E.A. POPENOE, Chairman

N.P. RATHVON, Jr., Alt. Chairman

Helen E. Connell  
H.R. CONNELL

G.A. Price  
L.D. HAMILTON  
G.A. PRICE

P.S. PAPAVASILIOU

R.A. LOVE

D.N. SLATKIN, Alternate

S.H. COHN, Alternate

U. Reincke  
U. REINCKE

A.P. WOLF, Alternate

TO Dr. Atkins,

THE ABOVE TITLED AND NUMBERED PROPOSAL IS Approved SUBJECT TO THE FOLLOWING:

Investigational consent #71 to be used on this CIRC.

E. P. Cronkite 16 Jan '74  
E.P. CRONKITE, M.D., Chairman, Medical Department Date

Minutes CIRC Meeting

14 January 1974

Present: E.A. Popenoe, H.R. Connell, R.A. Love, G.A. Price, U. Reincke

Absent: P.S. Papavasiliou, N.P. Rathvon, Jr.

The meeting was held in the Small Conference Room of the Medical Research Center. Dr. Popenoe opened the meeting at 1400.

The minutes of the previous meeting, 3 December 1973 were accepted as distributed.

CIRC #10A was approved for recertification. However, it was questioned why compound <sup>47</sup>Ca Cl<sub>2</sub>, IND#4390 was included in the previous CIRC Status Memo of 19 October 1972 but not in the Status Memo of 5 December 1973.

Other CIRC's reviewed and approved for recertification are:

~~#26~~  
~~27 & 27A~~  
~~62~~

CIRC #79 Addendum was reviewed next. Dr. Zanzi was invited into the meeting to clarify the sentence, "In addition, the patients may be screened for eventual modifications of their immunological responses." Dr. Zanzi replied that what is intended is a routine tuberculin skin test.

Subsequently, CIRC 79 Addendum was approved.

CIRC #110, "Studies of Antigen-Induced Mechanisms in Human Lymphocytes" was approved.

CIRC #111 was next discussed. The Committee found this proposal confusing and took no action on it. It was noted that the proposal contains several contradictory statements and is not consistent with the supportive documents attached.

In the discussion of CIRC 111 reference was made to the DHEW recommendations on the Protection of Human Subjects published in the Federal Register, Vol. 38, No. 221, Part II, particularly as pertains to children. Consequently the Committee declared that it will not approve any program that includes the use of children from the Children's Shelter.

CIRC #112 was reviewed and approved.

CIRC #103-The memorandum to CIRC from I. Zanzi, M.D., 14 December 1973 was reviewed and found acceptable with the provision that item 1, sentence 2 read: "These procedures will be performed, in the case of premenopausal women, during the 6 days following initiation of menstruation, after a negative pregnancy test, or other reasonable assurance that no pregnancy exists."

1180141

Other communications received and accepted:

- 1) Memorandum from I. Zanzi, M.D., 30 November 1973 listing the values of the approximate radiation doses from x-ray exposures as requested by CIRC for proposal #103.
- 2) A copy of the memorandum to the Medical Staff from E.P. Cronkite, M.D., 4 January 1974 in regard to the age of research participants.
- 3) Memorandum to CIRC from Dr. C. Wu, 14 December 1973 stating the patients to be included in CIRC #104 will be between 21 and 65 years of age.
- 4) Memorandum to CIRC from Dr. J. Iwai, 18 December 1973 stating the patients to be included in CIRC #105 will be between 21 and 65 years of age.
- 5) Memorandum to CIRC from R.B. Aronson, Ph.D., 5 December 1973 reporting the occurrence of a possible adverse reaction re CIRC 63 Rev. 7/20/73 and applicable to IND#7677.
- 6) Memorandum to Dr. Popenoe from R.B. Aronson, Ph.D., 18 December 1973 re Patient Consent #104 applicable to CIRC #106 and #36D. The CIRC acknowledges that this consent is now inactive.

The meeting was adjourned at 1530.

Respectfully submitted,



Helen R. Connell

HRC/ck

1180142

CIRC No. 27 and 27A

Title: Evaluation of Lung Scanning with <sup>99m</sup>Tc-macroaggregated human serum albumin

To: Dr. Atkins

Date: 12/5/73

Please indicate below whether this proposal is continuing or inactive. If continuing, complete the entire form, and 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), since the last CIRC approval date. Also please add any additional information which may be of use to the Committee in its deliberations. If inactive, merely sign and return this form.

If this form is not returned by 12/31/73, approval of the proposal will automatically be discontinued.

R. B. Aronson 12/17/73  
R.B. Aronson, Ph.D., Associate Chairman Date

To R.B. Aronson,

CIRC PROPOSAL NUMBER 27 IS: Continuing  Inactive

Proposed substantive changes are attached —

Adverse effects that have not already been reported to the Department Chairman include: —

Since the last approval 0 patients have been submitted to the experimental regimen.

The Sponsoring Physician as of this date is Harold L. Golden

The following changes in Investigators should be noted: —

The following IND #'s have been obtained for specific compounds used in this proposal:

Compound <sup>99m</sup>Tc HSA(S<sub>2</sub>) IND = D249 Compound — IND = —

The investigational consent form(s) used in this project are numbered 71 and copies are attached.

Patients involved in this study are referrals from or also studied at the following institution(s) —

Attach statement from institution(s) indicating the review committee approval is current.

