725552

RECAP SHEET

CIRC 26R

Title: Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-HSA(Sn).

Spon.Phys: H.L. Atkins
Prin. Invest.: A. Ansari
Others: J. Klopper
I. Zanzi

The Medical Research Center

Brookhaven National Laboratory

Consent: 243

Upton, L. I., New York

Approvals	
HSRC	DEPT
Initial	
11/8/71	11/9/71
Recertification	
12/12/72	12/19/72
Recertification	
1/14/74	1/15/74
Recertification	
2/7/75	2/11/75
Recertification	
4/13/76	4/16/76
* Modification	
7/16/76	8/10/76
Recertification	
5/11/77	5/17/77
Addendum (Comparison studies between 56 and 26R)	
6/8/77	6/10/77
Recertification	

IND#12000 - ^{99m}Tc-HSA(Sn) - Annual ~~report~~ to ~~FDA due now~~

Pts. studied:

1971-72 - 1 pt.
1972-73 - 29 pts.
1973-75 - 0 pts.
1975-77 - 0 pts.
1977-78 -

REPOSITORY Records Holding Area Bldg 494
COLLECTION Committee - Clinical Investigations and uses of Radioisotopes
BOX No. 4
FOLDER CIRC #26

*To include phase III Union Carbide Trial
(IND 12026 Union Carbide IND)

Purpose: To delineate the major blood vessels and heart blood pool for evaluation of vascular disease or possible impaired heart function. This is to support other clinical programs in the hospital.

To compare ^{99m}Tc-labeled red blood cells with ^{99m}Tc human serum albumin. In order to compare the same patients under CIRC's 26R and 56, the drawing of blood samples is necessary.

Radiation Dosimetry: The estimated absorbed radiation doses to an average pt. (70 kg) from an intravenous injection of a maximum dose of 5 millicuries of Technetium Tc 99m are:

Brain	0.047
Marrow	0.076
Kidneys	0.063
Bladder	0.166
Ovaries	0.082
Testes	0.079
Total Body	0.073

1180041

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: October 25, 1978

TO: Dr. Chanana, A. Harrison, J. Matkovich

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

SUBJECT: CIRC 26R

CIRC 26R entitled " Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-HSA(Sn)" and consent 243 are now inactive.

RBA/ck
cc: Dr. Atkins
Dr. Zanzi
HSRC

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: October 25, 1978

TO: Dr. Chanana, A. Harrison, J. Matkovich

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

SUBJECT: CIRC 26R

CIRC 26R entitled " Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-HSA(Sn)" and consent 243 are now inactive.

RBA/ck
cc: Dr. Atkins
Dr. Zanzi
HSRC

1180043

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

CIRC STATUS MEMO

CIRC No. 26R

Title:

Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99}Tc-HSA(Sn).

To: Dr. Atkins Date: 9/21/78

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 9/30/78, approval of the proposal will automatically be discontinued.
Recap sheet attached

R.B. Aronson 9/21/78
R.B. Aronson, Ph.D., Associate Chairman Date

To R.B. Aronson,

CIRC PROPOSAL NUMBER 26R IS: Continuing ☐ Inactive ☒

Proposed substantive changes are attached _____

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

_____

_____

Since the last approval 0 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 10/12/78
Principal Investigator Date

Harold L. Atkins 10/12/78
Sponsoring Physician Date

1180044

Form 1970A

RECAP SHEET

CIRC 26R

Title: Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-HSA(Sn).

Spon.Phys: H.L. Atkins
Prin. Invest.: A. Ansari
Others: J. Klopper
I. Zanzi

Consent: 243

IND#12000 — ^{99m}Tc-HSA(Sn) — Annual report to FDA due now

Pts. studied:

1971-72 - 1 pt.
1972-73 - 29 pts.
1973-75 - 0 pts.
1975-77 - 0 pts.
1977-78 -

Approvals

HSRC	DEPT
Initial	
11/8/71	11/9/71
Recertification	
12/12/72	12/19/72
Recertification	
1/14/74	1/15/74
Recertification	
2/7/75	2/11/75
Recertification	
4/13/76	4/16/76
* Modification	
7/16/76	8/10/76
Recertification	
5/11/77	5/17/77
Addendum (Comparison studies between 56 and 26R)	
6/8/77	6/10/77
Recertification	

*To include phase III Union Carbide Trial
(IND 12026 Union Carbide IND)

Purpose: To delineate the major blood vessels and heart blood pool for evaluation of vascular disease or possible impaired heart function. This is to support other clinical programs in the hospital.

To compare ^{99m}Tc-labeled red blood cells with ^{99m}Tc human serum albumin. In order to compare the same patients under CIRC's 26R and 56, the drawing of blood samples is necessary.

Radiation Dosimetry: The estimated absorbed radiation doses to an average pt. (70 kg) from an intravenous injection of a maximum dose of 5 millicuries of Technetium Tc 99m are:

Brain	0.047
Marrow	0.076
Kidneys	0.063
Bladder	0.166
Ovaries	0.082
Testes	0.079
Total Body	0.073

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

PAV. ____
O.P. ____
I.M. ____

CONSENT FOR PROCEDURE, STUDY, OR
DRUG UNDER CLINICAL INVESTIGATION

-243-

I understand that research patients of the Hospital of the Medical Research Center, Brookhaven National Laboratory, are asked to participate in procedures and studies not established as current medical practice but which are undertaken to discover and evaluate new methods of diagnosis and treatment of certain diseases and to study the nature of a disease, or the effectiveness of current methods of treatment, in the hope that a better understanding will lead to more effective control and even its eradication.

I understand that the procedure explained below 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 the study may not be revealed to me.

The following has been stated to me by Dr. .....:

Blood Pool Imaging with Technetium-99m Human Serum Albumin

Technetium-99m labeled human serum albumin is to be injected intravenously and scintiphotos obtained of its distribution in the body. Following the injection of the radioactivity a number of blood samples may be collected using an indwelling butterfly type needle which may be kept in place for several hours. No more than 50 ml of blood will be collected. Urine samples may also be obtained. Collection of blood and urine samples is for experimental purposes.

Discomforts and risks: One or two venipunctures which rarely but conceivably could give rise to infection and/or localized bleeding into tissues. The radiation dose received in this procedure is approximately 1/50 of the dose permitted radiation workers each year.

The examination is believed to be of some benefit to the patient in outlining the major blood vessels and heart blood pool for evaluation of vascular disease or possible impaired heart function.

Alternative procedures such as radiographic angiography entail much greater hazards in terms of radiation, the need for catheterization, and the possiblity of a drug reaction.

I have been advised that if I wish a more detailed explanation of any of these matters it will be given. (If additional information is given, a summary should be attached.)

I understand I am free to withdraw my consent and discontinue participation in this activity at any time, without prejudice to me.

I have read the foregoing and hereby consent to participate in this procedure.

PATIENT'S NAME _____

SIGNED BY: _____
(Patient and, when necessary, Legal Guardian) (Date)

WITNESS: _____
(Date)

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 _____

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

CIRC STATUS MEMO

CIRC No. 26 Rev.

Title: Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-HSA(Sn).

To: ~~Dr. Atkins~~

Date: ~~4/12/78~~

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 ~~4/30/78~~ R.B. Aronson 4/12/78 Approval of the proposal will automatically be discontinued.

Recap sheet attached
Annual report due to FDA

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

To R.B. Aronson,

CIRC PROPOSAL NUMBER _____ IS: Continuing ☐ Inactive ☐

Proposed substantive changes are attached _____

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 _____
Principal Investigator Date

_____
Sponsoring Physician Date

1180047

Form 1970A

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: March 1, 1978

TO: HSRC

FROM: H. L. Atkins

SUBJECT:

Please include Dr. Zanzi's name on the following CIRCs:

15R
26R
42
45R
56
63R
99R
109
113
120
126
144
145

He will be helping out in Nuclear Medicine with patient care during times that I must be away.

cc: I. Zanzi
A.D. Chanana

1180048

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: October 5, 1977

TO: HSRC

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

SUBJECT:

Please resume carrying my name as sponsoring physician for the following CIRC numbers which have been under Dr. Ansari in my absence:

15B	101	130
15R	107	136
17	109	139
26R	112	144
42	113	145
63R	120	45R
70	123	
84	126	
99R	128	

cc: Dr. Chanana
A. Harrison
J. Matkovich

1180049

Minutes of the

BNL Human Studies Review Committee

8 June 1977

Present: A. Ansari, D. Christman, R. Love, C. Meinhold, N.P. Rathvon, Jr., I. Zanzi
Also present: Alternate - J. Stone
Secretary - C. Kerr
Absent: D. Borg
Excused: H. Connell, R. Doremus, G. Price

The meeting was held in the Hospital Conference Room of the Medical Research Center and called to order by Mr. Rathvon at 1400.

The minutes of 11 May 1977 were accepted as distributed.

CIRC 145 - "Evaluation of Pulmonary Ventilation Using Kr-81m" is a new proposal. The Committee approved this CIRC contingent upon the following:

1. CIRC form 2-2, F4d - Should be marked "not applicable"
2. CIRC form 2-3, A3 - The abbreviation for BLIP should be spelled out as Brookhaven Linac Isotope Producer (BLIP).
3. On both new consent forms spell out the name of the isotope, e.g., radiokrypton (Kr 81m) and xenon(Xe 121).
4. Page 3 of protocol, first three lines should read:

   "ed to a disposable presterilized 0.45-μm bacterial filter (Millipore Corp., Bedford, MA) through a stainless steel adapter (Clay-Adams Inc., New York, NY)."
5. Page 3 of protocol, last sentence should read:

   "The latter system has been developed further by miniaturizing the generator (11,12) and by the addition of a 0.45-μm filter (1) to produce a sterile effluent."
6. CIRC is approved for patients 18 years and over.

CIRC 56 - "Blood Pool and Spleen Scanning with ^{99m}Tc-Labeled Red Cells". Annual recertification was approved providing:

1. The purpose of the study will be to evaluate the use of technetium-labeled red cells as scanning agent for blood pools, and of denatured technetium-labeled red cells as scanning agent for the spleen.
2. Consent form for Blood Pool Imaging with Technetium-99m Red Blood Cells, first paragraph, fourth sentence should read:

   "Following the injection of the radioactivity a number of blood samples may be collected using an in-place butterfly type needle which may be kept in place for several hours."

Permission was granted to do comparative studies with the same patients in CIRC 56 and 26 Rev.

CIRC 26 Rev. - "Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-SHA(Sn)" - Addendum. This addendum was approved as stated above with the recommendation that the consent form for Blood Pool Imaging

with Technetium-99m Human Serum Albumin, first paragraph, second sentence be changed to read:

"Following the injection of the radioactivity a number of blood samples may be collected using an indwelling butterfly type needle which may be kept in place for several hours."

CIRC 119 - "Disorders of Skeletal Metabolism in Hematological Diseases". Approved for annual recertification.

CIRC 126 - "Whole Body Imaging with with Radioactive ^{67}Ga as Gallium Citrate". Approved for annual recertification with the stipulation that the first sentence in the last paragraph on the new consent form be changed to:

"The procedure is done for diagnostic reasons."

CIRC 135 - "Chromosomal Aberrations in Genetic Diseases". Approved for annual recertification providing The Johns Hopkins University School of Medicine's Institutional Review Committee approval is obtained.

The Committee acknowledged receipt of the following:

1. Memo of 6/1/77 from Dr. Ansari declaring CIRC 125 inactive.
2. An article entitled "Neglected Aspects of Informed Consent".
3. Dr. Christman's report to HSRC on"Effects & Problems of Injections of High Specific-Activity Particle Emitters".

The Chairman requested that item 3 be deferred and discussed at a future meeting. Mr. Rathvon will send a memo to all Committee members asking them to be present when this topic is discussed.

Dr. Ansari mentioned that he has noticed some inconsistencies in relation to the Committee's wording and approval of various consents.

One of the Committee members suggested that perhaps Mr. Meinhold give a lecture to the Committee informing them of the natural radiation exposure received per year per individual.

The next meeting of HSRC is scheduled for July 13, 1977 at 2:00 PM in the Hospital Conference Room.

The meeting adjourned at 1500.

Respectfully submitted,

Carole Kerr
Secretary

Minutes of the

BNL Human Studies Review Committee

11 May 1977

Present: A. Ansari, D. Christman, H. Connell, R. Doremus, R. Love, N.P. Rathvon, I. Zanzi
Also present: Alternate - L. Owen
Secretary - C. Kerr
Absent: D.C. Borg
Excused: C. Meinhold

The meeting was held in the Large Conference Room of the Medical Research Center and called to order by Mr. Rathvon at 1405.

The minutes of the previous meeting held on 9 March 1977 were accepted as distributed.

