Minutes CIRC Meeting

725539

10 February 1975

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) 3HCdR should be replaced with $^{3}$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

and

Investigational Consent #71

REPOSITORY Records Holding Area Bldg. 494
COLLECTION Committee - Clinical Investigations and use of Radioisotope
BOX No. 4
FOLDER CIRC # 15F

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

1179757

Before adjourning 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

Helen R. Connell

HRC/ck

1179758

Minutes CIRC Meeting

6 January 1975

Present: G.C. Cotzias, H.R. Connell, L.D. Hamilton, E.A. Popenoe, G.A. Price, N.P. Rathvon, Jr., U. Reincke

Absent: R. Doremus

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

The minutes of the previous meeting, 18 November 1974, were accepted as distributed.

Communications received and noted:

1) Memoranda to CIRC from R.B. Aronson indicating that CIRC's 88,114 and 15F Rev. 10/2/73 and Investigational Consent #67 have been declared inactive.

2) Letter from Dr. Cronkite to Dr. Gyarfas of the DHEW dated 12/5/74 containing notification that IND 9700 and IND 10144 are to be terminated.

CIRC 124 was approved following a discussion in which it was emphasized that the approval is for those procedures being done at BNL.

The recertification of CIRC 56 was discussed next. Dr. Atkins' memorandum re the continuation of this study was deemed not entirely clear. Therefore, the recertification was approved subject to the submittal of a memorandum from Dr. Atkins explaining the reason for extending these studies from the originally proposed 6 patients to a much larger number.

CIRC 15 Rev. 9/7/72 was approved for recertification on the understanding that $^{99m}Tc$ as pertechnetate is used only for approved procedures.

CIRC 105 recertification was approved for up to an additional 40 patients. As regards this proposal, it was noted that a variance for the inclusion in this study of a 16 year old was approved at an unconvened meeting of the CIRC 13 August 1974.

CIRC 83 Addendum was approved.

CIRC 96 Rev. 3/19/74 Addendum was approved - with one member abstaining and the approval being subject to Dr. Cohn submitting evidence concerning:

1) risk - benefit considerations
2) protocols and dosages
3) safeguards of patients

CIRC 107 recertification was approved.

1179759

CIRC 123 was reviewed next and approved for only that portion of the protocol which will be conducted at Brookhaven. The portion of the protocol to be conducted elsewhere was too sketchy for an opinion.

Next, the CIRC reviewed further the matter of pregnancy tests and concluded that it should consult with expert opinion before formulating any judgements.

The meeting was adjourned at 1510.

Respectfully submitted,

Helen R. Connell

Helen R. Connell

HRC/ck

1179760

BROOKHAVEN NATIONAL LABORATORY

# MEMORANDUM

DATE: January 6, 1975

TO: CIRC

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

SUBJECT: CIRC's 15F Rev., 56, 105

The subject CIRC's have been forwarded to the Committee for annual review at the January 6, 1975 meeting.

Please note the following changes:

1. CIRC 15F Rev. is to be inactivated (see attached CIRC status memo amended by Dr. Atkins on 6 January, 1975).

2. Clarification of the status of CIRC 56 is made in the attached memo from Dr. Atkins dated 6 January, 1975.

3. A request is made to increase the number of patients studied under CIRC 105. (Memo of 6 January, 1975 from J. Iwai to CIRC is attached.

RBA/ck
Enc.

1179761

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

CIRC STATUS MEMO

CIRC No. 15F Rev. 10/2/73

Title: Comparison of $^{125}$I-Iothalamate and $^{99m}$Tc-DTPA

To: Dr. Atkins

Date: 12/6/74

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, approval of the proposal will automatically be discontinued.

R B Aronson Dec 13, '74
R.B. Aronson, Ph.D., Associate Chairman Date

To R.B. Aronson,

CIRC PROPOSAL NUMBER 15F R IS: Continuing ☒ Inactive ☒

HLA 01/06/74

Proposed substantive changes are attached We use commercially available kits so consent form is no longer required. Soln. is also USP.

Adverse effects that have been first noted since the last approval include:

none

Since the last approval 17 patients have been submitted to the experimental regimen.

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

The following changes in Investigators should be noted: delete Dr. Bradley-Moore

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

Compound $^{99m}$Tc-DTPA IND# 4344 Compound _____ IND# _____

The investigational consent form(s) used in this project are numbered Y 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 12/23/74 Harold L. Atkins 12/23/74
Principal Investigator Date Sponsoring Physician Date

1179762

Form 1970A

1179763

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

CIRC STATUS MEMO

CIRC No. 15F Rev. 10/2/73

Title: Comparison of $^{125}$I-Iothalamate and $^{99m}$Tc-DTPA

To: Dr. Atkins

Date: 12/6/74

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, approval of the proposal will automatically be discontinued.