Signed Harold L. Golden 12/18/73  
Principal Investigator Date

Signed Harold L. Golden 12/18/73  
Sponsoring Physician Date

1180143

HOSPITAL OF THE MEDICAL RESEARCH CENTER,  
BROOKHAVEN NATIONAL LABORATORY  
-71- Upton, New York 11973

NAME

UNIT NO

CONSENT FOR PROCEDURE, STUDY, OR  
DRUG UNDER CLINICAL INVESTIGATION

PAVILION

OP

I understand that the physicians at the Hospital of the Medical Research Center, Brookhaven National Laboratory are engaged in research and study of the nature of diseases and of new methods of diagnosis and treatment. I have been informed of the anticipated duration of hospitalization and the nature of the procedure, study, or drug under clinical investigation known as:

Lung scanning with radioactive <sup>99m</sup>Tc-macroaggregated human serum albumin

I understand that the nature of this procedure, study, or drug is experimental, and that at the present time no assurance can be given that my participation will be directly beneficial to me. I have been informed that the timing and sequence of these studies may not be revealed to me. I understand that in the opinion of the investigators responsible for this project and of the Review Board (Clinical Investigations Committee), I should be informed of the following possible hazards and inconveniences before agreeing to this clinical investigation:

The compound cannot be tested for sterility and pyrogens before use. Rare instances of allergic reactions have occurred. The system and components are tested periodically.

I have been informed of the above. I have also been informed of the customary procedures. These may or may not be used. I have been offered the opportunity for further discussion of this procedure, study, or drug with the attending physician.

I voluntarily consent to participate in the above studies with an understanding of the known possible effects or hazards that might occur in the course thereof, and with the further understanding that not all effects of such procedure, study, or drug are known.

PATIENT'S NAME \_\_\_\_\_

SIGNED BY: \_\_\_\_\_  
(Patient or Legal Guardian)

WITNESS: \_\_\_\_\_

I, the undersigned, herewith affirm that I have explained the above to Mr. (Mrs.) (Miss) \_\_\_\_\_ and I am willing to answer further inquiries.

\_\_\_\_\_ M D DATE \_\_\_\_\_

1180144

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

CIRC No. 27 and 27A

CLINICAL INVESTIGATION AUTHORIZATION FORM

TITLE: Evaluation of Lung Scanning with <sup>99m</sup>Tc-macroaggregated human serum albumin

- PURPOSE OF REVIEW:
- INITIAL
  - ADDENDUM
  - REVISION
  - RECERTIFICATION
  - REACTIVATION

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 4 Dec 72  
E.P. Cronkite, M.D., Chairman, Medical Department Date

TO CHAIRMAN, MEDICAL DEPARTMENT:

THE CIRC REVIEWED THE ABOVE IDENTIFIED PROPOSAL ON 13 December 72 AND RECOMMENDS APPROVAL WITH THE FOLLOWING MODIFICATIONS:

-none-

J.S. Robertson  
J.S. ROBERTSON, Chairman

G. PRICE  
G. PRICE

D.N. SLATKIN  
D.N. SLATKIN, Alternate

G.C. COTZIAS  
G.C. COTZIAS, Alternate Chairman

Edwin A. Popenoe  
E.A. POPENOE, Alternate

G. CHIKKAPPA  
G. CHIKKAPPA

A.P. WOLF  
A.P. WOLF, Alternate

Helen R. Connell  
H.R. CONNELL

R.A. LOVE  
R.A. LOVE

N.P. RATHVON, JR.  
N.P. RATHVON, JR.

TO H.L. Gilmanis

THE ABOVE TITLED AND NUMBERED PROPOSAL IS approved SUBJECT TO THE FOLLOWING:

Consent #71 to be used.

1180145

E.P. Cronkite 19 Dec 72  
E.P. CRONKITE, M.D., Chairman, Medical Department Date



Minutes CIRC Meeting

13 December 1972

Present: J.S. Robertson, H.R. Connell, R.A. Love, E.A. Popenoe, G.A. Price

Absent: S. Cohn, G. Chikkappa, N.P. Rathvon, Jr.

The meeting was held in the Small Conference Room of the Medical Research Center. Dr. Robertson opened the meeting at 1400.

The minutes of the previous meeting, 11 December 1972 were accepted as distributed.

CIRC #95 was reviewed first. Dr. Atkins was invited into the Conference Room to answer questions raised by the Committee. CIRC #95 was approved subject to the following changes agreed to by Dr. Atkins:

1. Clarification of pertinent statements to remove ambiguity as to whether pregnant females will be excluded unconditionally.
2. The dose for normal subjects will be 1/10 or less of the dose stated in the proposal for subjects with malignancies.
3. The Consent Form should contain a statement that a radiation dose will be received and relate the dose to accepted procedures.

CIRC #96 was approved subject to these provisos:

1. It is requested that in the case where a patient will have to sign more than one Consent Form, all the appropriate Consent Forms will be signed at the same time.
2. It is recommended that an estimate of the radiation dose from the skeletal survey be included in the cumulative dose record in the patient's chart.

CIRC #7 was approved for recertification. However, it is noted that the previous requirement that <sup>13</sup>C be included in Consent Form #30 has not been implemented and it is requested that this be done.

The following proposals were reviewed and approved for recertification:

CIRC #26

#27 and #27A

#46

#57

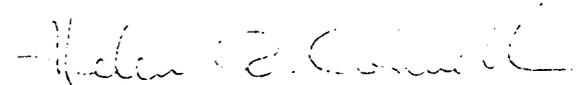
#77

CIRC #10C was reviewed next and approved for recertification with the condition that when applicable, the necessary Consent Form for 10A will be signed at the same time that the Consent Form for #10C is signed.