All of the following CIRC's were approved for annual recertification:

CIRC#	Title
15 Rev.	Clinical Use of ^{99}Tc Sulfur Colloid
26 Rev.	Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-SHA(Sn)
42	^{18}F Bone Scanning
62	Medical Studies of Marshallese People Accidentally Exposed to Radioactive Fallout in 1954
63 Rev.	Evaluation of Iodine-123 as Sodium Iodide
70	Detection of Impaired Pulmonary Function with Mass-Spectrographic Tracer Technique
113	Labeling of Blood Elements with Radioactive Nuclides
123	Clinical and Metabolic Evaluation of the Response of Renal Osteodystrophy to the Treatment of Diet; 25 Hydroxycholecalciferol; 1-alpha Hydroxycalciferol and 1,25 Dihydroxycholecalciferol
136	Evaluation Human Calcitonin BA 47175 Treatment of Pagent's Disease of Bone

CIRC 10A Rev. "Studies of Calcium Kinetics in Man" and CIRC 108 "Glucagon in the Treatment of Paget's Disease of Bone" were approved for annual recertification providing that the third paragraph on consent form 175 be changed to read:

> "The attendant discomforts and risks derived from the vein puncture necessary for the injection of ^{47}Ca and for several blood samples (approximately 2 ml (cc) of plasma per day up to ten days) are the remote possibility of pain, bleeding or infection at the site of the vein punctures."

CIRC 109 Rev. - "^{201}Thallium as Thallous Chloride in Sodium Chloride for Myocardial Visualization." Revision and recertification were the purpose of this review. Both were approved. Dr. Ansari's request for the continuation of the Thallium 201 project between BNL and the Special Procedures Laboratory of the Nassau Hospital X-ray Department and the Cardiopulmonary Laboratory was requested and also approved. Drs. P. Mandel and H. Epstein from Nassau Hospital will be added to the list of investigators.

CIRC 99 Rev. - "Detection of Melanoma with I-123 4-(3-dimethylaminopropylamino)-7-iodoquinoline". This addendum to change the method of the production of ^{123}I-43IMQ and to include North Shore University Hospital was approved. It is the Committee's understanding that biopsies will be done elsewhere - not at BNL.

CIRC 144 - "Evaluation of ^{18}FDG in the Diagnosis of Disease of the Brain and Heart" - Initial proposal. Drs. Ansari and Christman explained the protocol to the Committee and suggested that the Committee view the PETT III in operation. The meeting adjourned at 1500 hrs. and reconvened at 1515 and the CIRC was approved with the recommendation that the consent form reads:

First paragraph:

"Approximately 5 mCi of radioactive ^{18}FDG (a glucose-like compound) will be administered intravenously. When the compound has been transported to the heart and brain, images will be taken using imaging devices (a gamma camera and the PETT III tomograph). The images obtained show the distribution of ^{18}FDG and indicate the location and extent of any defect present. Serial blood samples (total of 20 ml - about two tablespoons) will be drawn through an in-place needle or an intra-arterial catheter inserted in the arm vein or artery. The blood samples will be obtained for a total time not exceeding 60 minutes. Urine will also be collected at the end of the study. Blood and urine will be assayed for radioactivity and ^{18}FDG metabolites. The use of ^{18}FDG is experimental."

Last sentence on the consent should read:

"Alternative metabolical procedures available are also experimental."

The Committee acknowledged receipt of the following:

1. Two memorandums (4/13/77 and 4/22/77) from Drs. Ansari and Zanzi changing the Sponsoring Physician on CIRC's 10A,67,121 and 123.

2. Dr. Cronkite's memo of 4/15/77 stating that CIRC 110 entitled "Studies of Antigen-Induced Mechanisms in Human Lymphocytes" is inactive.

3. CIRC 120 - Dr. Ansari's response to questions raised by the Committee at the 3/9/77 meeting.

CIRC 112 - "Clinical Evaluation of 25 Hydroxycholecalciferol Hydrate in the Therapy of Bone Disease Resulting from Malabsorption of Calcium". On 4/13/77 this CIRC was hand delivered to various committee members and was approved for annual recertification.

The next HSRC meeting will be held on Wednesday, 8 June 1977 at 1400 hrs. in the Large Conference Room.

The meeting adjourned at 1610.

Respectfully submitted,

Carole Kerr
Secretary

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: June 15, 1977

TO: HSRC

FROM: A. N. Ansari

SUBJECT: Discontinuation of Consents 178, 186, and 187

Would you please discontinue the use of the following consents:

1. For CIRC 26R, discontinue Consent 178, retaining Consent # 243.
2. For CIRC 56, discontinue Consents 186 and 187, retaining Consents 241 and 242.

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

CIRC No. 26 Rev.

PURPOSE OF REVIEW:

☐ INITIAL ☒ ADDENDUM

☐ REVISION ☐ RECERTIFICATION

☐ REACTIVATION

CLINICAL INVESTIGATION AUTHORIZATION FORM

TITLE: Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-SHA(Sn)

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

Addendum
(See 6/3/77 memo from Dr Ansari)

P B Aronson — Acting Chairman, Medical Deparment — June 3, '77 Date

TO CHAIRMAN, MEDICAL DEPARTMENT:
THE HSRC REVIEWED THE ABOVE IDENTIFIED PROPOSAL ON 6/8/77 AND RECOMMENDS approval
WITH THE FOLLOWING MODIFICATIONS:

Consent form for Blood Pool Imaging with Technetium-99m Human Serum Albumin be changes to read:

First paragraph, 2nd sentence:

"Following the injection of the radioactivity a number of blood samples may be collected using an indwelling butterfly type needle which may be kept in place for several hours."

		U. Reincke, Alternate
N.P. Rathvon, Jr., Chairman	D.D. Joel, Alternate	C.W. Flood, Alternate
	R. Doremus	J.P. Stone, Alternate
L.D. Hamilton (Alternate Chairman)	D.R. Christman	G.A. Price, Alternate
H.R. Connell	C.B. Meinhold	L. Owen, Alternate
A.N. Ansari	D.C. Borg	W. Shreeve, Alternate
R.A. Love	A. Upton, Alternate	I. Zanzi

TO Drs. Ansari, Atkins, Klopper,

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

Investigational consents 178 and 243 to be used on this CIRC.

E.P. Cronkite — E.P. Cronkite, M.D., Chairman, Medical Department — 10 Jun 77 Date

1180055

cc: Above investigators, Dr. Chanana, A. Harrison, J. Matkovich

Form 1936C

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: June 3, 1977

TO: HSRC

FROM: A. N. Ansari

SUBJECT: CIRC 26R and CIRC 56

It is planned to compare the same patients under CIRC 26R and CIRC 56, i.e., using ^{99m}Tc-labeled red blood cells and ^{99m}Tc human serum albumin (HSRC minutes Dec. 8, 1976). The following changes to CIRC 26R and 56 are therefore necessary:

CIRC 26R:

A. Purpose

1. To delineate the major blood vessels and heart blood pool for evaluation of vascular disease or possible impaired heart function. This is to support other clinical programs in the hospital.
2. To compare ^{99m}Tc-labeled red blood cells with ^{99m}Tc human serum albumin. In order to compare the same patients under CIRC's 26R and 56, the drawing of blood samples is necessary.

B. Revised consent form --Blood Pool Imaging with Tc-99m Human Serum Albumin

CIRC 56:

A. Purpose: It is planned to evaluate the feasibility of using Tc-labeled red cells as scanning agent for blood pools, and of denatured Tc-labeled red cells as scanning agent for the spleen. Further we will compare ^{99m}Tc-labeled red blood cells with ^{99m}Tc human serum albumin. In order to compare the same patients under CIRC's 26R and 56, the drawing of blood samples is necessary.

Main clinical uses in case of success of this labeling procedure should be:

1. To delineate the major blood vessels and heart blood pool for evaluation of vascular disease or possible impaired heart function. This is to support other clinical programs in the hospital.
2. Placental localization
3. Spleen scanning for determination of size, location, infarcts, etc.

B. Revised consent forms for Blood Pool Imaging with Tc-99m Red Blood Cells and Spleen Imaging with Tc-99m Red Blood Cells.

Applicable forms are attached.

1180056

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

CONSENT FOR PROCEDURE, STUDY, OR
DRUG UNDER CLINICAL INVESTIGATION

PAV. ____
O.P. ____
I.M. ____

I understand that research patients of the Hospital of the Medical Research Center, Brookhaven National Laboratory, are asked to participate in procedures and studies not established as current medical practice but which are undertaken to discover and evaluate new methods of diagnosis and treatment of certain diseases and to study the nature of a disease, or the effectiveness of current methods of treatment, in the hope that a better understanding will lead to more effective control and even its eradication.

I understand that the procedure explained below 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 the study may not be revealed to me.

The following has been stated to me by Dr. .....:

Blood Pool Imaging with Technetium-99m Human Serum Albumin

Technetium-99m labeled human serum albumin is to be injected intravenously and scintiphotos obtained of its distribution in the body. Following the injection of the radioactivity a number of blood samples may be collected using an indwelling butterfly type needle. No more than 50 ml of blood will be collected. Urine samples may also be obtained. Collection of blood and urine samples is for experimental purposes. which may be kept in patient for several hours.

Discomforts and risks: One or two venipunctures which rarely but conceivably could give rise to infection and/or localized bleeding into tissues. The radiation dose received in this procedure is approximately 1/50 of the dose permitted radiation workers each year.

The examination is believed to be of some benefit to the patient in outlining the major blood vessles and heart blood pool for evaluation of vascular disease or possible impaired heart function.

Alternative procedures such as radiographic angiography entail much greater hazards in terms of radiation, the need for catheterization, and the possibility of a drug reaction.

I have been advised that if I wish a more detailed explanation of any of these matters it will be given. (If additional information is given, a summary should be attached.)

I understand I am free to withdraw my consent and discontinue participation in this activity at any time, without prejudice to me.

I have read the foregoing and hereby consent to participate in this procedure.

PATIENT'S NAME _____

SIGNED BY: _____
(Patient and, when necessary, Legal Guardian) (Date)

WITNESS: _____
(Date)

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 1913B

1180057

2-3

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

PAV. ____
O.P. ____
I.M. ____

CONSENT FOR PROCEDURE, STUDY, OR
DRUG UNDER CLINICAL INVESTIGATION

-178-

I understand that research patients of the Hospital of the Medical Research Center, Brookhaven National Laboratory, are asked to participate in procedures and studies not established as current medical practice but which are undertaken to discover and evaluate new methods of diagnosis and treatment of certain diseases and to study the nature of a disease, or the effectiveness of current methods of treatment, in the hope that a better understanding will lead to more effective control and even its eradication.

I understand that the procedure explained below 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 the study may not be revealed to me.

The following has been stated to me by Dr. .....:

Technetium-99m labeled human serum albumin is to be injected intravenously and scintiphotos obtained of its distribution in the body. No particular hazards or inconveniences are associated with its use. The radiation dose is of the same magnitude as the radiation dose received by tissues in many standard diagnostic procedures. The radiation dose received in this procedure is approximately one tenth of the dose permitted occupational radiation workers each year. The chance of introducing an infection by the needle puncture is extremely rare. The examination is believed to be some benefit to the patient in outlining the major blood vessels and heart blood pool for evaluation of vascular disease or possible impaired heart function. No non-experimental alternate method is available at lesser risk.

I have been advised that if I wish a more detailed explanation of any of these matters it will be given. (If additional information is given, a summary should be attached.)

I understand I am free to withdraw my consent and discontinue participation in this activity at any time, without prejudice to me.

I have read the foregoing and hereby consent to participate in this procedure.

PATIENT'S NAME _____

SIGNED BY: _____
(Patient and, when necessary, Legal Guardian) (Date)

WITNESS: _____
(Date)

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 _____

1180058

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

CIRC No. 26 Rev.

PURPOSE OF REVIEW:
☐ INITIAL ☐ ADDENDUM
☐ REVISION ☒ RECERTIFICATION
☐ REACTIVATION

CLINICAL INVESTIGATION AUTHORIZATION FORM

TITLE: Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-SHA(Sn).

TO CHAIRMAN, HSRC.
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 15 Apr 77
E.P. CRONKITE, M.D., Chairman, Medical Deparment — Date

TO CHAIRMAN, MEDICAL DEPARTMENT:
THE HSRC REVIEWED THE ABOVE IDENTIFIED PROPOSAL ON May 11, 1977 AND RECOMMENDS Approval
WITH THE FOLLOWING MODIFICATIONS:

N Peter Rathvon
N.P. RATHVON, JR., Chairman

L.D. HAMILTON (Alternate Chairman)

Helen R. Connell
H.R. CONNELL

A.N. ANSARI

R.A. LOVE

D.D. JOEL, Alternate

Robert R. Doremus
R. DOREMUS

D.R. Christman
D.R. CHRISTMAN

C.B. MEINHOLD

D.C. BORG

A. UPTON, Alternate

U. REINCKE, Alternate

C.W. FLOOD, Alternate

J.P. STONE, Alternate

Linda Owen
G.A. PRICE, Alternate
L. OWEN, Alternate

W. SHREEVE, Alternate

TO Drs. Ansari, Atkins and Klopper,

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

Investigational consent # 178 to be used on this CIRC.