R B Aronson Dec 13, 74
R.B. Aronson, Ph.D., Associate Chairman Date

To R.B. Aronson,

CIRC PROPOSAL NUMBER 15F R. IS: Continuing ☒ Inactive ☒

HLA 01/06/74

Proposed substantive changes are attached We use commercially available kits so consent form is no longer required. Soln. is det USP.

Adverse effects that have been first noted since the last approval include:

none

Since the last approval 17 patients have been submitted to the experimental regimen.

The Sponsoring Physician as of this date is N. L. Atkins

The following changes in Investigators should be noted: delete Dr. Bradley-Moore

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

Compound $^{99m}$Tc-DTPA IND # 4344 Compound _____ IND # _____

From C. Kerr

SUBJECT
-FOLD Inactive Investigational Consents

DATE
1/2/75

**MESSAGE**

Please be advised that Investigational Consent #4 used on CIRC's 15F Rev 10/2/73 and 31A is inactive. Also, Investigational Consent #70 used on CIRC 15 Rev 9/7/73 is inactive.

SIGNED

**REPLY**

DATE

-FOLD

SIGNED

SENDER—RETAIN YELLOW COPY - SEND WHITE AND PINK COPIES WITH CARBON INTACT

1179764

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

CIRC No. 15F Rev. 10/2/73

# CLINICAL INVESTIGATION AUTHORIZATION FORM

PURPOSE OF REVIEW:

- [ ] INITIAL
- [ ] ADDENDUM
- [ ] REVISION
- [x] RECERTIFICATION
- [ ] REACTIVATION

TITLE:

Comparison of $^{125}$I-Iothalamate and $^{99m}$Tc-DTPA

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

E P Cronkite 23 Dec '74

E.P. CRONKITE, M.D., Chairman, Medical Deparment — Date

TO CHAIRMAN, MEDICAL DEPARTMENT:

THE CIRC REVIEWED THE ABOVE IDENTIFIED PROPOSAL ON _____ AND RECOMMENDS _____

WITH THE FOLLOWING MODIFICATIONS:

G.C. COTZIAS, Chairman

| | | |
|---|---|---|
| N.P. RATHVON, JR. (Alternate Chairman) | G.A. PRICE | A.D. CHANANA, Alternate |
| H.R. CONNELL | R. DOREMUS | R.A. LOVE, Alternate |
| L.D. HAMILTON | U. REINCKE, Alternate | S.H. COHN, Alternate |
| E.A. POPENOE | J. FOWLER, Alternate | A.P. WOLF, Alternate |

TO _____

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

E.P. CRONKITE, M.D., Chairman, Medical Department — Date

CIRC Form 1 7/1/74

Form 1936B

1179765

HOSPITAL OF THE MEDICAL RESEARCH CENTER,
BROOKHAVEN NATIONAL LABORATORY
-4- Upton, New York 11973

CONSENT FOR PROCEDURE, STUDY, OR
DRUG UNDER CLINICAL INVESTIGATION

NAME

UNIT NO.

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:

Kidney scan with technetium 99m-DTPA (Diethylenetriaminepentaacetic Acid)

Duration: Approximately ½ hour

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:

Hazards: The radiopharmaceutical (99mTc-DTPA) has not been tested for sterility or presence of pyrogens (substances that cuase fever) because of the short physical half-life of technetium 99m. However, the system used for production is checked periodically.

Inconvenience: Intravenous injection.

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 _____

Form 1913 -4- 1179766

Minutes CIRC Meeting

14 October 1974

Present: G.C. Cotzias, H.R. Connell, L.D. Hamilton, G.A. Price, E.A. Popenoe, N.P. Rathvon, Jr., U. Reincke

Absent: R. Doremus

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

First considered was the memorandum from Dr. Cronkite to the Chairman, CIRC requesting authorization for the treatment of one patient with multiple myeloma and extensive bone disease using salmon calcitonin, sodium fluoride and vitamin D. The authorization requested was unanimously approved.

Communications received and noted:

1) from R.B. Aronson, 11 October 1974 concerning the conditional recertifications in 1973 of CIRC's 61,67,79, and 87. The CIRC acknowledges that these approvals are no longer conditional.

2) Dr. Cronkite's letter dated 10/1/74 to the FDA covering Dr. Atkins' protocol and request to add two investigators to IND 10402 (CIRC 109).