The Committee considered next Dr. S.H. Cohn's memorandum to Dr. J.S. Robertson of 12/12/72 re CIRC #91. The questions raised by the Committee on 11 December 1972 concerning proposal #91 were found to be satisfactorily answered by this memorandum and CIRC #91 was approved.

The meeting was adjourned at 1630.

Respectfully submitted,



Helen R. Connell

1180147

HOSPITAL OF THE MEDICAL RESEARCH CENTER,  
BROOKHAVEN NATIONAL LABORATORY  
- 71 - Upton, New York 11973

NAME

UNIT NO.

CONSENT FOR PROCEDURE, STUDY, OR  
DRUG UNDER CLINICAL INVESTIGATION

PAVILION

OP

I understand that the physicians at the Hospital of the Medical Research Center, Brookhaven National Laboratory are engaged in research and study of the nature of diseases and of new methods of diagnosis and treatment. I have been informed of the anticipated duration of hospitalization and the nature of the procedure, study, or drug under clinical investigation known as:

Lung scanning with radioactive <sup>99m</sup>Tc-macroaggregated human serum albumin.

I understand that the nature of this procedure, study, or drug is experimental, and that at the present time no assurance can be given that my participation will be directly beneficial to me. I have been informed that the timing and sequence of these studies may not be revealed to me. I understand that in the opinion of the investigators responsible for this project and of the Review Board (Clinical Investigations Committee), I should be informed of the following possible hazards and inconveniences before agreeing to this clinical investigation:

The compound cannot be tested for sterility and pyrogens before use. Rare instances of allergic reactions have occurred. The system and components are tested periodically.

I have been informed of the above. I have also been informed of the customary procedures. These may or may not be used. I have been offered the opportunity for further discussion of this procedure, study, or drug with the attending physician.

I voluntarily consent to participate in the above studies with an understanding of the known possible effects or hazards that might occur in the course thereof, and with the further understanding that not all effects of such procedure, study, or drug are known.

PATIENT'S NAME \_\_\_\_\_

SIGNED BY: \_\_\_\_\_  
(Patient or Legal Guardian)

WITNESS: \_\_\_\_\_

I, the undersigned, herewith affirm that I have explained the above to Mr. (Mrs.) (Miss) \_\_\_\_\_  
and I am willing to answer further inquiries.

\_\_\_\_\_ M.D. DATE \_\_\_\_\_

1180148

BROOKHAVEN NATIONAL LABORATORY  
MEMORANDUM

DATE: December 4, 1972

TO: CIRC Committee (Dr. Robertson)  
FROM: R.B. Aronson, Ph.D. *R.B. Aronson*  
SUBJECT: CIRC Meeting

The following proposals are attached for your consideration at the CIRC meeting scheduled for December 11, 1972 in the Small Conference Room at 2:00 PM:

Initial: CIRC 91  
92  
93  
94  
95  
96

Recertification: CIRC 7  
26  
27 & 27A  
46  
57  
77

Reactivation: CIRC 10C

RBA/ck  
ENC.

1180149

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

NAME \_\_\_\_\_

UNIT NO. \_\_\_\_\_

PAVILION \_\_\_\_\_

OF \_\_\_\_\_

-40-  
CONSENT FOR PROCEDURE, STUDY, OR  
DRUG UNDER CLINICAL INVESTIGATION

I understand that the physicians at the Hospital of the Medical Research Center, Brookhaven National Laboratory are engaged in research and study of the nature of diseases and of new methods of diagnosis and treatment. I have been informed of the anticipated duration of hospitalization and the nature of the procedure, study, or drug under clinical investigation known as:

*radioactive*  
Lung scanning with <sup>99m</sup>Tc-macroaggregated human serum albumin.

I understand that the nature of this procedure, study, or drug is experimental, and that at the present time no assurance can be given that my participation will be directly beneficial to me. I have been informed that the timing and sequence of these studies may not be revealed to me. I understand that in the opinion of the investigators responsible for this project and of the Review Board (Clinical Investigations Committee), I should be informed of the following possible hazards and inconveniences before agreeing to this clinical investigation:

The compound cannot be tested for sterility and pyrogens before use. Rare instances of allergic reactions have occurred. *The system and components are tested periodically.*

OLD  
CONSENT

I have been informed of the above. I have also been informed of the customary procedures. These may or may not be used. I have been offered the opportunity for further discussion of this procedure, study, or drug with the attending physician.

I voluntarily consent to participate in the above studies with an understanding of the known possible effects or hazards that might occur in the course thereof, and with the further understanding that not all effects of such procedure, study, or drug are known.

PATIENT'S NAME \_\_\_\_\_

SIGNED BY: \_\_\_\_\_  
(Patient or Legal Guardian)

WITNESS: \_\_\_\_\_

I, the undersigned, herewith affirm that I have explained the above to Mr. (Mrs.) (Miss) \_\_\_\_\_ and I am willing to answer further inquiries.

\_\_\_\_\_ M.D. DATE \_\_\_\_\_

1180150

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

CIRC No.

27 and 27A

CIRC STATUS MEMO

Title: Evaluation of Lung Scanning with <sup>99m</sup>Tc-macroaggregated human serum albumin

To: Dr. Atkins

Date: 11/6/72

Please indicate below whether this proposal is continuing or inactive. If continuing, complete the entire form, and 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), since the last CIRC approval date. Also please add any additional information which may be of use to the Committee in its deliberations. If inactive, merely sign and return this form.

If this form is not returned by 11/14/72, approval of the proposal will automatically be discontinued.