1180059

E.P. Cronkite 17 May 77
E.P. CRONKITE, M.D., Chairman, Medical Department — Date

cc: Dr. Chanana, A. Harrison, J. Matkovich

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

CIRC STATUS MEMO

CIRC No. 26 Rev.

Title: Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-SHA(SN).

To: Dr. Ansari Date: 3/24/77

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 4/15/77, approval of the proposal will automatically be discontinued.

Recap sheet attached.

R B Aronson 3/28/77
R.B. Aronson, Ph.D., Associate Chairman Date

To R.B. Aronson,

CIRC PROPOSAL NUMBER 26R IS: Continuing [X] Inactive [ ]

Proposed substantive changes are attached None

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

None

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

The Sponsoring Physician as of this date is Dr. A. Ansari

The following changes in Investigators should be noted: None

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

Compound ^{99m}Tc-HSA(Sn) IND# 12000 Compound _____ IND# _____

The investigational consent form(s) used in this project are numbered 178 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 _____ 4/12/77
Principal Investigator Date

_____ 4/12/77
Sponsoring Physician Date

Form 1970A

1180060

RECAP SHEET

CIRC 26 Rev.

TITLE: Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-HSA(Sn).

Spon. Phys.: A. Ansari
Prin. Invest.: H. L. Atkins
Others: J. Klopper

Investigational Consent: 178

IND#12000 - ^{99m}Tc-HSA(Sn) - Annual Report due 12/77

Approvals	
HSRC	Dept.
Initial	
11/8/71	11/9/71
Recertification	
12/12/72	12/19/72
Recertification	
1/14/74	1/15/74
Recertification	
2/7/75	2/11/75
Recertification	
4/13/76	4/16/76
* Modification	
7/16/76	8/10/76
Recertification	

Pts. studied:
1971-1972 - 1 pt.
1972-1973 - 29 pts.
1973-1975 - 0 pts.
1975-1976 - 0 pts.
*To include phase III Union Carbide Trial

Purpose: To delineate blood pools such as heart aneurysms in pts. in whom this is clinically indicated. No specific research program is intended. This is to support other clinical programs in the hospital.

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: 1/17/77

TO: HSRC

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

SUBJECT: Sponsoring Physician

This is to inform you that I will be on leave for professional advancement from December 19, 1976 to June 19, 1977. In my absence, Dr. Ansari has agreed to assume the role of sponsoring physician for the various research projects for which I am presently sponsoring physician.

jf
cc: A.N. Ansari
R.B. Aronson

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: 1/17/77

TO: HSRC

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

SUBJECT: Sponsoring Physician

This is to inform you that I will be on leave for professional advancement from December 19, 1976 to June 19, 1977. In my absence, Dr. Ansari has agreed to assume the role of sponsoring physician for the various research projects for which I am presently sponsoring physician.

jf
cc: A.N. Ansari
R.B. Aronson

1180063

Minutes of the
BNL Human Studies Review Committee
8 December 1976

Present: A. Ansari, D. Borg, D. Christman, H. Connell, R. Doremus, R. Love, C. Meinhold, I. Zanzi
Also present: Alternate - J. Stone
Secretary - C. Kerr
Excused: N.P. Rathvon, Jr.

The meeting was held in the Large Conference Room of the Medical Research Center and called to order by Dr. Christman at 1400 hrs.

The minutes of the previous meeting held on 10 November 1976 were accepted as distributed.

CIRC 69 - "Culture of Human Bone Marrow, its DNA Content and Morphology" was approved for annual recertification.

CIRC 101 - "Evaluation of ^{11}C-dopamine for Adrenal Visualization" - Annual recertification. It was the Committee's recommendation that this CIRC be returned for the following changes on the consent form: 1) Consent should be modified to include the title as it appeared on the old consent form. 2) In paragraph 1, instead of the word "tested" it should specify "tested for sterility and pyrogenicity (substances causing fever)." 3) The purpose and procedure should be given in laymen's terms as per instructions on the reverse side of the consent form (items 1 & 3). The Committee would like to review the revised consent at its next meeting.

CIRC 128 - "^{11}C-octylamine for Pulmonary Function and Imaging" - Annual recertification. Dr. Ansari informed the Committee that a different procedure will be used to minimize the probability of high local radiation dose at the injection site. The original procedure was to inject a needle with syringe directly into the vein. Now, a scalp needle with a tube connected to the syringe will be used. The Committee discussed the risk of extravasation and whether it would be reduced by using this new method, vis a vis the hazards of alternative methods such as a catheter. Not all members of the Committee were in agreement.

The question concerning the effects of high local dose during all high specific activity injections will be considered and reported on by the Radiation Safety subcommittee with respect to all such CIRCs. CIRC 128 was approved for annual recertification providing the consent form include the title of the CIRC.

CIRC 129 - "Changes in Exchangeable Sodium, Chlorine and Potassium in Patients with Chronic Renal Failure and Hypertension" - Annual recertification. Approved, providing consent 181 be modified for this particular CIRC to specify all elements being determined and the purpose of the procedure in laymen's terms.

CIRC 141 - "Measurement of Total-Body Nitrogen by Prompt-Gamma Neutron Activation Analysis" - Initial proposal. Approved for 24 normal subjects. Consent form should have a statement of purpose added.

CIRC 142 - "Testing Sensitivity of Leukemic Cells to Drugs" - Initial proposal. Approved as submitted.

CIRC 26 and 56. The Committee acknowledged receipt of Dr. Atkins 23 November 1976 memo and approves the use of subjects under both CIRCs.

The meeting adjourned at 1600.

Respectfully submitted,

Carole Kerr

Carole Kerr
Secretary

Minutes of the

BNL Human Studies Review Committee

13 July 1976

Present: A. Ansari, D. Borg, D. Christman, H. Connell, R. Doremus, R. Love, C. Meinhold, N. P. Rathvon, Jr.

Absent: I. Zanzi

Also Present: Alternates: U. Reincke, J. P. Stone
Secretary: S. McKenna

The meeting was held in the Large Conference Room of the Medical Research Center and called to order by Mr. Rathvon at 1400 hrs.

The minutes of the 11 May 1976 meeting were accepted as distributed.

The file on each of the following annual recertifications and modifications previously had been assigned to a certain member of the Committee for an in-depth review and recommendation to the Committee.

CIRC 32 "Polycythemia Vera Study Group" - Recertification was approved.

CIRC 94 "Administration of daunorubicin in patients with acute non-lympocytic leukemias" - Recertification was approved, subject to submission of a more informative consent form, which will be reviewed at the next meeting of the Committee.

CIRC 36D3 "In vivo activation analysis of patients with severe Cushing's Disease" - Recertification was approved provided that the consent form is made more understandable to a layperson. In this procedure, as in all others involving venipuncture, it was suggested that the following be used as standard language:

> "Whenever blood is removed or a substance is injected by venipuncture, there is minor discomfort and a slight possibility of local bleeding into the tissues."

CIRC 74 "Growth and differentiation of bone marrow and blood cells of normal human beings, pts. with acute and chronic leukemias, polycythemia vera, myelofibrosis, aplastic and hypoplastic states of the bone marrow, and drug induced abnormalities of bone marrow function" - Recertification was approved. The Chairman will convey to the principal investigator the consensus of the Committee that the statements in the consent form might well be limited to facts necessary for a reasonable person to make an informed decision. Paragraphs 1 and 2 could be replaced with the language in the consent form for volunteers; the danger discussed in paragraph 6 is unrealistic; and the danger discussed in paragraph 7 is trivial.

CIRC 84 "Vitamin C (Ascorbic Acid) Metabolism in Scorbutic Patients with Hemosiderosis" - Recertification was approved.

CIRC 103 "Osteoporosis in Rheumatoid Arthritis (RA)" - Recertification was approved provided the following sentence is inserted at the beginning of paragraph 2 of the consent form: "The isotope will be injected using methods to assure intravenous flow."

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: Nov. 23, 1976

TO: HSRC and PCEC

FROM: H.L. Atkins

SUBJECT: CIRC 26R and 56

This is to inform you that we intend to use the same subjects in CIRC 26R and 56. The procedures are as outlined in these CIRC's with no change. This memo is to keep you informed of this fact and that the radiation dose is well below the limits as set by the guidelines of the FDA (per minutes of HSRC, 4/13/76).

jf

CIRC 118 "Evaluation of ^{123}I-orthoiodohippurate (^{123}I-OIH)" - Recertification was neither approved nor disapproved. The Committee requests current information on the stability of the compound to be used. The recap sheet should set forth the exclusion of pregnant women.

CIRC 26R "Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-SHA(Sn)." - Modification was approved on the condition that Consent #178 will be used in place of, or in addition to, the Union Carbide form.

CIRC 127 "Total Body Calcium in Patients Receiving Chronic Anti-convulsant Therapy" - Modification was approved.

Attachments 1, 2, and 3 to the notice of meeting were discussed by the Committee. The Committee noted that Dr. Zanzi is the sponsoring physician on CIRCs 103, 106, 108, 124, and 127.

Mr. Rathvon invited general discussion of HSRC procedures and recommendations for changes. Approval was expressed of the practice of assigning to a specific member the duty of an in-depth review of the complete file. New procedures should, however, be studied completely by all HSRC members. It was noted that the IND file contains additional relevant information and should also be made available for the review.

The next HSRC meeting will be held on Tuesday, 10 August 1976, at 1400 hrs. in the Large Conference Room.

The meeting was adjourned at 1545.

Respectfully submitted,

Shirley McKenna

Shirley McKenna
Secretary

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

CIRC No. 26

PURPOSE OF REVIEW:

☐ INITIAL ☐ ADDENDUM
☐ REVISION ☐ RECERTIFICATION
☐ REACTIVATION ☒ Modificati

CLINICAL INVESTIGATION AUTHORIZATION FORM

TITLE: Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-SHA(Sn).

TO CHAIRMAN, ~~CIRC~~ HSRC.

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

To use Union Carbide's product

E.P. Cronkite 7 July 76
E.P. CRONKITE, M.D., Chairman, Medical Deparment — Date

TO CHAIRMAN, MEDICAL DEPARTMENT:

THE ~~CIRC~~ HSRC REVIEWED THE ABOVE IDENTIFIED PROPOSAL ON July 13, 1976 AND RECOMMENDS Approval

WITH THE FOLLOWING MODIFICATIONS:

Approved on condition Consent form 178 be used either in lieu of or in addition to the U.C. form.

H. Reincke
U. Reincke, Alt.

N.P. Rathvon, Jr., Chairman	D.D. Joel, Alt.	C.W. Flood, Alt.
	R. Dorfman	
L.D. Hamilton (Alternate Chairman)	D.R. Christman	J.P. Stone, Alt.
H.R. Connell	C.B. Meinhold	G.A. Price, Alt.
	D.C. Borg	L. Owen, Alternate
A.N. Ansari		W. Shreeve, Alt.
R.A. Love	J.A. Laissue, Alternate	I. Zanzi

TO Drs. Atkins, Ansari, Klopper

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

Modification approved to include the phase III trial of Union Carbide's product under their IND 12026.

Consent #178 will be used in place of, or in addition to, the Union Carbide form.

1180069

E.P. Cronkite 8/10/76
E.P. CRONKITE, M.D., Chairman, Medical Department — Date

CIRC Form 1 7/25/75 cc: Dr. Chanana, J. Holder, A. Harrison, J. Matkovich and other investigators

Tolcher
HSRC
CBR 7/1/76

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: June 30, 1976

TO: HSRC

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

SUBJECT: CIRC 26

Please amend our CIRC 26 for ^{99m}Tc-labeled human serum albumin to include the phase III trial of Union Carbide's product under their IND #12,026. Enclosed is the requisite information from Union Carbide.

jf
enclosures

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
5500 FISHERS LANE
ROCKVILLE, MARYLAND 20852

STATEMENT OF INVESTIGATOR

Form Approved
OMB No. 57-R0029

TO: SUPPLIER OF DRUG (Name and address, include Zip Code)

Union Carbide Corporation
P. O. Box 324
Tuxedo, N.Y. 10987

NAME OF INVESTIGATOR (Print or Type)
Harold L. Atkins, M.D.

DATE
6-30-76

NAME OF DRUG
TECHNETIUM 99m HSA

Dear Sir:

The undersigned, _____, submits this statement as required by section 505(i) of the Federal Food, Drug, and Cosmetic Act and §130.3 of Title 21 of the Code of Federal Regulations as a condition for receiving and conducting clinical investigations with a new drug limited by Federal (or United States) law to investigational use.