3) the request of Dr. Atkins and Dr. Zanzi dated 1 October 1974 to include Dr. Vaswani as an investigator on CIRC's 10A,36,36C,36D,36D3,36F,36G,67, 79,87,96R,103,106,108. Approved.

4) the annual report to the FDA for IND 9768 submitted by Dr. Cotzias 24 September 1974. The Chairman was commended for its perspicuity.

5) the request of Dr. Atkins and Dr. Zanzi of 8 October 1974 to include Dr. Petrak as an investigator on CIRC's 15 Rev, 15B, 15F, 31B,36D3,36G, 42,56,63 Rev,67,79,101,103,106,108,109. Approved.

Next the Chairman read to the Committee a memorandum from Dr. Cronkite re the procedure for Women in Clinical Investigations. Consideration of this subject was postponed until the members could familiarize themselves with the contents of the memorandum.

CIRC# 120 was reviewed next and approved subject to two changes:

1) the title of the clinical investigation be changed to "Evaluation of Lung Function with Radioactive Xenon-127" as it is given on the Consent Form and

2) the Consent Form be changed thus: from "No hazards or inconveniences" to "No inconveniences".

1179767

Approved for recertification were: CIRC's 101,100 and 99 Rev. 8/17/73.

CIRC #109 Addendum was reviewed next. One member reported that the principal investigator informed him that the subjects involved in the study will be highly knowledgeable members of the medical staff. The proposal was found acceptable and was approved.

The meeting was adjourned at 1435.

Respectfully submitted,

Helen R. Connell

Helen R. Connell

HRC/ck
Enc.:
Dr. Cronkite's memo dated 10/7/74

1179768

BROOKHAVEN NATIONAL LABORATORY

# MEMORANDUM

DATE: 10/7/74

TO: Chairman, CIRC

FROM: E. P. Cronkite, M.D. E P Cronkite

SUBJECT: Procedure for Women in Clinical Investigations

I have read with interest the proposal in respect to pregnancy (September 23, 1974 CIRC minutes).

There is no mention of the pill.

Statement 2 should read: "before the menarche" since this takes place at a variable age such as does puberty.

Statement 3 should read: "past the menopause" which also takes place at a variable age.

Statement 4 appears reasonable.

I don't know what fraction of women in the present day would give a true answer to statement 5 but in the past it would have been relatively low.

It is my general understanding that there is some concern on the part of the Committee of invasion of privacy. May I state emphatically that a proper medical history unquestionably results in invasion of privacy, prying into all aspects of human behavior. This is a major reason for the confidentiality of medical records.

There is no question in my mind that there should be a standard approach for the best determination of whether female participants in clinical investigation involving radiation are pregnant.

mb

1179769

Minutes CIRC Meeting

29 October 1973

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

Absent: 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, 24 September 1973 were accepted as distributed.

Communications received:

Copy of the letter to Dr. Atkins from Dr. Robertson dated 9 October 1973 requesting Dr. Atkins assume responsibility of Sponsoring Physician for CIRC's 28,28A,31A,31B,36,36C,36D,36F,42,52,53, and 54.

Memorandum to CIRC from Dr. Zanzi dated 18 October 1973, concerning the modification to CIRC's #103 and 86.

Memorandum to CIRC from Dr. Atkins of 24 October 1973 amending CIRC 15F-Revised 10/2/73.

CIRC#103 was reviewed first and approved with the following qualifications:

1) It be specified that no pregnant women will be involved.
2) Consent form #3 for $^{18}F$ bone scan should include the extent of the radiation involved.
3) The total radiation dose from all procedures involved in this study should be stated-per quarter.
4) It is noted that the letter to Dr. Roginsky from Dr. Crampton 27 September 1973 is unsigned.
5) It is understood that Consent Form #60 will be modified to include $^{125}I$.

CIRC #92 Addendum for FD1571 (Supplements#3 & 4) and CIRC #36H Addendum were approved without modification, Dr. Papavasiliou abstaining.

CIRC #15F Revised 10/2/73 was reviewed for revision and reactivation. Dr. Atkins was asked into the meeting to answer questions about the dose of DTPA to be used and to clarify some of the answers given in the Authorization form.

Dr. Atkins informed the Committee there is a consent form for this procedure even though it was not included in the material distributed to the Committee.

CIRC 15F Revised 10/2/73 was approved with the following modifications in

1179770

CIRC form 2-1:

1) Paragraph A should read: "and 2-3 mCi of $^{99m}$Tc-DTPA"
2) Paragraph F, question 1 is answered "Yes".