R B Aronson

7 Nov. '72

R.B. Aronson, Ph.D., Associate Chairman

Date

To R.B. Aronson,

CIRC PROPOSAL NUMBER 27, 27A IS:

Continuing

Inactive

Proposed substantive changes are attached \_\_\_\_\_

Adverse effects that have not already been reported to the Department Chairman include: \_\_\_\_\_

Since the last approval 0 patients have been submitted to the experimental regime.

The Sponsoring Physician as of this date is H. L. ATKINS

The following changes in Investigators should be noted: \_\_\_\_\_

The following IND #'s have been obtained for specific compounds used in this proposal:

Compound <sup>99m</sup>Tc IND # 249 Compound \_\_\_\_\_ IND # \_\_\_\_\_

The investigational consent form(s) used in this project are numbered 40 and copies are attached.

Signed

Harold L. Atkins  
Principle Investigator

11/7/72  
Date

Harold L. Atkins  
Sponsoring Physician

11/7/72  
Date

1180151

Minutes CIRC Meeting

8 November 1971

Present: G.C. Cotzias, H.R. Connell, R.A. Love, E.A. Popenoe, G.A. Price,  
N.P. Rathvon, Jr.

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

Dr. Cotzias opened the meeting at 1400.

The following proposals, presented for annual recertification, were approved:

CIRC #24, #26, and combined #27-27A.

A discussion followed concerning the jurisdiction of the Committee in such cases as the experiment proposed in CIRC #73.

Mr. Rathvon reported that he attended a meeting with Dr. Bond and Dr. Cronkite at which a proposed Standard Operating Procedure for Non-Medical Department Research was discussed. The Standard Operating Procedure would be that whenever any experiment concerning human beings was proposed the Director of the Laboratory would form a select committee to study the proposed experiment and make recommendations.

It was concluded at that meeting that the CIRC Committee should not be used for this purpose. It would be more desirable if the Director appoint an ad hoc committee, the appointees being chosen with a view to the particular problems involved. The flexibility of this kind of committee yields advantages not available in the use of a standing committee such as CIRC.

The meeting was adjourned at 1445.

Respectfully submitted,



Helen R. Connell

cc: CIRC Committee  
Mr. Finn  
Dr. Aronson  
File

1180152

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

CLINICAL INVESTIGATION AUTHORIZATION FORM

Purpose of Review: Initial  Revision  Continuing  Addendum

Title: *Evaluation of lung Scanning with <sup>99m</sup>Tc -  
macroaggregated Human Serum Albumin*

CIRC# *27 and 27A*  
Assigned  
on (date) *29 Sept 1971*

To Chairman, CIRC,

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

*Annual recertification of CIRC 27 and 27A combined*

*- E.P. Cronkite*

*14 Oct 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 *X* and recommends *that it be* with the following modifications:

*Recertified.*

J.S. Robertson, Chairman

*George C. Cotzias*  
G.C. Cotzias, Alt. Chairman

*Helen R. Connell*  
H.R. Connell

S.H. Cohn

*Edwin A. Popenoe*  
E.A. Popenoe, Alternate

*R.A. Love*  
R.A. Love

G. Price

*Glen A. Price*  
G. Price

J.F. Klopfer

N.P. Rathvon, Jr.

S.E. Duby, Alternate

A.P. Wolf, Alternate

To *Drs Robertson and Atkins*

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

*Investigational Consent Form # - 40 - has been established for this CIRC.*

*+ See minutes of CIRC meeting 8 Nov 1971 re appropriate date*

*E.P. Cronkite*

*9 Nov 71*

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

Date

1180153

BROOKHAVEN NATIONAL LABORATORY  
MEMORANDUM

DATE: 10/14/71

TO: CIRC Committee (Cotzias Comm.)

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

SUBJECT: Agenda for CIRC Meeting to be  
held 18 October 1971

CIRC proposals 24, 26 and combined 27-27A will be presented for annual recertification.

CIRC 26 is to be reviewed again due to conflict of interest because of Dr. Robertson's and Dr. Klopper's attendance.

1180154

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: 11/2/71

TO: CIRC Committee (Cotzias Comm.)  
FROM: R.B. Aronson, Ph.D. *RBA*  
SUBJECT: Agenda for CIRC Meeting to be held  
8 November 1971 at 2:00 PM

Since the Committee was unable to obtain a quorum for the October 18th meeting it was cancelled. CIRC proposals 24, 26 and combined 27-27A will be presented for annual recertification.

CIRC 26 is to be reviewed again due to conflict of interest because of Dr. Robertson's and Dr. Klopper's attendance.

All necessary papers required for the above have been previously distributed.

1180155

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: 29 Sept 1971

TO: H. L. Atkins MD

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

SUBJECT: CIRC Proposal 27 and 27A

In compliance with recent FDA and HEW notices requiring periodic reviews of clinical research projects, your CIRC proposal, number 27/27A 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 18 Oct 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? NO. Please include the nature and frequency of such effects.

Approximately how many patients have been submitted to the experimental regime since the last approval? 2

The Sponsoring Physician on this proposal is JS Robertson. Has there been a change of Sponsoring Physician or Responsible Investigators? yes Dr Schiffer has left the study.