1. STATEMENT OF EDUCATION AND EXPERIENCE

a. COLLEGES, UNIVERSITIES, AND MEDICAL OR OTHER PROFESSIONAL SCHOOLS ATTENDED, WITH DATES OF ATTENDANCE, DEGREES, AND DATES DEGREES WERE AWARDED

See attached curriculum vitae.

b. POSTGRADUATE MEDICAL OR OTHER PROFESSIONAL TRAINING (Indicate dates, names of institutions, and nature of training)

See attached curriculum vitae.

c. TEACHING OR RESEARCH EXPERIENCE (Indicate dates, institutions, and brief description of experience)

See attached curriculum vitae.

d. EXPERIENCE IN MEDICAL PRACTICE OR OTHER PROFESSIONAL EXPERIENCE (Indicate dates, institutional affiliations, nature of practice, or other professional experience)

See attached curriculum vitae

e. REPRESENTIVE LIST OF PERTINENT MEDICAL OR OTHER SCIENTIFIC PUBLICATIONS (Indicate titles of articles, names of publications and volume, page number, and date)

See attached curriculum vitae/bibliography

1180071

2a. If the investigation is to be conducted on institutionalized subjects or is conducted by an individual affiliated with an institution which agrees to assume responsibility for the study, assurance must be given that an institutional review committee is responsible for initial and continuing review and approval of the proposed clinical study. The membership must be comprised of sufficient members of varying background, that is, lawyers, clergymen, or laymen as well as scientists, to assure complete and adequate review of the research project. The membership must possess not only broad competence to comprehend the nature of the project, but also other competencies necessary to judge the acceptability of the project or activity in terms of institutional regulations, relevant law, standards of professional practice and community acceptance. Assurance must be presented that the investigator has not participated in the selection of committee members; that the review committee does not allow participation in its review and conclusions by any individual involved in the conduct of the research activity under review (except to provide information to the committee) that the investigator will report to the committee for review any emergent problems, serious adverse reactions, or proposed procedural changes which may affect the status of the investigation and that no such change will be made without committee approval except where necessary to eliminate apparent immediate hazards; that reviews of the study will be conducted by the review committee at intervals appropriate to the degree of risk, but not exceeding 1 year, to assure that the research project is being conducted in compliance with the committee's understanding and recommendations; that the review committee is provided all the information on the research project necessary for its complete review of the project; and that the review committee maintains adequate documentation of its activities and develops adequate procedures for reporting its findings to the institution. The documents maintained by the committee are to include the names and qualifications of committee members, records of information provided to subjects in obtaining informed consent, committee discussion on substantive issues and their resolution, committee recommendations, and dated reports of successive reviews as they are performed. Copies of all documents are to be retained for a period of 3 years past the completion or discontinuance of the study and are to be made available upon request to duly authorized representatives of the Food and Drug Administration. (Favorable recommendations by the committee are subject to further appropriate review and rejection by institution officials. Unfavorable recommendations, restrictions, or conditions may not be overruled by the institution officials.) Procedures for the organization and operation of institutional review committees are contained in guidelines issued pursuant to Chapter 1-40 of the Grants Administration Manual of the U.S. Department of Health, Education, and Welfare, available from the U.S. Government Printing Office. It is recommended that these guidelines be followed in establishing institutional review committees and that the committees function according to the procedures described therein. A signing of the Form FD 1573 will be regarded as providing the above necessary assurances; however, if the institution has on file with the Department of Health, Education, and Welfare, Division of Research Grants, National Institutes of Health, an "accepted general assurance," and the same committee is to review the proposed study using the same procedures, this is acceptable in lieu of the above assurances and a statement to this effect should be provided with the signed FD 1573. (In addition to sponsor's continuing responsibility to monitor the study, the Food and Drug Administration will undertake investigations in institutions periodically to determine whether the committees are operating in accord with the assurances given by the sponsor.)

b. A description of any clinical laboratory facilities that will be used. (If this information has been submitted to the sponsor and reported by him on Form FD 1571, reference to the previous submission will be adequate).

3. OUTLINE THE PLAN OF INVESTIGATION *(Include approximation of the number of subjects to be treated with the drug and the number to be employed as controls, if any; clinical uses to be investigated; characteristics of subjects by age, sex and condition; the kind of clinical observations and laboratory tests to be undertaken prior to, during, and after administration of the drug; the estimated duration of the investigation; and a description or copies of report forms to be used to maintain an adequate record of the observations and tests results obtained. This plan may include reasonable alternates and variations and should be supplemented or amended when any significant change in direction or scope of the investigation is undertaken.)*

As per protocol supplied by Union Carbide.

1180072

a. The sponsor is required to supply the stigator with full information concerning the preclinical investigations that justify clinical trials, together with fully informative material describing any prior investigations and experience and any possible hazards, contraindications, side-effects, and precautions to be taken into account in the course of the investigation.

b. The investigator is required to maintain adequate records of the disposition of all receipts of the drug, including dates, quantities, and use by subjects, and if the investigation is terminated to return to the sponsor any unused supply of the drug.

c. The investigator is required to prepare and maintain adequate and accurate case histories designed to record all observations and other data pertinent to the investigation on each individual treated with the drug or employed as a control in the investigation.

d. The investigator is required to furnish his reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained by various investigators. The sponsor is required to present progress reports to the Food and Drug Administration at appropriate intervals not exceeding 1 year. Any adverse effect that may reasonably be regarded as caused by, or probably caused by, the new drug shall be reported to the sponsor promptly, and if the adverse effect is alarming, it shall be reported immediately. An adequate report of the investigation should be furnished to the sponsor shortly after completion of the investigation.

e. The investigator shall maintain the records of disposition of the drug and the case histories described above for a period of 2 years following the date a new-drug application is approved for the drug; or if the application is not approved, until 2 years after the investigation is discontinued. Upon request of a scientifically trained and properly auth... zed employee of the Department, at reasonable times, the investigator will make such records available for inspection and copying. The subjects' names need not be divulged unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual cases studied, or do not represent actual results obtained.

f. The investigator certifies that the drug will be administered only to subjects under his personal supervision or under the supervision of the following investigators responsible to him,

_____

_____

_____

and that the drug will not be supplied to any other investigator or to any clinic for administration to subjects.

g. The investigator certifies that he will inform any subjects, including subjects used as controls, or their representatives, that drugs are being used for investigational purposes, and will obtain the consent of the subjects, or their representatives, except where this is not feasible or, in the investigator's professional judgement, is contrary to the best interests of the subjects.

h. The investigator is required to assure the sponsor that for investigations involving institutionalized subjects, the studies will not be initiated until the institutional review committee has reviewed and approved the study. (The organization and procedure requirements for such a committee should be explained to the investigator by the sponsor as set forth in form FD 1571, division 10, unit c.)

Very truly yours,

Harold L. Atkins

(Name of investigator)

Brookhaven National Laboratory

(Address)

Upton, New York 11973

(This form should be supplemented or amended from time to time if new subjects are added or if significant changes are made in the plan of investigation.)

1180073

UNION CARBIDE CORPORATION
P. O. BOX 324, TUXEDO, NEW YORK 10987
TELEPHONE: 914-351-2131

CLINICAL DIAGNOSTICS

June 21, 1976

Dr. Harold L. Atkins
Brookhaven National Laboratory
Upton, L.I., New York 11973

Dear Dr. Atkins:

We appreciate your interest in TECHNETIUM 99m HSA. The following information about our product is provided for your review:

1. Package Insert.
2. Summary of Initial Clinical Trials.
3. Protocol for Phase III Clinical Trials of TECHNETIUM 99m HSA.
4. Statement of Investigator, Form 1573.
5. Examples of Clinical Report Forms.
6. Examples of Patient Consent Forms.

Our TECHNETIUM 99m HSA is currently in the extended clinical trial period (Phase III) under IND #12,026.

After appropriate in-house review of the enclosed information, the enclosed Statement of Investigator, Form 1573, should be completed and one copy returned to us. If you do not have your "Curriculum Vitae" filed at Union Carbide, please send one to us or complete Item 1 (Statement of Education and Experience) on the first page of the form. Complete Item 4.f., sign your name and address on the second page, and send the form to us. Save a copy of the completed form for your files.

Investigators may order TECHNETIUM 99m HSA by calling collect (914-351-2131, Exts. 328 or 333).

Sincerely yours,

Kathleen Jensen

Kathleen Jensen
Drug Regulatory Affairs

KJ:sk
Encls.

1180074

TECHNETIUM 99m HSA

(TECHNET[illegible]1 Tc 99m SERUM ALBUMIN (HUMAN)[illegible]T)

DIAGNOSTIC - FOR INTRAVENOUS USE

DESCRIPTION: The kit consists of 5 reaction vials each containing 21 mg Human Serum Albumin (HSA) and 0.23 mg stannous tartrate, HCl added for pH adjustment. All components are sterile and pyrogen free. When a solution of sterile and pyrogen free Sodium Pertechnetate Tc 99m in isotonic saline is mixed with these components following the instructions provided with the kit, Technetium Tc 99m Serum Albumin (Human) is formed. The product so derived is intended for intravenous injection. The precise structure of Technetium Tc 99m Serum Albumin is not known at this time.

The Serum Albumin (Human) in this preparation was supplied by a manufacturer licensed to do so by the U.S. Food and Drug Administration. The lot tested negative for hepatitis associated (Australia) antigen and was released by the F.D.A. for use.

Physical Characteristics: Technetium ^{99m}Tc decays by isomeric transition with a physical half-life of 6.03 hours(1). Photons that are useful for detection and imaging studies are listed in Table I.

TABLE I: PRINCIPAL RADIATION EMISSION DATA

Radiation	Mean % Disintegration	Mean Energy (keV)
Gamma-2	87.9	140.5

External Radiation: The specific gamma ray constant for ^{99m}Tc is 0.8 R/mCi-hr. at 1 cm. The first half value thickness of lead (Pb) for ^{99m}Tc is 0.2 mm. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb is shown in Table II. For example, the use of 2.7 mm of Pb will decrease the external radiation exposure by a factor of 1,000.

TABLE II: RADIATION ATTENUATION BY LEAD SHIELDING

Shield Thickness (Pb) mm	Coefficient of Attenuation
0.2	0.5
0.95	10^{-1}
1.8	10^{-2}
2.7	10^{-3}
3.6	10^{-4}
4.5	10^{-5}

To correct for physical decay of this radionuclide, the fractions that remain at selected intervals relative to the time of calibration are shown in Table III.

TABLE III: PHYSICAL DECAY CHART: ^{99m}Tc, HALF-LIFE 6.03 HOURS

Hours	Fraction Remaining	Hours	Fraction Remaining
-5	1.777	5	.563
-4	1.584	6	.502
-3	1.412	7	.447
-2	1.259	8	.399
-1	1.122	9	.355
0*	1.000	10	.317
1	.891	11	.282
2	.795	12	.252
3	.708	18	.126
4	.631	24	.063

*Calibration Time

(1) Dillman, L.T. and Von der Lage, F.C., Radionuclide Decay Schemes and Nuclear Parameters for Use in Radiation-Dose Estimation, MIRD Pamphlet No. 10, p. 62, 1975.

1180075

CLINICAL PHARMACOLOGY: Human serum albumin, being a normal component of blood, leaves the vascular space at a rate slow enough to permit imaging procedures utilizing radioactive tags. Technetium Tc 99m Serum Albumin does not rapidly leak from the vascular space, nor is there significant accumulation in organs other than those of excretion, the kidney and bladder. Therefore, the vascular system may be imaged with a minimum of background and organ interference. In humans, a two component blood clearance rate is observed, the T 1/2 slow component ranging from 10 to 16 hours. Twenty-four hour urine clearance averaged 39%.

INDICATIONS AND USAGE: Technetium Tc 99m Serum Albumin is used as an agent for imaging the heart blood pool, to assist in the detection of pericardial effusion and ventricular aneurysm, and for determining cardiac ejection fraction.

CONTRAINDICATIONS: None known.

WARNINGS: The contents of the kit are not radioactive. However, after the Sodium Pertechnetate Tc 99m is added, adequate shielding of the final preparation must be maintained.

This radiopharmaceutical preparation should not be administered to children or to patients who are pregnant or to nursing mothers unless the expected benefits to be gain outweigh the potential hazards.

Ideally, examinations using radiopharmaceuticals, especially those elective in nature, of women of childbearing capability should be performed during the first few (approximately 10) days following the onset of menses.

PRECAUTIONS: The components of the kit are sterile and pyrogen-free. It is essential that the user follows the directions carefully and adheres to strict aseptic procedures during preparation of the radiodiagnostic.

Technetium Tc 99m Serum Albumin must not be used after three hours from the time of formulation.

Adequate reproduction studies have not been performed in animals to determine whether this drug affects fertility in males or females, has teratogenic potential, or has other adverse effects on the fetus. Technetium Tc 99m Serum Albumin should be used in pregnant women only when clearly needed.