Approved for recertification were:

CIRC#15 Rev. 9/7/72
CIRC#56

The Committee then discussed CIRC # 64 Rev. 10/17/73 which had been approved for reactivation on an emergency basis 18 October 1973.

The meeting was adjourned at 1510.

Respectfully submitted,

Helen R. Connell

Helen R. Connell

1179771

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

CIRC No. 15F Rev. 10/2/73

PURPOSE OF REVIEW:

☐ INITIAL ☐ ADDENDUM

☐ REVISION ☐ RECERTIFICATION

☒ REACTIVATION

# CLINICAL INVESTIGATION AUTHORIZATION FORM

TITLE:

Comparison of $^{125}$I-Iothalamate and $^{99m}$Tc-DTPA

TO CHAIRMAN, CIRC:

THE PROPOSAL FOR CLINICAL INVESTIGATION IDENTIFIED BY THE ABOVE CIRC NUMBER AND TITLE IS FORWARDED HEREWITH FOR REVIEW AND RECOMMENDATION.

R B Aronson 8 Oct. 73

Acting ~~E.P. Cronkite, M.D.~~, Chairman, Medical Deparment Date

TO CHAIRMAN, MEDICAL DEPARTMENT:

THE CIRC REVIEWED THE ABOVE IDENTIFIED PROPOSAL ON October 29, 1973 AND RECOMMENDS Approval

WITH THE FOLLOWING MODIFICATIONS:

| | | |
|---|---|---|
| Edwin A. Popenoe<br>E.A. POPENOE, Chairman | ~~K.D. KNUDSEN, Vice Chairman~~ | Helen R. Connell<br>H.R. CONNELL |
| L.D. HAMILTON | P.S. Papavasiliou<br>P.S. PAPAVASILIOU | R.A. Love<br>R.A. LOVE |
| Glenn A. Price<br>G.A. PRICE | S.H. COHN, Alternate | N.P. RATHVON, JR., ALT. CHAIRMAN |
| D.N. SLATKIN, Alternate | A.P. WOLF, Alternate | Ursula Reinicke<br>U. REINICKE |

TO Drs. Atkins, Ansari, Bradley-Moore and Wu,

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

Investigational consent # 4 to be used on this CIRC

E.P. Cronkite 1 Nov '73

1179772

E.P. CRONKITE, M.D., Chairman, Medical Department Date

CIRC Form 1 7/1/73 cc: Atkins, Ansari, Bradley-Moore, Wu, Chanana, Dahl, Harrison, Clinic III

Form 1936B

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

CIRC STATUS MEMO

CIRC No. 15F Rev. 10/2/73

**Title:** Comparison of $^{125}$I-Iothalamate and $^{99m}$Tc-DTPA

To: Dr. Atkins Date: 1 /2/73

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 —, approval of the proposal will automatically be discontinued.

R B Aronson Oct. 2, '73
R.B. Aronson, Ph.D., Associate Chairman Date

To R.B. Aronson,

CIRC PROPOSAL NUMBER 15F IS: Reactivation [X] Continuing ☐ Inactive ☐

Proposed substantive changes are attached None

Adverse effects that have not already been reported to the Department Chairman include:
None

Since the last approval 1 /8/70 11 patients have been submitted to the experimental regimen.

The Sponsoring Physician as of this date is Harold L. Atkins, M.D.

The following changes in Investigators should be noted: Delete W. Hauser & J. Klopper

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

Compound $^{99m}$Tc-DTPA IND # 4344 Compound _____ IND # _____

The investigational consent form(s) used in this project are numbered 4 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 10/2/73
Principal Investigator Date

Harold L. Atkins 10/2/72
Sponsoring Physician Date

1179773

Form 1970A
CIRC Form 4 3/21/73

BROOKHAVEN NATIONAL LABORATORY

# MEMORANDUM

DATE: October 24, 1973

TO: CIRC

FROM: H.L. Atkins, M.D. HLA

SUBJECT: CIRC 15F Rev. 10/2/73

Please note that on CIRC form 2-1 (Rev.2/1/73), page 1 of 4, D, my typed statement of"Type of Patient to be Studied"is amended to read: About 15-20 patients of either sex over 18 years of age.