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 27/27A IS: Continuing [checked]

Inactive [unchecked]

Signed

[Signature]

9/29/71 Date

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

1180156

Hospital of the Medical Research Center  
Brookhaven National Laboratory  
Upton, New York 11973  
Area Code 516 Yaphank 4-6262

45  
CONSENT FOR PROCEDURE, STUDY, OR  
DRUG UNDER CLINICAL INVESTIGATION

Unit No:  
Pavilion:  
Date: OP

CIRC 27-27A

---

I understand that the physicians at the Hospital of the Medical Research Center, Brookhaven National Laboratory, are engaged in research and study of the nature of diseases and of new methods of diagnosis and treatment. I have been informed of the anticipated duration of hospitalization and the nature of the procedure, study, or drug under clinical investigation known as: Lung scanning with  $^{99m}\text{Tc}$  - macroaggregated human serum albumin.

I understand that the nature of this procedure, study, or drug is experimental, and that at the present time no assurance can be given that my participation will be directly beneficial to me. I have been informed that the timing and sequence of these studies may not be revealed to me. I understand that in the opinions of the investigators responsible for this project, and of the review board (Clinical Investigations Committee), I should be informed of the following possible hazards and inconveniences before agreeing to this clinical investigation: The compound cannot be tested for sterility and pyrogens before use. Rare instances of allergic reactions have occurred.

I have been informed of the above. I have also been informed of customary procedures. These may, or may not, be used. I have been offered the opportunity for further discussion of this procedure, study, or drug with the attending physician.

I voluntarily consent to participate in the above studies with an understanding of the known possible effects or hazards that might occur in the course thereof, and with the further understanding that not all effects of such procedure, study, or drug are known.

PATIENT'S NAME: \_\_\_\_\_

SIGNED BY: \_\_\_\_\_  
(Patient or Legal Guardian)

WITNESS: \_\_\_\_\_

I, the undersigned, herewith affirm that I have explained the above to Mr. (Mrs.) (Miss) \_\_\_\_\_ and I am willing to answer further inquiries.

\_\_\_\_\_ M. D. DATE: \_\_\_\_\_

1180157

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

CLINICAL INVESTIGATION AUTHORIZATION FORM

Purpose of Review: Initial  Revision  Continuing  Addendum

Title: EVALUATION OF LUNG SCANNING WITH <sup>99m</sup>Tc-ALBUMIN  
MACROAGGREGATES

CIRC# 27A

Assigned  
on (date) 9/28/66

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*

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

*5/14/71*  
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. Doby, Alternate

A.P. Wolf, Alternate

To \_\_\_\_\_,

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

1180158

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

Date

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

CLINICAL INVESTIGATION AUTHORIZATION FORM

Purpose of Review: Initial  Revision  Continuing  Addendum

Title:

SCANNING OF LUNGS

CIRC# 27

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*

*5/14/71*

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:

1180159

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

Date

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: 6 May 1971

TO: Dr. J. Robertson

FROM: G. C. Cotzias, M.D. *G.C.*

SUBJECT: CIRC 26 "BLOOD POOL SCANNING WITH  
 $^{99m}\text{Tc}$ -Albumin" and CIRC 27-a "EVALUATION OF  
LUNG SCANNING WITH  $^{99m}\text{Tc}$ -ALBUMIN MACROAGGREGATES

The enclosed CIRC #26 and 27-a were not reviewed by the CIRC Committee on May 3, 1971 because I did not know what the questions are that must be answered.

Please advise and I will be happy to run another meeting.

Many thanks,

George C. Cotzias, M.D.

Distribution:

J. S. Robertson  
S. H. Cohn  
E. A. Popenoe  
H. R. Connell  
J. F. Klopper  
R. A. Love  
G. Price  
N. P. Rathvon, Jr.

1180160

Minutes CIRC Meeting

3 May 1971

Present were: G. C. Cotzias, G. Price, H.R. Connell, J. F. Klopper, N.P. Rathvo  
E. A. Popenoe and R. A. Love.

Absent: J.S. Robertson and S. H. Cohn.

The Committee discussed first the general problem of informed consent with regard to spelling out possible hazards in more detail. The respective consent forms of CIRC #26, 27-a, 36, 61 and 68 were reviewed and found generally satisfactory.

The CIRC #67 was thereafter reviewed. This was submitted by Dr. H. L. Atkins under the title "Effects of Chronic Alcoholism on Calcium Metabolism". It was found unanimously acceptable but three comments were thought as perhaps helpful to the investigators:

- 1) That the irradiation doses of  $^{47}\text{Ca}$  and of whole body Neutron Activation should be added if this is not already being done.
- 2) That a total number of whole body activations per patient should be specified to form a part of the record. The record now specifies only upper limits of radiation dose but not times of exposure.
- 3) The amount of alcohol to be given may perhaps need to be elevated, in which case the investigators will be welcome to address themselves to the Committee.

The CIRC #36 was re-reviewed and found generally acceptable. The final acceptance will be signed by the members of the committee after Dr. Stanton Cohn specifies the following:

- 1) The total number of whole body neutron activations to be delivered per patient.
- 2) The upper limit of combined  $^{47}\text{Ca}$  and neutron activations per patient.

1180161

The Committee then reviewed CIRC #68 entitled "Pi Meson Radiotherapy". It found two specific merits to the proposed use of this technique: 1) That Pi Mesons have a Bragg effect which may be therapeutically useful. 2) That such therapy will be essentially independent of tissue oxygen tension. The Committee encouraged the Chairman of the Medical Department to proceed with plans of developing appropriate facilities and Dr. Atkins to proceed with animal experiments when the time comes. The Committee expressed willingness to review the data from animal experiments and to assist with possible extrapolations into human therapy.