It is not known whether this drug is excreted in human milk. As a general rule, nursing should not be undertaken while a patient is on a drug since many drugs are excreted in human milk.

Safety and effectiveness in children have not been established.

Technetium Tc 99m Serum Albumin, as well as other radioactive drugs, must be handled with care and appropriate safety measures should be used to minimize external radiation exposure to clinical personnel. Also, care should be taken to minimize radiation exposure to patients consistent with proper patient management.

ADVERSE REACTIONS: None known.

DOSAGE AND ADMINISTRATION: The suggested intravenous dose used in the average patient (70 kg) is 3-5 mCi for cardiac blood pool and 10-20 mCi for cardiac ejection fraction.

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

Radiopharmaceuticals should be used only by physicians who are qualified by specific training in the safe use and handling of radionuclides produced by nuclear reactor or particle accelerator and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

Preparation: The following directions must be carefully followed for optimum preparation of the Technetium Tc 99m Serum Albumin (Human). 1. Aseptically swab rubber septum of sterile vial containing the sterile, lyophilized HSA. 2. Aseptically inject 1.0 ml of sterile Water for Injection, withdraw an equal volume of air. 3. Mix contents by swirling until all the material is suspended. 4. Place vial in shield provided. 5. Aseptically swab rubber septum of shielded vial. 6. Aseptically inject up to 100 mCi Sodium Pertechnetate Tc 99m in a maximum of 3 ml into the vial, withdraw an equal volume of air. 7. Mix contents of vial by gentle shaking for 10 seconds. 8. Affix pressure-sensitive label to shielded vial. 9. Allow to stand for 20 minutes after

mixing to allow maximum tagging. 10. The TECHNETIUM 99m HSA is ready for use. 11. Mix contents of vial ep 7) prior to withdrawing pa nt dose. 12. Mix contents of syringe by repeated inversion immediately prior to injection. 13. Maintain adequate shielding of the radioactive preparation. 14. Do not use the preparation after 3 hours from the time of formulation. 15. The radioactivity concentration of the final Technetium Tc 99m Serum Albumin (Human) preparation may be calculated by using the following: C = A/V where C equals radioactivity concentration of the preparation (millicuries/ml). A = Tc 99m activity added to the reaction mixture vessel (millicuries). V = Total volume in the final mixture (ml).

Radiation Dosimetry: The estimated absorbed radiation doses[1] to an average patie (70 kg) from an intravenous injection of a maximum dose of 5 millicuries of Technetium Tc 99m Serum Albumin are shown in Table IV.

TABLE IV: ESTIMATED ABSORBED DOSE

Tissue	Absorbed Radiation Dose (rads/5 mCi)
Brain	0.047
Marrow	0.076
Kidneys	0.063
Bladder	0.166
Ovaries	0.082
Testes	0.079
Total Body	0.073

HOW SUPPLIED:

Kit Contents: 5 STERILE REACTION VIALS (10 cc, Silver Aluminum Overseal), each containing 21 mg Human Serum Albumin (HSA) and 0.23 mg stannous tartrate, lyophilized. 1 RADIATION SHIELD for preparation and storage of a Technetium Tc 99m Serum Albumin preparation. 10 PRESSURE SENSITIVE LABELS for final Technetium Tc 99m Serum Albumin preparation. 1 PACKAGE INSERT.

Storage: Store kit contents in refrigerator (2-8°C). Do not freeze.

Disposal: The residual materials may be discarded in ordinary trash provided the vials and syringes read background with an appropriate low range survey meter. It is suggested that all identifying labels be destroyed before discarding.

(1) A Schema for Absorbed-Dose Calculations for Biologically Distributed Radionuclides, Supplement No. 1, MIRD pamphlet No. 1, J. Nucl. Med., p. 7, 1968.

FOR ORDERING OR TECHNICAL INFORMATION,
CONTACT MANUFACTURER:

Clinical Diagnostics
UNION CARBIDE CORPORATION, Rye, N. Y. 10580
Telephone (914) 967-7800

CintiChem™

TECHNETIUM 99m HSA
TECHNETIUM Tc 99m SERUM ALBUMIN (HUMAN) KIT

This reagent kit is approved for use by persons licensed by the U.S. Nuclear Regulatory Commission pursuant to Sec. 35. 14 and Sec. 35. 100 Group III of 10 CFR Part 35 or under equivalent licenses of Agreement States.

June, 1976 Printed in U.S.A.
L-308-1

1180078

PHASE I CLINICAL STUDIES

TECHNETIUM 99m HSA was administered to 2 normal volunteers each at Milwaukee County General Hospital and Johns Hopkins Medical Institutions, according to the protocol supplied in BB-IND 832. The following is a summary of the findings:

Vital Signs - Unchanged.
Blood Chemistry - Unchanged.
Urinalysis - Unchanged.
Adverse Reactions - None.
Quality of Image - Good.

a) Hopkins - "The radiopharmaceutical performed satisfactorily and permitted determination of cardiac ejection fraction and brain scanning."

b) Milwaukee - "The quality of the image is satisfactory for interpretation."

Blood Clearance (T 1/2 slow component) - 10-16 hours.
Urine Clearance - 39% avg. in 24 hours.

The clinical report forms and raw data are attached. Copies of the scans from Milwaukee were lost in-hospital and therefore are missing from this report.

TABULATIONS - PHASE II HOPKINS STUDY

Male - 12

Female - 3

Age:

- 20-29 - 2
- 30-39 - 1
- 40-49 - 4
- 50-59 - 5
- 60-69 - 2
- Over 70 - 1

Diagnosis:

- Pericardial effusion - 1
- Myocardial infarction - 7
- Ventricular hypertrophy - 4
- By-pass follow-up - 1
- Dilatation - 1
- Normal - 1

Confirmation of diagnosis - 15

Adverse reactions - 0

False positives - 1 possible, see case 15

False negatives - 0

Scan quality (1-5, 5 being best):

- 1 - 0
- 2 - 0
- 3 - 0
- 4 - 0
- 5 - 15

PHASE II CLINICALS

A. JOHNS HOPKINS MEDICAL INSTITUTIONS

Fifteen patients received TECHNETIUM 99m HSA for blood pool/cardiac ejection/heart imaging. The quality of image was excellent in all cases, no adverse reactions were noted, and no confirmed false positives or negatives encountered. The following is a summary of the findings:

Case	Data	Age	Sex	Initial Diagnosis	Scan Diagnosis	Confirmation
1	3/8/75	27	F	Pericardial Effusion	P.E.	Yes - echo-cardiogram
2	3/12	55	M	Myocardial Infarction	M.I.	Yes - surgery
3	3/13	63	M	M.I.	M.I.	Yes - EKG, ^{201}Tl
4	3/18	61	M	Prosthetic valve follow-up	Left ventric-ular hyper-trophy	Yes - expected
5	4/25	49	M	M.I.	M.I.	Yes - EKG, CPK
6	4/25	51	M	M.I.	M.I.	Yes - EKG, CPK, history
7	4/29	44	M	Post coronary by-pass	Regions of hyperkinesis	Yes - history
8	4/29	53	M	M.I. follow-up	Old M.I.'s	Yes - history
9	4/29	40	M	Chest pain	Normal	Yes - catheteriza-tion
10	4/29	50	F	Hypertrophy	Hypertrophy	Yes - EKG
11	4/30	47	M	R/O M.I.	M.I.	Yes - ^{201}Tl, pyro-phosphate
12	4/30	70	F	Polymyosites with dilatation	Dilatation	Yes - history
13	4/30	33	M	M.I.	M.I.	Yes - catheteriza-tion
14	5/1	54	M	Aortic stenosis	Severe ventricular hypertrophy	Yes - surgery
15	5/1	28	M	Sarcoidosis	Gross ventricular hypertrophy	Yes - ^{201}Tl

PHASE II CLINICALS

B. MILWAUKEE COUNTY GENERAL HOSPITAL

Four patients received TECHNETIUM 99m HSA, one for brain imaging and three for cardiac imaging. In all cases the quality of the image was excellent, no adverse reactions were observed, nor were false positives or negatives encountered.

Case	Date	Age	Sex	Initial Diagnosis	Scan Diagnosis	Confirmation
16	4/18/75	25	F	Post-op kidney transplant	Dilatation and pericardial effusion	No
17	4/18/75	13	F	Cardiomegaly	Dilatation	Yes - X-ray
18	4/30/75	60	F	Post-op craniotomy	Abscess	Yes - ^{99m}Tc-DTPA
19	6/5/75	64	F	Congestive heart failure	Dilatation and pericardial effusion	Yes - autopsy

Tabulations:

Male - 0

Female - 4

Age:

Under 18 - 1

20-29 - 1

60-69 - 2

Diagnosis:

Dilatation and pericardial effusion - 2

Dilatation - 1

Cranial abscess - 1

Confirmation of diagnosis - 3

Adverse reactions - 0

False positives and negatives - 0

Scan quality (1-5, 5 being best):

5 - 3

4.5 - 1

PHASE III

1. TITLE: Phase III Clinical Trials with TECHNETIUM 99m HSA.

2. PURPOSE: As in Phase II, the ability of the drug to provide quality cardiac blood pool imaging and cardiac ejection fraction data that will aid in diagnosis will be the criteria. Possible false positives or negatives are to be explained fully.

3. METHOD: A. Selection of Study Subjects:

The drug will be used in place of the hospital's normal cardiac blood pool imaging preparation for no longer than 6 months. During this time it is estimated that a total of about 100 patients will receive the drug. All should require imaging as an aid to diagnosis. The only age and sex restrictions will be those stated in the warning section of the Informational Material. Patient consent will be obtained (see Consent Form which is attached to this protocol).

B. Product Information:

1) Chemical: Sodium pertechnetate ^{99m}Tc is reduced with stannous tartrate and bound to the Human Serum Albumin molecule.

2) How Supplied: Each vial contains:
21.0 mg Human Serum Albumin,
0.23 mg Stannous Tartrate.

3) Recommended mCi Dose: Cardiac Blood pool: 3-5 mCi
Cardiac Ejection Fraction: 10-20 mCi

4) Route of Administration: IV.

5) Imaging: Selective cardiac imaging to be performed immediately post injection.

4. RECORDING AND PROCESSING DATA:

All required data will be recorded on case report forms supplied to the investigator by the Drug Regulatory Department of Union Carbide. For each evaluation period and for each patient, all completed case report forms, signed and dated by the investigator, will be forwarded to the Clinical Monitor at Union Carbide Corporation, Drug Regulatory, Tuxedo, N.Y. 10987 within one week after the evaluation is completed. A reasonalble explanation must be given under "COMMENTS" for all required data or other information that is missing from any case report form submitted.

All numerical data and information required on all the case report forms will be recorded in type or legibly printed in black ink for ease of duplication, interpretation, and data processing.

Representative scans are requested to be submitted.

5. ADVERSE REACTIONS:

Any laboratory test reported to have an abnormal value, other than those associated with the patient's specific disease state, and that is considered to be clinically significant by the investigator must be repeated within 48 hours to rule out lab error. In tests where there is persistent abnormality, repeat analysis will be performed at intervals appropriate to the abnormality until the cause is determined or return to normalcy occurs. The question of the relationship of the adverse reaction to the drug administration will be determined by the investigator after thorough consideration of all the facts that are available to him. Significant and serious adverse reactions will be reported to Union Carbide's Drug Regulatory Department immediately by telephone (914-351-2131, Exts. 315 or 391) and subsequently in writing within 5 days of the occurrence.

6. STATISTICAL STATEMENT:

The data obtained during the course of this clinical study will be subjected to a statistical analysis by the Sponsor.

Within one month after receiving the statistical report from Union Carbide, the investigator will submit a written, final summary. This may be as brief or lengthy as desired. However, we suggest that it includes the standard sections: Objectives, Materials and Methods, Results, Discussion and Conclusions.

7. SPECIAL NOTES:

A. Alterations of the Protocol

No alterations or changes in this protocol will be permitted without the written approval of Mr. A. E. Westerfield or Miss K. Jensen of Drug Regulatory, Union Carbide.

B. Disclosure

All information provided to the investigator dealing with the investigational drug, will be regarded as confidential. The members of the Research Team agree not to disclose such information in any way without prior written permission from Union Carbide.

C. Monitoring

This study will be monitored by UCC Drug Regulatory at all stages of its development, from inception to its conclusion. This monitoring may be in the form of personal visits if necessary and communications (letter, telephone) to assure that the investigation is carried out according to the protocol design and specifications.

PROTOCOL REVIEW COMMITTEE

This protocol will, if approved, be submitted to a proper Institutional Review Committee, as required by the Code of Federal Regulations, for initial approval and proper follow-up.