HLA/ck

1179774

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

CIRC No.
15F Rev. 10/2/73

CLINICAL INVESTIGATION PROPOSAL

Title: Comparison of $^{125}$I-iothalamate acid $^{99m}$Tc-DTPA

Sponsoring Physician Harold L. Atkins Principal Investigator Harold L. Atkins

Other Investigators: A. Ansari
P. Bradley-Moore
C-H. Wu

A. **Brief Description of Proposed Study.** Include general goals and purpose, methods to be used. Mention any radiopharmaceuticals and unofficial drugs to be used, abnormal diets or deprivations (See E).
The purpose is to compare the renal clearance of $^{99m}$Tc-DTPA and $^{125}$I-iothalamate, both agents being cleared by glomerular filtration. Approximately 50 μCi of $^{125}$I-iothalamate and 2-3 ~~μ~~mCi of $^{99m}$Tc-DTPA will be administered simultaneously by the intravenous route. Blood samples will be obtained at appropriate intervals.
HAA 10/29/73

B. **Pertinent Information on Related Prior Clinical, Animal and Laboratory Studies.** Include quantitative toxicity data for drugs. Cite literature by author, title and publication.
Only tracer quantities will be used. Both compounds are in widespread use. Iothalamate in much larger doses is used routinely as a contrast agent in urography and angiography.

C. **Reasons for Performing the Studies on Human Beings and Approximate Number to be Studied.**
The studies will be performed on patients whose renal function is to be evaluated. The patients will have uricemia.

D. **Type of Patient to be Studied.** Include age range, sex, disease, stage of treatment, inclusion or exclusion of pregnant or potentially pregnant females.
Patients involved in this study are referrals from or also studied at the following institution(s)
About 15-20 patients of either sex over ~~16~~ 18 years of age. HAA 10/29/73

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

E. **Dose Schedule for Drugs or Radiopharmaceuticals to be Used.**
50 μCi $^{125}$I-iothalamate and 2-3 mCi $^{99m}$Tc-DTPA i.v.

1179775

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

CIRC No.
15F Rev. 10/2/73

CLINICAL INVESTIGATION PROPOSAL (Cont'd.)

F. **Details of Special Materials or Procedures.**

| | *YES | NO |
|---|---|---|
| 1. Is any drug that falls into one or more of the following categories to be used? (If yes, indicate which) | X | ~~X~~ |
| a) unofficial drug or biological product (drug not listed in the USP or NNR) | X | |
| b) official drug but for purposes other than those listed? | | X |
| c) official drug in doses exceeding or means of administration different from those listed? | | X |
| (An answer "no" to 1. indicates that either no drugs, or only official drugs for the listed purposes and in the listed doses is/are to be used.) | | |
| 2. Are any unlicensed biological products to be administered? | | X |
| 3. Is external or internal radiation other than accepted diagnostic or therapeutic procedures to be administered? | | X |
| **4. Is a radionuclide to be administered? (If no, skip to question 5) | X | |
| a) Specify nuclide and chemical form $^{99m}$Tc-DTPA, $^{125}$I-iothalamate | | |
| b) Is the radionuclide one not listed in the USP? | X | |
| c) Is the purpose for its use one not listed in the USP? | | X |
| d) Does the dose exceed that listed in the USP? | | X |
| 5. Are any other procedures to be used that exceed the ordinary diagnostic and therapeutic measures for the patient concerned and that may entail a hazard, discomfort or embarassment to the patient? | | X |
| ***6. a. Is a direct benefit to the patient to be expected? | X | |
| b. Will the study contribute to the diagnosis, treatment or knowledge of the patient's disease? | X | |

HWA 10/29/

G. I am familiar with the AEC requirement to abide by (a) the HEW's policies on institutional review of experiments involving human subjects and (b) FDA policies on investigational drugs and activities. This clinical investigation will be carried out in conformance with these policies. In particular, informed consent statements will be obtained.

Harold L. Atthe 10/3/73
Sponsoring Physician Date

Harold L. Atthe 10/3/73
Principal Investigator Date

*If any question 1 through 5 is answered yes, append a discussion of the potential hazards including pertinent literature citations or indicate where discussed in accompanying IND request. (Note that an answer NO to 4b, c, and d is sufficient for question 4.)
**If answer to 4 is yes, and the answer to 4b is yes, append a completed CIRC form 2-3 and 2-4 (Supplementary Information on Radionuclide Administration).
***If answer to both 6a and 6b are no, append explanation.

SUPPLEMENTARY INFORMATION ON RADIONUCLIDE ADMINISTRATION

A. Radionuclide

1. **Species:** (Radionuclide or labeled compound, eg. $^{24}$NaCi or 1-$^{14}$C-glucose)
   $^{125}$I-iothalamate

2. **Physical Characteristics:** (Physical half-life; decay scheme, or type, energy, and relative frequency of major emissions; average $\beta$ energy if known)
   $T\frac{1}{2}$ = 60d. Decays by electron capture with emission of low energy & (35.5 keV) and x-rays (27.5 keV) as well as Anger electrons.