*George C. Cobble*  
*Chairman (pro tem.)*

Distribution:

J. S. Robertson  
S. H. Cohn  
E. A. Popenoe  
H. R. Connell  
J. F. Klopper  
R. A. Love  
G. Price  
N. P. Rathvon, Jr.  
✓ R. Aronson

Minutes CIRC Meeting

6 April 1971

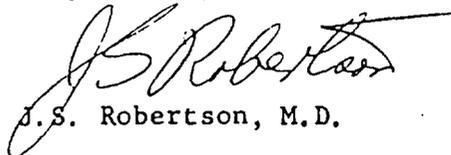
Members Present: Drs. Cohn, Klopper, Love, Robertson and Steck

Absent: Dr. Hamilton

*Refer to 26 Revised*

1. The Committee met at 1100, first in the Large Conference Room, then moving to Room 5-5.
2. A proposal submitted by Dr. Atkins incorporating features of CIRC's 26 and 27a, but involving a revised method of preparation of the pharmaceutical was considered. The proposal was submitted as an amendment to DBS-IND 299. It is noted that in addition to the change in preparation, the types of patients to be studied differs from those in the old CIRC's. It was agreed to designate the new proposal as CIRC 26 (3/30/71), with Dr. Atkins as the sponsor. With these understandings, the proposal was approved.
3. Notice was taken of the recent promulgation of notices by the FDA (Federal Register, vol. 36, No.52, Wednesday, March 17, 1971) and the HEW (Policy Statement to be issued April 15) which affect the constitution of and responsibilities of CIRC. Among the new requirements is an annual review of clinical programs. In anticipation of this, lists of CIRC proposals have been distributed among the investigators with the request that they indicate which ones are active. The responses received indicate that there are 34 inactive proposals, and 64 active ones, of which 45 are now over one year old. No further action was taken, pending further clarification and interpretation by the appointing authorities.
4. Further consideration was given to revision of CIRC forms.
5. A proposal submitted by Dr. Cohn to modify CIRC#36D by lowering the age limits for patients with Cushing's disease and those with thyrotoxicosis was considered. Specific proposals with clinical data were submitted for four patients. After getting information from Dr. Cohn he was excused from the meeting. The remaining members passed the general request and the four special requests.
6. The meeting adjourned at 1205.

Respectfully submitted,

  
J.S. Robertson, M.D.

/ck

cc: CIRC Committee  
Mr. Finn  
File

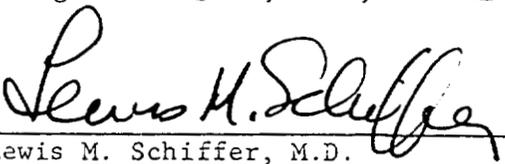
1180163

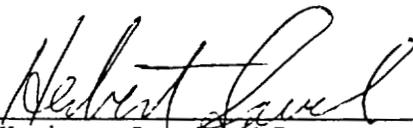
The Committee on Clinical Investigations and Use of Radioisotopes  
hereby approves the program with the following title:

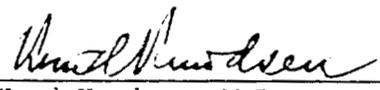
EVALUATION OF LUNG SCANNING WITH  $^{99m}\text{Tc}$ -ALBUMIN  
MACROAGGREGATES

CIRC # 27-a has been assigned to this program.

  
George C. Cottias, M.D., Chairman

  
Lewis M. Schiffer, M.D.

  
Herbert Savel, M.D.

  
Knud Knudsen, M.D.

Date: Oct 18, 1966

Place: Medical Research Center  
Brookhaven National Laboratory  
Upton, New York 11973

1180164

Received:

VB

FORM FOR INITIATION OR REVIEW OF CLINICAL  
INVESTIGATIVE PROGRAMS

V. P. Bond, M. D.  
Chairman

CIRC #27-a

(Submit original only to Department Chairman) Date: Oct. 5, 1966

- A. Title of the proposal: Evaluation of lung scanning with  $^{99m}\text{Tc}$ -albumin macroaggregates
- B. Sponsoring physician(s): J. S. Robertson
- C. Responsible investigator(s): H.L. Atkins, L. Schiffer
- D. Brief description of the study, including its general goals and purpose; and pertinent information on past studies: (Attach additional sheets if necessary.)

Macroaggregates of  $\text{I}^{131}$  human serum albumin are being used routinely in many medical centers for diagnosis of a number of lung conditions. Primarily the study evaluates distribution of blood flow to the various segments of the lung. Scanning of the lungs is carried out 5 minutes following intravenous injection of the macroaggregates. Scans are performed in supine and prone positions.

The advantages of using  $^{99m}\text{Tc}$  are 1) much reduced radiation dose due to short  $T_{1/2}$  and virtual absence of beta; 2) scanning can be performed more rapidly and accurately due to higher count rates; 3) material can be prepared when needed, whereas keeping commercially-available  $\text{I}^{131}$ -labeled material on hand is inconvenient and expensive; and 4) no premedication with stable iodide is required to prevent irradiation to thyroid since material has largely decayed by the time free  $\text{Tc}^{99m}$  is released.

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

Clinical need in patients undergoing ECI and other therapy.

- 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.): Those patients will be studied who have pulmonary symptomatology with no or minor X-ray changes.