I understand that I have been asked to participate in a study that involves my receiving an investigational and radioactive drug. Before giving my consent by signing this form I have been sufficiently informed of the purpose of this study, of the nature of the drug and radiation exposure that I will receive, of the possible beneficial effects, of the methods, and the means and duration of administration of the drug, of the inconveniences, hazards, or adverse effects that might result from use of the drug, and of the alternatives to this course of diagnosis.

In giving my consent, I acknowledge that my participation in this research project is voluntary and that I may withdraw at any time.

_____
Investigational Drug

_____
Protocol Number

_____
Patient Signature

_____
Date

_____
Witness

_____
Date

CintiChem

TECHNETIUM 99m HSA

HOSPITAL_____ INVESTIGATOR_____ DATE OF INJECTION:_____

Lot No._____ Amount Injected: Activity_____mCi Volume_____ml Concentration_____mCi/ml

PATIENT Initials or Name_____ Hospital Admission #_____

Age_____ Sex_____

INITIAL CLINICAL DIAGNOSIS_____

Symptoms:_____

_____

CLINICAL DATA:

Time following scan, patient observed_____hours, _____days.

IMAGE INFORMATION: Camera_____ Rectilinear_____ Quality of Image_____ (1 to 5 5 being best)

Clinical Diagnosis as a Result of Image:_____

_____

_____

_____

ADVERSE REACTIONS: None_____ Serious_____ Slight_____

Explain any reactions_____

_____

_____

Was reaction due to the radiodiagnostic_____Yes _____No

(If Yes, explain)_____

_____

Time of reaction following injection_____ Time of duration of reaction_____

SUMMARY STATEMENT (including confirming data of other departments if possible):_____

_____

_____

_____

_____

_____

Signed:_____ Date:_____

1180086

CIRC 26R

Minutes
of the
BNL Human Studies Review Committee

13 April 1976

Present: N.P. Rathvon, Jr., D.C. Borg, D.R. Christman, H.R. Connell, R.A. Love, C.B. Meinhold, I. Zanzi

Absent: R. Doremus

Also present: Alternates - W.W. Shreeve
Others - J. Holder, C. Kerr

The meeting was held in the Large Conference Room of the Medical Research Center and called to order by Mr. Rathvon at 1400 hrs.

The minutes of the previous meeting, 10 February 1976 were accepted as distributed.

CIRC 109, "^{201}Thallium as Thallous Chloride in Sodium Chloride for Myocardial Visualization", approved 3/24/76 at an unconvened meeting of the Committee was noted for the record. The annual recertification was approved with a revised investigational consent #176 (replacing 111) by Dr. Cronkite on 3/25/76.

The Committee acknowledged for the record the letter from Dr. Chalkley to Dr. Vineyard stating that the Laboratory's General Assurance has been approved by the DHEW.

Many of the proposals submitted to the Committee for recertification at this meeting warranted a complete review of the original protocol, addendums, revisions, etc. Mr. Rathvon stated that in order to speed up the process of approval, he had asked various members for their help and assigned to them the task of reviewing the files of certain proposals prior to the meeting. The Committee agreed that this seemed to be a worthwhile method of proceding.

There followed extensive discussion of the possible total radiation exposure of a research patient from all procedures including the various diagnostic studies routinely prescribed on admission and participation in other studies as a volunteer. The view was expressed that the Committee should establish guidelines and a radiation limit. It was the consensus that: a) each proposal hereafter submitted contain an estimate of the total radiation the patient would be given in the planned program; b) the Committee should request the Medical Staff to reconsider its previous decision to discontinue the radiation exposure summary for each patient; c) the radiation limits of the FDA set forth in the Federal Register, Vol. 40, No. 144, Section 361.1, page 31309 should be observed; and d) the Patient Care Evaluation Committee should be requested to determine if excessive use was being made of patients as volunteers in other programs.

Investigational consent 147, "Extracorporeal Irradiation of Blood" was reviewed as requested in Dr. Cronkite's memo dated 2/4/76 to the Committee. Approval was granted to change the consent. Investigational consent 182 will now be used on CIRC's 18R and 122 replacing consent 147.

CIRC 62, "Medical Studies of Marshallese People Accidentally Exposed to Radioactive Fallout in 1954"; CIRC 110, "Studies of Antigen - Induced Mechanisms in Human Lymphocytes"; and CIRC 113, "Labeling of Blood Elements with Radioactive Nuclides" were reviewed and recertification was approved.

CIRC 70, "Detection of Impaired Pulmonary Function with Mass-Spectrographic Tracer Technique" was reviewed and approved for recertification with the following change on the consent form #62: "The specific study in which I shall participate is "Measurement of Respiratory Dynamics (breathing motions) Using Helium" be changed to "The specific study in which I shall participate is "Measurement of Respiratory Dynamics (breathing functions) Using Helium" and also provide a signature of a witness. Revised investigational consent 177 will be used to replace #62.

CIRC 36G and 96R - Addendum and Recertification: The addendum was approved for both CIRC's. Because of the amount of procedures and changes requested on both of these CIRC's, the Committee did not approve the annual recertification. HSRC is requesting that both CIRC's be resubmitted as originals when they are due for annual recertification.

CIRC 105, "Study of the Effects of Thiazide on Essential Hypertension". An addendum was submitted and approved.

CIRC 10A, "Studies of Calcium Kinetics" was forwarded for revision and annual recertification originally at the 2/10/76 meeting when the Committee decided to defer action awaiting additional information. This data was supplied and approval was granted after changes were made on the consent #74. The new consent is #175.

CIRC 135 - Initial proposal entitled "Chromosomal Aberrations in Genetic Diseases" was approved.

CIRC 42, "^{18}F Bone Scanning" was submitted for annual recertification. Approval was given subject to revision of the consent form to include a) a statement of the procedure in language the patient can understand, and b) a description of hazards of the intravenous injection.

CIRC 15R, "Clinical Use of ^{99m}Tc Sulfur Colloid" was submitted for annual recertification and approved with the recommendation that both consent forms #179 and 180 be revised to include the following statement: "This procedure will result in a radiation dose of one fifth of the dose permitted occupational workers each year". Investigational consent #179 (replacing 87) and 180 (replacing 69) are to be used on this CIRC. The Committee also reviewed the waiver given to minors and agreed to continue it.

CIRC 26R, "Technetium 99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-SHA(sn)" presented for annual recertification was approved with the understanding that the following statement be added to the new consent form to be numbered 178 replacing 72: "The radiation dose is of the same magnitude as the radiation dose received by tissues in many standard diagnostic procedures. The radiation dose received in this procedure is approximately one tenth of the dose permitted occupational radiation workers".

CIRC 63R, "Evaluation of Iodine-123 as Sodium Iodide" was approved for annual recertification provided that a statement be included in the present consent form #114 concerning the hazards of intravenous injection. Once again the Committee reviewed the waiver given to minors and agreed to continue it.

CIRC 95, "Indium-111 for Marrow Imaging" was forwarded to the Committee for annual recertification. The Chairman had asked Dr. Zanzi to review the complete CIRC file prior to the meeting. Dr. Zanzi reported that Dr. Atkins intends to inactivate this CIRC and therefore no action was taken.

CIRC 123, "Clinical and Metabolic Evaluation of the Response of Renal Osteodystrophy to the Treatment of Diet; 25 Hydroxycholecalciferol; 1-alpha Hydroxycalciferol and 1,25 Dihydroxycholecalciferol" presented for annual recertification of BNL's only participation in the study - TBNAA. The CIRC was approved with the recommendation that a statement of the procedure be added to the consent in language understandable to the patient. This revised consent will be numbered 181 and replaces 55.

The Committee noted with concern that procedures outside the Laboratory in CIRC 123 include the withdrawal of 216cc of blood over a 24 hour period and 100cc over the next 2 days totaling 316cc in a 72 hour period taken from sick patients. Mr. Rathvon will bring this to Dr. Atkins attention.

CIRC 136, "Evaluation: Human Calcitonin BA 47175 Treatment in Paget's Disease of Bone" is an initial proposal and was approved with the following stipulations: 1) Only TBNAA will be performed at BNL, 2) Consent form should be supplemented by inclusion of a statement of the procedure to be followed in language understandable to the patient, and 3) Answer to F3 on page 2 of 4 of the proposal should be corrected.

CIRC 108, "Glucagon in the Treatment of Paget's Disease of Bone" was approved for annual recertification with the following as a 3rd sentence in the first paragraph: "Since Glucagon is a protein, a hypersensitivity reaction is possible".

The next HSRC meeting will be held on Tuesday, May 11, 1976 at 1400 hrs. the Large Conference Room.

The meeting adjourned at 1630.

Respectfully submitted,

Carole Kerr

Carole Kerr
Executive Secretary

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

CIRC No. 26 Rev.

PURPOSE OF REVIEW:

CLINICAL INVESTIGATION AUTHORIZATION FORM

TITLE: Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-SHA(Sn).

☐ INITIAL ☐ ADDENDUM
☐ REVISION ☒ RECERTIFICATION
☐ REACTIVATION

TO CHAIRMAN, ~~CIRC~~ HSRC.

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 26 Feb 76
E.P. CRONKITE, M.D., Chairman, Medical Deparment Date

TO CHAIRMAN, MEDICAL DEPARTMENT:

THE ~~CIRC~~ HSRC REVIEWED THE ABOVE IDENTIFIED PROPOSAL ON 4/13/76 AND RECOMMENDS Approval

WITH THE FOLLOWING MODIFICATIONS:

Change the third sentence of the consent form to read:

The radiation dose is of the same magnitude as the radiation dose received by tissues in many standard diagnostic procedures. The radiation dose received in this procedure is approximately one-tenth of the dose permitted occupational radiation workers each year

N.P. Rathvon, Jr., Chairman
L.D. Hamilton (Alternate Chairman)
H.R. Connell
A.N. Ansari
R.A. Love

D.D. Joel, Alt.
R. Doremus
D.R. Christman
C.B. Meinhold
D.C. Borg
J.A. Laissue, Alternate

U. Reincke, Alt.
C.W. Flood, Alt.
J.P. Stone, Alt.
G.A. Price, Alt.
L. Owen Alternate
W. Shreeve, Alt.
I. Zanzi

TO Drs. Atkins, Ansari & Klopper,

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

Revised investigational consent #178 (replacing #72) is to be used on this CIRC.

E.P. Cronkite 16 April 76
E.P. CRONKITE, M.D., Chairman, Medical Department Date

1180090

CIRC Form I 7/25/75 cc: Above investigators, Dr. Chanana, A. Harrison, J. Holder, J. Matkovich, Clinic

Form 1926B

CIRC 26 Rev.
RECAP SHEET as
of ~~2/9/76~~
2/24/76

TITLE: Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-SHA(Sn).

Spon. Phys.: H.L. Atkins
Prin.Invest.: H.L. Atkins
A. Anaani
J. Klopper

APPROVALS	
HSRC	DEPT.
Initial	
11/8/71	11/9/71
Recertification	
12/12/72	12/19/72
Recertification	
1/14/74	1/15/74
Recertification	
2/7/75	2/11/75
Recertification	

Investigational Consent: ~~72~~ New form submitted

IND#12000 - ^{99m}Tc-HSA(Sn) - Annual Report due
~~April 1976~~ 2/77

Pts. studied
1971-1972 - 1 pt.
1972-1973 - 29 pts.
1973-1975 - 0 pts.
1975-1976 - 0 pts

Purpose: To delineate blood pools such as heart aneurysms in pts. in whom this is clinically indicated. No specific research program is intended. This is to support other clinical programs in the hospital.

1180091

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

CIRC STATUS MEMO

CIRC No. 26 Rev.

Title: Technetium-99m Labeled Human Serum Albumin (produced by the stannous ion method): ^{99m}Tc-SHA(Sn).

To: Dr. Atkins Date: 2/9/76

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 2/20/76, approval of the proposal will automatically be discontinued.

RECAP SHEET ATTACHED

PLEASE REVISE CONSENT ON NEW FORM

R B Aronson Feb. 9, 76
R.B. Aronson, Ph.D., Associate Chairman Date

To R.B. Aronson,

CIRC PROPOSAL NUMBER 26 Rev IS: Continuing ☒ Inactive ☐

Proposed substantive changes are attached none

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

none

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

The Sponsoring Physician as of this date is A L Atkins

The following changes in Investigators should be noted: Include A Aussie, J. Klopper

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

Compound ^{99m}Tc HSA IND# 12 022 Compound _____ IND# _____

The investigational consent form(s) used in this project are numbered 72 and copies are attached.

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

0

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

Signed Harold L. Atkins 2/13/76
Principal Investigator Date

A L Atkins 2/13/76
Sponsoring Physician Date

1180092

Form 1970.A

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

CONSENT FOR PROCEDURE, STUDY, OR
DRUG UNDER CLINICAL INVESTIGATION

PAV. _____

O.P. _____

I.M. _____

I understand that research patients of the Hospital of the Medical Research Center, Brookhaven National Laboratory, are asked to participate in procedures and studies not established as current medical practice but which are undertaken to discover and evaluate new methods of diagnosis and treatment of certain diseases and to study the nature of a disease, or the effectiveness of current methods of treatment, in the hope that a better understanding will lead to more effective control and even its eradication.