3. **Source:** (BNL reactor, cyclotron, hot lab, commercial supplier, etc.)
   Abbott Laboratories

4. **Preparation:** (Target material, quantity, special problems)
   -

5. **Specific Activity and Isotopic Purity of Administered Material:**
   190-375 μCi/mg

6. **Radioassay and Calibration Procedures:** (Include validation to be performed at BNL prior to use)
   Use manufacturer's calibration

7. **Vehicle and Route of Administration:**
   i.v.

8. **Procedures for Control of Sterility and Pyrogenicity:** (Or note that commercially supplied isotopes are certified as ready for administration to human beings)
   Certified by manufacturer

9. **Side Effects, If Pertinent:** (Such as pharmacological or toxic actions of the parent compound or vehicle, etc.)
   None

B. Radiological Health Aspects

1. **Hazards to Other Patients and to Personnel From External or Internal Radiation** (e.g. mr/hr. at 1 meter)
   None

2. **Monitoring Procedures, If Necessary:**
   None

SUPPLEMENTARY INFORMATION ON RADIONUCLIDE ADMINISTRATION

B. **Radiological Health Aspects (Cont'd.)**

3. **Special Procedures for Handling Waste Products, Excreta, Biological Samples, etc., Where Indicated:**
   None

4. **Plan for Isotope Accountability, If Required:**
   None

C. **Radiation Dosage**

1. **Biological Half-Life or Half Lives:** (including slow components and fraction involved)
   $T\frac{1}{2}$(biol) = 12 min (40%); 98 min (50%); 14.8 hrs(10%)

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):**
      Kidney 3.7 mrem/50 μCi

   b. **Gonadal Exposure:**
      0.0006 mrem/50 μCi
      Whole body 0.15 mrem/50 μCi
      (from Abbott literature)

3. **Sample Calculations:** Dosage should be calculated for the whole body and for "target" or other separate organs, where indicated. Prototype equations are desired; not extensive calculations. Where applicable, the Medical Internal Radiation Dose (MIRD) Committee's recommended methods (J. Nuclear Medicine Supplements) should be used. Otherwise, standard dosage equations from references such as Hine and Brownell's *Radiation Dosimetry*, and the *National Bureau of Stanards Handbook 69*, should be used where possible and the reference cited. The relationship to the administered dose should be made clear.

   Assumptions 5% max. in kidneys, uniform distribution in body, $T\frac{1}{2}$ = 1.5 hr., 50 μCi dose.

   Gammas $\sum \Delta i \phi$ = .0358
   Betas $\sum \Delta i$ = .0258
   Whole body contribution to kidney dose in negligible sine $\phi$ = .003

   $$D = C \sum \Delta i \phi x T\tfrac{1}{2} x 1.44 = \frac{2.5}{300} (.0358)(1.5)(1.44) = .00065$$

   $$D_\beta = C \sum \Delta i x T\tfrac{1}{2} x 1.44 \frac{2.5}{300} x .0258(1.5)(1.44) = \underline{.00047}$$

   Total dose $\simeq$ .00112 rads

   For radiation dose from $^{99m}$Tc-DTPA sec CIRC31. Approx. 0.1 rad kidneys and .05 rad gonads for 3 mCi dose.



1179778

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

CIRC No. 15 F

CIRC STATUS MEMO

Title: Comparison of $^{125}$I-Iothalamate and $^{99m}$Tc-DTPA

To: Dr. Atkins

Date: 2/8/73

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 2/28/73, approval of the proposal will automatically be discontinued.

R B Aronson — R.B. Aronson, Ph.D., Associate Chairman — 10 Feb. '73 Date

To R.B. Aronson,

CIRC PROPOSAL NUMBER 15F 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 _____ patients have been submitted to the experimental regime.

The Sponsoring Physician as of this date is _____

The following changes in Investigators should be noted: Delete Drs. Hauser & Klopper

_____

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.

Signed Harold L. Atkins — Principle Investigator — Date 2/12/73

Harold L. Atkins — Sponsoring Physician — Date 2/12/73

1179779

Form 1970
CIRC Form 4 9/21/72

January 13, 1972

Dr. Earl L. Meyers, Director
Division of Oncology and Radio-
pharmaceutical Drug Products
Office of Scientific Evaluation
Bureau of Drugs
Department of Health, Education & Welfare
Rockville, Maryland 20852

Dear Dr. Meyers:

Enclosed is a summary of the administered radiopharmaceuticals in the Nuclear Medicine Service at Brookhaven National Laboratory during 1971. Included are data in the following IND's:

4316, 4172, 4344, 7677, 7440 and 5623.