1180165

SUPPLEMENTARY FORM FOR RADIOISOTOPE  
ADMINISTRATION TO HUMAN BEINGS

A. Radioisotope

1. Species: (Radioisotope or labeled compound, eg. Na<sup>24</sup>Cl or I-C<sup>14</sup>- glucose)  
Tc<sup>99m</sup>-albumin - macroaggregated
2. Physical characteristics: (Physical half-life; decay scheme (or type, energy and relative frequency of major emissions)  
T<sub>1/2</sub> = 6 hours, decay by  $\gamma$ : 0.142 keV (1.4%)  
0.140 keV (98.6%) No  $\beta$  decay, <10% I.C.  
0.002 keV (98.6%)
3. Source: (BNL reactor, cyclotron, hot lab.), commercial supplier, etc.)  
Hot lab.
4. Preparation: (Target material, quantity, special problems)  
At Hot lab according to previously-submitted and approved application for Tc-albumin and then macroaggregated by heating in water bath to 75°C for 15 min.
5. Specific activity and isotopic purity of administered material:  
Tc<sup>99m</sup> is carrier-free and isotopically > 99.9% pure. Labeling will be > 1 mCi/mgm albumin.
6. Radioassay and calibration procedures: (Include validation to be performed at BNL prior to use)  
Performed at Hot lab with same procedures presently used for Tc<sup>99m</sup>.
7. Vehicle and route of administration:  
Suspended in physiological saline and administered intravenously.
8. Procedures for control of sterility and pyrogenicity: (Or note that commercially supplied isotopes are certified as ready for administration to human beings.) Sterile and pyrogen-free reagents used throughout. Millipore filter 0.045  $\mu$  used prior to aggregation.
9. Extraneous effects, if pertinent: (Such as pharmacological or toxic actions of the parent compound or vehicle, etc.) None

B. Radiation Dosage

1. Biological half-life or half-lives, including slow components:  
In lungs 0.25 d and 3.2 d. In blood 0.44 d and 4.0 d (determined on I<sup>131</sup>-labeled albumin macroaggregates).
2. Organ, cellular, or subcellular localization: (Should account for the effects of special drugs or agents on altering the natural distribution of the radioisotope)
  - a. Critical or "target" organ(s): Lung
  - b. Gonadal exposure: Equivalent to whole-body exposure.

1180166

3. Sample calculations: (Dosage should be calculated for the whole body and for "target" or other separate organs, where indicated)  
 Summary equations are desired; not extensive calculations. Standard dosage equations from references such as Hine and Brownell's Radiation Dosimetry, National Bureau of Standards Handbook 69, and BNL Hospital Form 1167-A should be used where possible and the reference cited.

Lungs: $T_{1/2 b} = 6 \text{ h (0.25 d)}$	wt = 1000 gm	87% adm. dose in lungs
$T_{1/2 p} = 6 \text{ h (0.25 d)}$	g = 160	
$T_{1/2 \text{ eff}} = 3 \text{ h (1/8 d)}$	$\bar{E}_{\beta} = 0.014 \text{ MeV}$	(I <sup>2</sup> )
$D_{\beta} = 73.8 \times \bar{E}_{\beta} \times T_{1/2} \times C \frac{\mu\text{C}}{\text{g}} = 0.56 \text{ rad}$	$\Gamma = 0.696 \text{ cm}^2\text{-R/mCi-hr}$	
$D_{\gamma} = 0.0346 \times C \times T_{\text{eff}} \times \Gamma \times g = 2.16 \text{ rad}$	Density of lung assumed to be 1000 gm/1300 ml.	

Total  $D_{\beta+\gamma} = 2.73 \text{ rads}$  for 5 mCi administered dose

Whole-body dose is less than 0.070 rads which is value for 5 mCi non-aggregated Tc<sup>99m</sup> albumin

Ref. (see below)

C. Radiological Health Aspects

1. Hazards to other patients and to personnel from external or internal radiation: None
2. Monitoring procedures, if necessary: -
3. Special procedures for handling waste products, excreta, biological samples, etc., where indicated: -
4. Plan for isotope accountability, if required: -

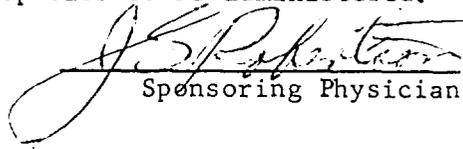
References:

1. McAfee, J.G. et al.: <sup>99m</sup>Tc labeled serum albumin for scintillation scanning. J. Nucl. Med. 5: 936, 1965.
2. Furth, E.D. et al.: The distribution, metabolic fate and radiation dosimetry of <sup>131</sup>I labeled macroaggregated albumin. J. Nucl. Med. 6: 506, 1965.
3. Gwyther, M.M. and Field, E.O.: Aggregated Tc<sup>99m</sup>-labeled albumin for lung scintiscanning. Int. J. Appl. Rad. and Isot. 17: 485, 1966.
4. Laken, M.K. and Bugby, R.D.: Visualization of the lung by methods of scintiphotography. Am. J. Roent., Rad. Therapy and Isot. 97: 850, 1966.

- 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):
- 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      No X
- Note the project number: 27

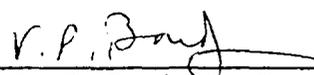
IF ANY OF QUESTIONS 1 THROUGH 5 ARE ANSWERED AFFIRMATIVELY, a detailed analysis of the potential hazards must be appended, including pertinent bibliographic citations and other relevant information.

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.

  
Sponsoring Physician

Committee on Clinical Investigations and  
Uses of Radioisotopes

Approval recommended ✓ Date 10/26/66  
Disapproval      Date     

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

1180168

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

SCANNING OF LUNGS

CIRC # 27 has been assigned to this program.

George C. Cotzias  
George C. Cotzias, M.D., Chairman

Absent  
Lewis M. Schiffer, M.D.