I understand that the procedure explained below 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 the study may not be revealed to me.

The following has been stated to me by Dr. .....:

Technetium-99m labeled human serum albumin is to be injected intravenously and scintiphotos obtained of its distribution in the body. No particular hazards or inconveniences are associated with its use. The radiation dose is similar to that incurred by having a chest x-ray. The chance of introducing an infection by the needle puncture is extremely rare. The examination is believed to be of some benefit to the patient in outlining the major blood vessels and heart blood pool for evaluation of vascular disease or possible impaired heart function. No non-experimental alternate method is availble at lesser risk.

I have been advised that if I wish a more detailed explanation of any of these matters it will be given. (If additional information is given, a summary should be attached.)

I understand I am free to withdraw my consent and discontinue participation in this activity at any time, without prejudice to me.

I have read the foregoing and hereby consent to participate in this procedure.

PATIENT'S NAME _____

SIGNED BY: _____
(Patient and, when necessary, Legal Guardian) (Date)

WITNESS: _____
(Date)

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 1913B

1180093

HOSPITAL OF THE MEDICAL RESEARCH CENTER,
BROOKHAVEN NATIONAL LABORATORY
Upton, New York 11973
-72-

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:

Radioactive ^{99m}Tc labeled human serum albumin for blood pool scanning

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. The system and components are checked periodically

Revised form submitted

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 _____

1180094

Form 1913 -72-

Minutes CIRC Meeting

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.

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

CIRC No.
26 Rev. 3/30/71

PURPOSE OF REVIEW:

CLINICAL INVESTIGATION AUTHORIZATION FORM

TITLE:
Technetium-99m labeled human serum albumin (produced by the Stannous ion method: ^{99m}Tc-HSA(Sn)

☐ 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.

ANNUAL RECERTIFICATION

E.P. Cronkite 10 Jan 75
E.P. CRONKITE, M.D., Chairman, Medical Deparment — Date

TO CHAIRMAN, MEDICAL DEPARTMENT:
THE CIRC REVIEWED THE ABOVE IDENTIFIED PROPOSAL ON 2/7/75 AND RECOMMENDS Approval
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 Dr. Atkins,

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

Investigational Consent #72 to be used on this CIRC.

E.P. Cronkite 11 Feb 75
E.P. CRONKITE, M.D., Chairman, Medical Department — Date

1180096

CIRC Form 1 7/1/74 2/11/75 cc: J. Holder, A. Harrison, Clinic and above

Form 19368

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

CIRC STATUS MEMO

CIRC No. 26 Rev. 3/30/71

Title: Technetium-99m labeled human serum albumin (produced by the stannous ion method: ^{99m}Tc-HSA(Sn)

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~~ Jan 20, 1974 RBA, approval of the proposal will automatically be discontinued.

Recap sheet attached

R.B. Aronson, Ph.D., Associate Chairman Date Dec 24, 74

To R.B. Aronson,

CIRC PROPOSAL NUMBER 26 IS: Continuing ☒ Inactive ☐

Proposed substantive changes are attached

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

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

The Sponsoring Physician as of this date is Harold 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 ^{99m}Tc-HSA(Sn) IND # D299 Compound IND #

The investigational consent form(s) used in this project are numbered 72 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

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

1180097

Form 1970A

HOSPITAL OF THE MEDICAL RESEARCH CENTER,
BROOKHAVEN NATIONAL LABORATORY
Upton, New York 11973
-72-

CONSENT FOR PROCEDURE, STUDY, OR
DRUG UNDER CLINICAL INVESTIGATION

NAME

UNIT NO

PAVILION OP

I understand that the physicians of 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 ^{99m}Tc labeled human serum albumin for blood pool scanning

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. The system and components are checked 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 _____

1180098

Form 1913 -72-

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

CIRC No. 26 Rev. 3/3c/71

PURPOSE OF REVIEW:

CLINICAL INVESTIGATION AUTHORIZATION FORM

TITLE:

Technetium-99m labeled human serum albumin (produced by the stannous ion method: ^{99m}Tc-HSA(Sn)

☐ 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 Deparment 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 R. Connell H.R. CONNELL
L.D. HAMILTON	P.S. PAPAVASILIOU	R.A. LOVE
G.A. PRICE	S.H. COHN, Alternate	U. REINCKE
D.N. SLATKIN, Alternate	A.P. WOLF, Alternate	

TO Dr. Atkins,

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

Investigational Consent #72 to be used on this CIRC.

E. P. Cronkite 15 Jan '74
E.P. CRONKITE, M.D., Chairman, Medical Department Date

CIRC Form 1 10/4/73 1180099
Form 1936B

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 $^{47}Ca\ Cl_2$, 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."

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

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

CIRC STATUS MEMO

CIRC No. 26

Title: Technetium-99m labeled human serum albumin(produced by the stannous ion method): ^{99m}Tc-HSA(Sn).

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 12/19/73
R.B. Aronson, Ph.D., Associate Chairman Date

To R.B. Aronson,

CIRC PROPOSAL NUMBER 26 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 29 patients have been submitted to the experimental regimen.

The Sponsoring Physician as of this date is Harold 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 ^{99m}Tc-HSA(Sn) IND# D2947 Compound _____ IND# _____

The investigational consent form(s) used in this project are numbered 72 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 12/1/73
Principal Investigator Date

H. L. Atkins 12/18/73
Sponsoring Physician Date

1180102

Form 1970A
CIRC Form 1 3/21/73

HOSPITAL OF THE MEDICAL RESEARCH CENTER,
BROOKHAVEN NATIONAL LABORATORY
Upton, New York 11973
-72-

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:

Radioactive ^{99m}Tc labeled human serum albumin for blood pool scanning

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. The system and components are checked 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 _____

1180103

Form 1913 -72-

To A. Harrison - Med Rec.

From E. Pen

SUBJECT Pt Consent # 42

DATE 12/19/72

MESSAGE

Please discontinue consent # 42 on CIRC 26. This has been replaced by consent # 72. A supply of the new consent form will be sent shortly.

SIGNED Carole

SIGNED

SENDER — A.P. WOLF, Alternate

TO H.L. Atkins

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

Consent # 72 to be used

E P Cronkite 19 Dec 72

1180104

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

CIRC Form 1 9/1/72

Form 1936A

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 ^{13}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 reactivation 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

HOSPITAL OF THE MEDICAL RESEARCH CENTER,
BROOKHAVEN NATIONAL LABORATORY
-72- 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:

Radioactive ^{99m}Tc labeled human serum albumin for blood pool scanning

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. The system and components are checked 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 _____

1180106

Form 1913 -72-

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.

1180107

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

CIRC No. 26

CIRC STATUS MEMO

Title: Technetium-99m labeled human serum albumin (produced by the stannous ion method): ^{99m}Tc-HSA (Sn).

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 26 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 1 patients have been submitted to the experimental regime.

The Sponsoring Physician as of this date is Harold 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 ^{99m}Tc-HSA(Sn) IND = DOS 299 Compound _____ IND = _____

The investigational consent form(s) used in this project are numbered 42 and copies are attached.

Signed Harold L. Atkins 11/7/72
Principle Investigator Date

Harold L. Atkins 11/7/72
Sponsoring Physician Date

1180108

Form 1970

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

NAME

UNIT NO.

-42-

CONSENT FOR PROCEDURE, STUDY, OR DRUG UNDER CLINICAL INVESTIGATION CIRC 26

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:

^{99m}Tc labeled human serum albumin for blood pool scanning

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.

New consent form attached

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 _____

1180109

Form 1913

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: Technetium - 99m labeled human serum albumin (produced by the stannous ion method): ^{99m}Tc - HSA (Sn).

CIRC# 26 (REVISED)
Assigned on (date) 3/30/71

To Chairman, CIRC,

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

Recertification by "Cotzias Committee" because of conflicts of interest at 6 April 71 meeting.

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 + 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. Colin	Edwin A. Popenoe E.A. Popenoe, Alternate	D. L. Love R.A. Love
Glenn D. Price G. Price	J.F. Klopper	N.P. Rathvon, Jr.
S.E. Duby, Alternate	A.P. Wolf, Alternate	

To Drs Atkins and Robertson

The above titled and numbered proposal is Approved subject to the following:
Investigational Consent no. -42- has been established for this CIRC
+ See minutes of CIRC meeting since 1971 for appropriate date

E P Cronkite 9 Nov 71
E.P. Cronkite, M.D., President of Staff Date

1180110

CIRC form #1 5/12/71

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.

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

Helen R. Connell

cc: CIRC Committee
Mr. Finn
Dr. Aronson
File

1180112

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: Oct 14 1971

TO: H. L. Atkins MD

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

SUBJECT: CIRC Proposal 26 Rev 3/30/71

In compliance with recent FDA and HEW notices requiring periodic reviews of clinical research projects, your CIRC proposal, number 26 Rev 3/30/71 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 April 6, 1971 but with conflict of interest 19____. Do you wish to make any substantive changes in your proposal? NO

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? 3

The Sponsoring Physician on this proposal is Dr J.S. Robertson. Has there been a change of Sponsoring Physician or Responsible Investigators? NO

DBS IND 799

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

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

Please add any additional information which may be of use to the Committee in its diliberations. Include a copy of the Patient Consent Form now in use for this study. 442

CIRC PROPOSAL NUMBER 26 Rev 3/30/71 IS: Continuing [X]

Inactive [ ]

Signed Harold L. Atkins J.S. Robertson 10/14/71
Date

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

1180113

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

-42-

CONSENT FOR PROCEDURE, STUDY, OR DRUG UNDER CLINICAL INVESTIGATION CMC 26

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:

^{99m}Tc labeled human serum albumin for blood pool scanning

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.

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 _____

1180114

Form 1913

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

CLINICAL INVESTIGATION AUTHORIZATION FORM

Purpose of Review: Initial ☐ Revision ☒ Continuing ☐ Addendum ☐

Title:
Technetium-99m labeled human serum albumin (produced by the stannous ion method): ^{99m}Tc-HSA (Sn).

CIRC# 26 (Revised 3/30/71)

Assigned on (date) 3/30/71

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

L. 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. Klopper	N.P. Rathvon, Jr.
S.E. Duby, Alternate	A.P. Wolf, Alternate	

To_____,
The above titled and numbered proposal is_____subject to the following:

1180115

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

CIRC form #1 5/12/71

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: 6 May 1971

TO: Dr. J. Robertson

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

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

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.

1180116

Rec'd 5/7/71

Minutes CIRC Meeting

3 May 1971

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

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

The Committe 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}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}Ca and neutron activations per patient.

The Committee then reviewed CIRC #68 entitled "π^- Meson Radiotherapy". It found two specific merits to the proposed use of this technique: 1) That π^- 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. Cotzias
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.

CPC

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

Technetium-99m labeled human serum albumin (produced by the stannous ion method): ^{99m}Tc-HSA (Sn).

CIRC # 26 (Revised 3/30/71) has been assigned to this program.

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

S. H. Cohn, Ph.D.

-ABSENT-
L. D. Hamilton, M. D.

J. F. Klopper, M. D.

R. A. Love, M. D.

A. J. Steck, M. D.

Date: 6 April 1971

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

Committee on Clinical Investigations and Uses of Radioisotoptes

Approval Recommended ✓ Date 4/6/71

Disapproval _____ Date _____

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

7 April 71
Date

1180119

Minutes CIRC Meeting

6 April 1971

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

Absent: Dr. Hamilton

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

J.S. Robertson, M.D.

/ck
cc: CIRC Committee
Mr. Finn
File

1180120

BROOKHAVEN NATIONAL LABORATORY
ASSOCIATED UNIVERSITIES, INC.
UPTON, L.I., N.Y. 11973
TEL. AREA CODE 516 YAPHANK 4-6262

REFER:

MEDICAL DEPARTMENT

7 April 1971

Division of Biologics Standards
National Institutes of Health
Public Health Service
Bldg. 29
9000 Rockville Pike
Bethesda, Maryland 20014

Dear Sir:

Enclosed is an amendment to DBS-IND 299 by Dr. Harold L. Atkins of this Department.

All investigation on human subjects within this Department has always been subject to continuing purview by the Chairman of the Department, the Head of the Hospital and our local Clinical Investigation Committee. This is a continuing policy of this Department which involves informed consent and adherence to the Helsinki Declaration, and is being conformed to the new regulations of the FDA and NIH to be effective April 15, 1971.