No adverse reactions were encountered.

Sincerely,

Harold L. Atkins, M. D.

HLA:ls
Enclosure
CC: Mr. W. A. Finn

1179780

# NUCLEAR MEDICINE BNL, 1971 ISOTOPE ADMINISTRATIONS

| | Circ # | Ind # | Jan | Feb | Mar | April | May | June | July | Aug | Sept. | Oct | Nov | Dec | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $^{99m}TcO_4^-$ | 15 | 4316 | 18 | 16 | 28 | 23 | 28 | 25 | 20 | 23 | 24 | 21 | 17 | 23 | 266 |
| $^{131}I^-$ Thyroid | | | 16 | 15 | 24 | 9 | 16 | 19 | 4 | 11 | 5 | 3 | | 6 | 128 |
| $^{123}I^-$ Thyroid | 63 | 7677 | | | | 13 | 11 | 6 | 15 | 12 | 20 | 17 | 17 | 17 | 128 |
| $^{99m}TcO_4^-$ Brain | 15 | 4316 | | | 2 | | | | | | | | | | 2 |
| $^{99m}$TcS, Liver, Spleen and Marrow | 15A | 4172 | 2 | 3 | 3 | 2 | 2 | 3 | 1 | 3 | 7 | 1 | 2 | 1 | 30 |
| $^{99m}$TcS, Lymph Node | 15C | 4172 | 2 | 1 | | 1 | | 1 | | 1 | 1 | 2 | | | 9 |
| $^{99m}$Tc-DTPA, Brain | 31 | 4344 | 11 | 5 | 9 | 6 | 6 | 4 | 10 | 15 | 8 | 10 | 11 | 6 | 101 |
| $^{99m}$Tc-DTPA, Kidney | 31 | 4344 | 1 | 6 | 4 | 6 | 5 | 4 | 4 | 5 | 5 | 3 | 2 | 4 | 49 |
| $^{99m}$Tc-RBC, Spleen & blood pools | 56 | DBS 469 | 1 | 3 | 0 | 1 | 3 | 1 | 1 | 3 | 3 | 1 | | 1 | 18 |
| $^{99m}$TcHSA, blood pools | 26 | DBS 299 | 1 | | | | | | | | | | | | 1 |
| $^{99m}$Tc-gelatin Kidney | 59 | 7440 | | 4 | 2 | 2 | 2 | | | | | | | | 10 |
| $^{18}$F-fluoride-Bone | 42 | 5623 | | | 1 | | | | | | | | | | 1 |
| $^{131}$I-hippuran Kidney | | | 1 | 10 | 3 | 6 | 4 | 4 | 3 | 6 | 2 | 6 | 2 | 2 | 49 |
| $^{131}$I-Rose Bengal Liver | | | | 1 | | | | | | | | | | | 1 |
| $^{125}$I-iothalamate Kidney | | | | 3 | 2 | | | | | | | | | | 5 |
| $^{57}$Cr-RBC-Red blood cell val.or survival | | | | 1 | | 1 | 3 | 1 | 1 | 3 | 3 | 1 | 1 | | 15 |
| $^{57}$Co-$B_{12}$-Shilling Test | | | | | | | | | 1 | | | | 2 | 0 | 3 |
| TOTAL | | | 53 | 68 | 78 | 70 | [illegible] | 68 | 60 | 82 | 78 | 65 | 54 | 60 | [illegible]46 |

1816111

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

COMPARISON OF $^{125}$I-IOTHALAMATE AND $^{99m}$Tc-DTPA

CIRC # 15 (f) has been assigned to this program.

J. S. Robertson, M.D., Chairman

S. H. Cohn, Ph.D.

L. D. Hamilton, M. D.

J. F. Klopper, M. D.

R. A. Love, M. D.

A. J. Steck, M. D.

Date:

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

Committee on Clinical Investigations and Uses of Radioisotoptes

Approval Recommended ✓ Date 6 Oct 7

Disapproval Date

E. P. Cronkite, M.D.
Chairman, Medical Department

8 Oct 70
Date

1179782

Minutes CIRC Meeting

6 October 1970

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

The committee considered these proposals:

1) CIRC 57, by Dr. Cotzias et al, for Potentiation of L-Dopa by MK-486.

2) CIRC 15(f) by Dr. Atkins et al, for Comparison of $^{125}$I-iothalamate and $^{99m}$Tc-DTPA.

3) CIRC 58 by Dr. Cotzias et al, for Administration of Melatonin to Patients.

Actions taken were:

1) Approved

2) Approved

3) Deferred for additional information.