Knud D. Knudsen  
Knud D. Knudsen, M.D.

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

Date: JUN 20 1966

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

1180169

June 20, 1966

The Committee on Clinical Investigations and Use of Radioisotopes has reviewed the Circ. #27 entitled: "Scanning of Lungs" and submitted by Drs. J.S. Robertson, L.M. Schiffer and H.L. Atkins. It was ascertained from Dr. Atkins that 300  $\mu\text{c}$  of  $^{131}\text{I}$  will be given.

The Committee recommended approval of this proposal.

1180170

SUPPLEMENTARY FORM FOR RADIOISOTOPE  
ADMINISTRATION TO HUMAN BEINGS

A. Radioisotope

1. Species: (Radioisotope or labeled compound, eg. Na<sup>24</sup>Cl or 1-C<sup>14</sup>-glucose)  
<sup>131</sup>I-human serum albumin macroaggregates 10-50 μ size
2. Physical characteristics: (Physical half-life; decay scheme (or type, energy and relative frequency of major emissions)  
 $T_{1/2} = 8.1$  days Decay by β and γ emission 0.364 MeV γ 87%
3. Source: (BNL reactor, cyclotron, hot lab.), commercial supplier, etc.)  
Commercial supplier (Squibb)
4. Preparation: (Target material, quantity, special problems)
5. Specific activity and isotopic purity of administered material:  
Carrier-free <sup>131</sup>I 800-1500 μCi/mgm albumin
6. Radioassay and calibration procedures: (Include validation to be performed at BNL prior to use)  
Calibration by supplier
7. Vehicle and route of administration: Intravenous administration.
8. Procedures for control of sterility and pyrogenicity: (Or note that commercially supplied isotopes are certified as ready for administration to human beings.) Supplied as sterile, pyrogen-free suspension, certified by supplier.
9. Extraneous effects, if pertinent: (Such as pharmacological or toxic actions of the parent compound or vehicle, etc.) None reported.

B. Radiation Dosage

1. Biological half-life or half-lives, including slow components:  
Lung  $T_{1/2} = 120$  min      Whole body ~24 hrs  
Liver  $T_{1/2} = 20$  min
2. Organ, cellular, or subcellular localization: (Should account for the effects of special drugs or agents on altering the natural distribution of the radioisotope)
  - a. Critical or "target" organ(s): Lung 3 rads/300 μc  
Whole body 0.7 rads
  - b. Gonadal exposure:  
Equiv. to whole-body exposure.

*Administered dose = 300 μCi*

1180171

3. Sample calculations: (Dosage should be calculated for the whole body and for "target" or other separate organs, where indicated)  
Summary equations are desired; not extensive calculations. Standard dosage equations from references such as Hine and Brownell's Radiation Dosimetry, National Bureau of Standards Handbook 69, and BNL Hospital Form 1167-A should be used where possible and the reference cited.

Dosage calculations taken from the literature.

Ref: Wagner, H. N. Jr. et al. N.E.J. Med. 271: 377, 1964.

Smith, E. J. Nucl. Med. 6: 231, 1965 (Comparison of <sup>99m</sup>Tc and other radiopharmaceuticals)

#### C. Radiological Health Aspects

1. Hazards to other patients and to personnel from external or internal radiation: -
2. Monitoring procedures, if necessary: -
3. Special procedures for handling waste products, excreta, biological samples, etc., where indicated: -
4. Plan for isotope accountability, if required:

- Ref:
1. Colloidal radioalbumin aggregates for organ scanning. Exhibit at 10th Annual Meeting, Soc. Nuclear Medicine, Montreal, June 26-29, 1963, George V. Taplin et al.
  2. Wagner, H. N. Jr., et al., N. Eng. J. Med. 271: 377, 1964.
  3. Sabiston, D. C. and Wagner, H. N. Jr., Ann. Surg. 160: 575, 1964.
  4. Haynie, T. P., et al., J. Nucl. Med. 6: 613, 1965.

JUN 6 1966

FORM FOR INITIATION OR REVIEW OF CLINICAL  
INVESTIGATIVE PROGRAMSV.P. Bond, M.  
Chairman

(Submit original only to Department Chairman)

CIRC #27

- A. Title of the proposal: Scanning of lungs
- B. Sponsoring physician(s): J.S. Robertson, L.M. Schiffer
- C. Responsible investigator(s): H.L. Atkins
- D. Brief description of the study, including its general goals and purpose, and pertinent information on past studies: (Attach additional sheets if necessary.)

Pulmonary scanning is now an accepted clinical procedure for the diagnosis of embolism and other pulmonary pathology. The purpose of this application is for permission to perform such studies in patients in whom clinical symptoms and signs suggest pulmonary pathology, particularly in those patients undergoing extracorporeal irradiation of blood.

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

As a clinical service on research patients.

- 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.):

See above.

1180173

- G. 1. Are drugs not in the U. S. Pharmacopoeia (USP) or the NNR being used or contemplated for use? Yes \_\_\_ No X
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 X No \_\_\_
- Describe the radioisotopic preparation(s):  
<sup>131</sup>I-labeled macroaggregates of human serum albumin.
- 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 \_\_\_ No X
- Note the project number: \_\_\_\_\_

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. Robertson*  
 Sponsoring Physician

Committee on Clinical Investigations and Uses of Radioisotopes

Approval recommended ✓ Date 6/23/63  
 Disapproval \_\_\_\_\_ Date \_\_\_\_\_

*V. P. Bond*

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

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