Respectfully submitted,

E P Cronkite

Eugene P. Cronkite, M.D.
Chairman

/ck
Enclosures

cc: Dr. Atkins
Dr. Dahl
File

1180121

DBS-IND 299

Amendment No. 1

1. Drug: Technetium-99m labeled human serum albumin (produced by the stannous ion method): ^{99m}Tc-HSA (Sn).

2. The components of the diagnostic agents and their sources are:

Stannous chloride, reagent grade (J. T. Baker Chemical Co., Phillipsburg, N. J.).

Hydrochloric acid, reagent grade (J. T. Baker Chemical Co.)

Sterile water for injection, U. S. P., pyrogen-free (Travenol Lab., Morton Grove, Ill.).

Human serum albumin 5%, U. S. P. (Hyland Labs.,)

Sodium hydroxide, reagent grade (J. T. Baker Chemical Co.).

Nitrogen, prepurified grade (Matheson, Coleman and Bell, East Rutherford, N. J.).

Sodium chloride 0.9% injection U. S. P. (The Vitamine Co., New York, N. Y.).

Technetium-99m-pertechnetate (see IND 4136, as amended on May 12, 1969).

3. Method for production (Stannous ion method).

^{99m}Tc-HSA (Sn) is prepared in the Hot Laboratory of the Department of Applied Science, Brookhaven National Laboratory. To ensure uniformity of the final product, the following procedure is strictly followed. All solutions and equipment used are sterile and pyrogen-free.

A. Preparation of the stannous solution.

25 mg $SnCl_2 \cdot 2\ H_2O$ are added to 2.5 ml conc. HCl. The solution is heated until all stannous chloride is dissolved. It is then diluted to 25 ml with sterile water.

B. Preparation of the HSA stock solution.

4 ml of HSA (250 mg/ml) are added to 2 ml of the freshly prepared $SnCl_2 \cdot 2\ H_2O$ solution (1 mg/ml). After thorough mixing the pH is adjusted to 6 with NaOH. The entire solution is put into a 35 cm Sephadex G 25 column, and eluted across the column with 0.9% NaCl. The HSA fraction is collected in sterile multi-injection vials after it has passed through a presterilized 0.22 μ Swinnex-type filter.

One cc. of the solution is put into each vial. The vials are stored at 4°C with the HSA stock solution under nitrogen.

Usually four vials can be filled with HSA stock solution when the amount of chemicals described above is used.

C. Labeling of the HSA stock solution.

0.1 ml sterile $^{99m}TcO_4^-$ in physiological saline containing the derived amount of radioactivity is added to one vial containing 1 cc. of the HSA stock solution. The solution is allowed to mix for two minutes, and is then ready for administration to patients.

4. Assay and calibration procedures.

A. Radioactivity

Radioactivity/unit volume is determined for every sample by

1. determination of the radioactivity with a well-type ionization chamber ("Mediac" Dose Calibrator, Nuclear Chicago) which is calibrated daily with a ^{226}Ra standard, and by

2. determination of the volume by weighing of the sample

B. Radionuclide purity

The only detectable impurity is molybdenum -99. The ^{99}Mo contamination is determined quickly and accurately by using a commercially available well-type ionization chamber and lead shield (P. Richards and M. O'Brien: Rapid determination of ^{99}Mo in separated $^{99m}TcO_4^-$. J. Nucl. Med. 10: 517, 1969).

C. Radiochemical purity

Periodically the adequacy of the production system will be tested by determining the radiochemical purity by gel chromatography. The final product should have at least the same purity as the product obtained with the previously used procedure (> 90% of radioactivity associated with HSA).

D. Sterility and pyrogenicity

1. Presterilized Swinnex-type filters (Millipore Corp., Bedford, Mass.) are used for sterilization of both the HSA stock solution and the TcO_4^- solution. The integrity of the filters is tested immediately following use by a standard bubble point test. The 0.22 μ filters should require at least 50 p.s.i. pressure to force air through the filter.

2. Pyrogen testing is performed periodically by an independent laboratory (Leberco Laboratory, Roselle Park, N. J.)

5. Metabolic behavior of ^{99m}Tc-HSA (Sn).

This modified diagnostic agent has been tested in mice and rabbits.

a. Mice:

Groups of 6 animals each were injected i.v. with 0.2 ml ^{99m}Tc-HSA (Sn) and with 0.2 ml of ^{131}I-RISA obtained from commercial sources. The mice were sacrificed after 1 hour. The total body retention of activity (after removal of the urinary bladder) and the renal uptake of the radioactive material were measured by scintillation counting and comparison with an injection standard. The results were

	RISA	Tc-HSA
Total body	84.2 ± 3.4%*	63.8 ± 2.3
Kidneys only	4.2 ± 0.3	4.8 ± 0.4

* % of administered dose ± 1 S. D.

The reason for the discrepancy in the amount of total-body retention for these compounds at 1 hour was not determined. However, the amount of Tc-HSA retained in the mice is by far the largest of any compound tested other than radiocolloids.

The most likely explanation of the result is that the two compounds did not contain albumin of the same molecular weight.

b. Rabbits

Whole body scans of rabbits obtained with several different preparations always showed retention of the Tc-HSA (Sn) in the blood pool with loss

of some radioactivity in the urine.

A comparison of the of disappear of radi ty from the blood (corrected ay) for the n ^{99m}Tc-HSA compound A with the current ^{99m}Tc-HSA-com B is sh low. The of counts obtained at 1? min. a taken as Scintip taken at that time did not demonstrate radioact it in any organ other than the blood pool.

	Compound A	Compound B
12 min.		
30 min.		
60 min.		
90 min.		
120 min.		
180 min.		

This study demonstrated clear better retentio radioactivity in the blood pool of rabbits wit new Tc-HSA compound in comparison with the Tc-HSA compound prep by the curr y used procedure.

A further study was carried o o demonstrate that the radioactivity in the blood is indeed assoc with proteins. The distribution of radioactivity in Tc-HSA (Sn) pared by the procedure described (post-Sephadex) and in Tc-HSA (Sn) prepared without purification by gel chromatography (pre-Sephadex) were analyzed by gel chromatography before administration to rabbits. Plasma obtained from the rabbits 1 hour after i.v. injection were analyzed in the same manner.

The results of this analysis are shown in the following table:

	^{99m}Tc-HSA	^{99m}Tc Adsorbed Onto Column	$^{99m}TcO_4^-$
FINAL PRODUCT			
post-Sephadex	95%*	5	
pre-Sephadex	89	11	
PLASMA (1 hour)			
post-Sephadex	84		16
pre-Sephadex	93		7

* % of total radioactivity in sample.

c. Man

Only these studies will demonstrate the usefulness of the ^{99m}Tc-HSA (Sn) obtained with this simple and rapid labeling procedure. The animal studies have shown sufficient similarity of this new compound Tc-HSA (Sn) with compounds currently in use to warrant study of this new compound in man.

6. Evaluation of the safety of ^{99m}Tc-HSA (Sn)

a. Chemical toxicity

The only potentially toxic component of Tc-HSA (Sn) is $SnCl_2 \cdot 2\ H_2O$. Recovery studies with radioactive tracers have indicated that ~ 10% (200 μg) of the $SnCl_2 \cdot 2\ H_2O$ used in the preparation remain with the 1 g of HSA after the gel chromatography step. Since this amount is usually distributed into four vials the usual dosages of $SnCl_2$ to be administered to one patient should be 50 μg. The normal level of this in the blood is 13 μg/100 gm (Biological Handbook-Blood and Other

Body Fluids. Federation of American Societies for Experimental Biology, Washington, D. C. 1961, page 21). No toxic reaction is expected, and none have been observed with another technetium-99m labeled compound, ^{99m}Tc-DTPA (Sn) in which up to 250 μg are administered to one patient (H. L. Atkins, et al.: Evaluation of ^{99m}Tc-DTPA prepared by three different methods. Radiology 98: 674-677, March 1971).

The lethal dose of $SnCl_2 \cdot 2 H_2O$ for animals is 25-50 mg/kg (W. S. Spector, ed.: Handbook of Toxicology, Vol. I, W. B. Saunders Co., Philadelphia and London, 1956, p. 300).

b. Chemical impurity

No significant impurity is introduced into the compound ^{99m}Tc-HSA with this new stannous ion method.

c. Radiation dose

d. Radionuclide impurity

e. Sterility and pyrogenicity.

The same considerations as for the compound prepared by the procedure currently in use apply.

7. Outline of the prepared evaluation of the new compound ^{99m}Tc-HSA (Sn).

Five patients referred for blood pool scans will receive approximately 5.0 mCi of the preparation intravenously. Blood and plasma samples will be obtained at frequent intervals to determine the rate of disappearance of the compound from the blood. 24-hour urine collections will be carried out to measure the rate of breakdown. Both urine and plasma samples will

be analyzed by gel chromatography to determine the chemical form of technetium-99m in these samples at different times.

Scans of the blood pools and of the whole body will be performed and compared with those obtained with the ^{99m}Tc-HSA compound used up to now.

If all these data indicate substantial agreement in the behavior of the new compound ^{99m}Tc-HSA (Sn) with that found with the compound prepared by our current method, we plan to substitute this new method of preparation for that currently used.

The preparation of technetium-99m labeled human serum albumin macroaggregates will continue with the procedure described in our original Notice of January 15, 1968.

For further details of the labeling procedure, see the enclosed copy of the manuscript "^{99m}Tc Human Serum Albumin," by W. C. Eckelman, G. Meinken and P. Richards.

ls

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

BLOOD POOL SCANNING WITH ^{99m}Tc-ALBUMIN

CIRC # 26 has been assigned to this program.

George C. Cotzias

George C. Cotzias, M.D., Chairman

Absent

Lewis M. Schiffer, M.D.

Knud D. Knudsen, M.D.

Walton W. Shreeve

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

Date: June 20, 1966

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

1180130

June 20, 1966

The Committee on Clinical Investigations and Use of Radioisotopes has reviewed the Cir. 26 entitled: "Blood pool scanning with ^{99m}Tc albumin" by Drs. J.S. Robertson and H.L. Atkins. The dose given will be 1 millicurie as was confirmed by contacting Dr. Atkins.

The Committee recommends approval of this proposal.

JUN 6 1966

V

V.P. Bond, M.
Chairman
CIRC #26

FORM FOR INITIATION OR REVIEW OF CLINICAL

INVESTIGATIVE PROGRAMS

(Submit original only to Department Chairman)

A. Title of the proposal: Blood pool scanning with ^{99m}Tc-albumin

B. Sponsoring physician(s): J.S. Robertson

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.)

The purpose is to delineate blood pools such as heart, aneurysms in patients in whom this is clinically indicated. No specific research program is intended. This is to support other clinical programs in the hospital.

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

As a service function.

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.):

Patients with possible pericardial effusion or abdominal aneurysm.

1180132

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: _____

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 6/21/63

Disapproval _____ Date _____

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

1180133

6/25/63
mlk

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)
^{99m}Tc-human serum albumin

2. Physical characteristics: (Physical half-life; decay scheme (or type, energy and relative frequency of major emissions)
$T_{1/2}$ = 6 hours; γ = 0.140, 0.142, 0.002 MeV; no β, 10% int. conversion.

3. Source: (BNL reactor, cyclotron, hot lab.), commercial supplier, etc.)
Hot lab.

4. Preparation: (Target material, quantity, special problems)
Method in: MacAfee, J. G. et al., J. Nucl. Med. 5: 936-946, 1964.

5. Specific activity and isotopic purity of administered material:
Carrier-free ^{99m}Tc better than 99.99% isotopically pure.

6. Radioassay and calibration procedures: (Include validation to be performed at BNL prior to use) Performed at hot lab with ionization chamber calibrated with ^{57}Co.

7. Vehicle and route of administration: Intravenous.

8. Procedures for control of sterility and pyrogenicity: (Or note that commercially supplied isotopes are certified as ready for administration to human beings.) Sterile, pyrogen-free reagents and commercially-supplied human serum albumin to be used. Same procedure used as for preparation of Tc-Fe-ascorbate in initial stage. Millipore filter used in final stage.

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:
$T_{1/2}(a)$ = 6 hours; $T_{1/2}(b)$ = 3 days (see reference above).

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): Blood = 47 mrads/mCi

b. Gonadal exposure: Same as whole-body dose = 5 mrads/mCi

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.

Calculations performed by McAfee, et al., J. Nucl. Med. 5: 936-946, 1964, and Smith, E., J. Nucl. Med. 6: 231-251, 1965.

Assumptions are I_γ = 0.56 r/mCi/h at 1 cm.
$T_{1/2}$ eff = 6 hrs
Blood vol. = 60 ml/kg
$\bar{g}$ = 178 (for pregnant woman)

C. Radiological Health Aspects

1. Hazards to other patients and to personnel from external or internal radiation: None

2. Monitoring procedures, if necessary: None

3. Special procedures for handling waste products, excreta, biological samples, etc., where indicated: None

4. Plan for isotope accountability, if required: None