Respectfully submitted,

J.S. Robertson, MD

/ck

cc: CIRC Committee
Mr. W.A. Finn
File

1179783

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: Comparison of $^{125}$I-iothalamate and $^{99m}$Tc-DTPA

B. Sponsoring physician(s): H.L. Atkins

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

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

Both agents are excreted by glomerular filtration. This has been proved with iothalamate by simultaneous measurements with inulin. We would like to compare the Tc-DTPA with iothalamate by measuring plasma clearance and urinary excretion to determine if it truly can be used to measure glomerular filtration. Both compounds will be administered simultaneously (50 μCi $^{125}$I-iothalamate and 3 mCi $^{99m}$Tc-DTPA) and plasma samples and fractional urine collections made over the next 24 hours.

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

Both compounds are used for diagnostic purposes in humans. The patients to be used will require the studies anyway and urine collections for 24 hours are easiest with people.

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.):

Five patients will be the maximum number. These will all be over 18 years of age and referred for renal function studies by the hypertension study group.

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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 X No ____

Describe the radioisotopic preparation(s): $^{125}$I-iothalamate

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: CIRC 15

H. I am familiar with the AEC requirement to abide by the Public Health Service policy on protection of the individual as a research subject. The brochure has been read and this clinical program will be carried out in conformance with those policies.

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

1179785

SUPPLEMENTARY FORM FOR RADIOISOTOPE

ADMINISTRATION TO HUMAN BEINGS

A. Radioisotope

1. Species: (Radioisotope or labeled compound, eg. $Na^{24}Cl$ or 1-$C^{14}$-glucose)
   $^{125}$I-iothalamate
2. Physical characteristics: (Physical half-life; decay scheme (or type, energy and relative frequency of major emissions) $T\frac{1}{2}$ = 60 d., with decay by electron capture with emission gamma, X-ray and Auger electrons.
3. Source: (BNL reactor, cyclotron, hot lab., commercial supplier, etc.)
   Abbott Laboratories
4. Preparation: (Target material, quantity, special problems)
5. Specific activity and isotopic purity of administered material:
   190-375 μCi/mg
6. Radioassay and calibration procedures: (Include validation to be performed at BNL prior to use) Mediac dose calibrator
7. Vehicle and route of administration: I.V.
8. Procedures for control of sterility and pyrogenicity: (Or note that commercially supplied isotopes are certified as ready for administration to human beings.) Certified by manufacturer
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:
   (a) 12 min. (b) 98 min. (c) 14.8 hr.
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): Kidney 3.7 mrem/50 μCi
   b. Gonadal exposure: 0.0006 mrem/50 μCi
      Whole body 0.15 mrem/50 μCi
      (Above dose stated in Abbott literature.)

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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.

Assuming 5% maximum in kidneys, 100% in bladder, uniform distribution in body, $T\frac{1}{2}$ = 1.5 hr for kidney, 2.0 hr whole body, 50 μCi dose.

$D_{kidney}$ = .0006 rad

$D_{bladder}$ = .009 rad/hr

$D_{whole\ body}$ = .0002 rad

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: -

BROOKHAVEN NATIONAL LABORATORY
CLINICAL RESEARCH CENTER
UPTON, NY 11973-5000

Funding Assumed to be from: Department of Energy

Collaborator (if any) mentioned in the text below.

Clinical Investigation Research Proposal (CIRC) 15

---

**Project Name:** Appraisal of $Tc^{99m}$ as a Scanning Agent **Date Started:** April 10, 1964

---

**Identification:**

**Principal Investigator(s):** H.L. Atkins, M.D., L. Schiffer, M.D.

---

**Short description and objectives:**

SEE ATTACHED

| | | |
|---|---|---|
| Appraisal of $Tc^{99m}$ as a Scanning Agent | CIRC 15A | April 10, 1964 |
| Evaluation of $Tc^{99m}$ as a Scanning Agent | CIRC 15B | February 2, 1965 |
| Technitium-99m Sulfur Colloid for Lymph Node Scanning | CIRC 15C | June 21, 1968 |
| Modification of Tissue Distribution of $^{99m}$Tc-sulfur Colloid by Gelatin | CIRC 15D | March 8, 1969 |
| $^{99m}$Tc-S Colloid | CIRC 15E | February 20, 1970 |
| Comparison of $^{125}$I-Iothalamate and $^{99m}$Tc-DTPA | CIRC 15F | October 2, 1973 |
| Clinical Use of $^{99m}$Tc as Pertechnetate and Sulfur Colloid | CIRC 15 (Revised) | September 7, 1972 |

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