

BROOKHAVEN NATIONAL LABORATORY
MEMORANDUM

R

DATE: 24 March 1971

TO: A. Harrison
FROM: E. P. Cronkite, M.D. *E.P. Cronkite*
SUBJECT: CIRC Numbers

The following CIRC #s are inactive. Except for completing old records, they should not be used for identifying patient activity until reactivation is formally approved.

<u>Principal Investigator</u>	<u>CIRC #</u>
Dr. Cronkite	3 4 20 23 35 35A
Dr. Dahl	5 6 14 25
Dr. Jesseph	1
Dr. Robertson	9 10 16 28
Dr. Schiffer	22

EPC/ck
cc: CIRC Committee
Mr. Finn
Dr. Dahl

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

REPOSITORY Records Holding Area Bldg. 494
COLLECTION Committee - Clinical Investigations
and use of Radioisotopes
BOX No. 4
FOLDER CIRC # 25

File
60111
1000

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

INULIN - C¹⁴ - RENAL CLEARANCE

CIRC # 25 has been assigned to this program.

George C. Cozias
George C. Cozias, M.D., Chairman

Lewis M. Schiffer
Lewis M. Schiffer, M.D.

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

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

Date: February 23, 1966

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

1180035

February 11, 1966

The Committee on Clinical Investigations and Isotopes met on February 11, 1966 and discussed the proposal "Inulin-C¹⁴ renal clearance" by Drs. Dahl, Knudsen and Ben-Ishay. Dr. Knudsen answered questions concerning the radiation dose, the reason for not using Co⁵⁷, B₁₂, the number of times C¹⁴ inulin will be used per person and the reasons for not using non-radioactive inulin. The Committee understood that while inulin is listed in the U.S. Pharmacopoea, C¹⁴ inulin is not. Similarly, it is understood that C¹⁴ inulin is not an accepted routine procedure. The sum of the evidence submitted indicates that approval is warranted.

1180036

Date received: FEB 11 1966

Initial Approval: VB
V.P. Bond, M.D.
Chairman, Med. Dept.

Date: FEB 17 1966

FORM FOR INITIATION OR REVIEW OF CLINICAL
INVESTIGATIVE PROGRAMS

(Submit original only to Department Chairman)

CIRC No. 25

- A. Title of the proposal: Inulin - C¹⁴ - renal clearance
- B. Sponsoring physician(s): Lewis K. Dahl, Knud Knudsen, Drori Ben-Ishay
- C. Responsible investigator(s): Same
- D. Brief description of the study, including its general goals and purpose, and pertinent information on past studies: (Attach additional sheets if necessary.)

GFR - using C¹⁴-inulin has been determined in rats, using a single injection technique.

The same technique will be tested in patients.

One dose of 50 μ c Inulin-C¹⁴ will be injected IV. Blood samples and fractionated urine collections during the next 24 hours. The results will be compared to a simultaneous endogenous creatinine clearance.

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

The test promises to be of clinical value. Our interest in hypertension is, basically, oriented toward studying the disease process in man, for which there is no substitute.

- 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 and without hypertension on high and low NaCl intake. No special requirements or restrictions except reasonably good renal function and no frank heart failure. Consent will be obtained directly from patient.

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- G. 1. Are drugs not in the U. S. Pharmacopoeia (USP) or the NNR being used or contemplated for use? Yes ___ No x
- 2. Is an unusual use of a drug(s) accepted by the USP or NNR contemplated? (An example would be the use of an accepted drug in dosages far exceeding the recommended limits or for purposes distinctly different from the usual indications cited.) Yes ___ No x
- 3. Are any biological products to be administered that do not bear on their containers or labels notation of approval by the Biological Control Division of the National Institutes of Health? Yes ___ No x
- 4. Is external or internal radiation other than accepted diagnostic or therapeutic procedures to be administered? Yes x No ___
- 5. Are any (other) unusual procedures being performed or proposed which in your judgment may entail a special hazard - particularly a hazard above and beyond any imposed by accepted diagnostic and therapeutic measures for that patient? Yes ___ No 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): ¹⁴C-inulin
 - 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.

Lewis K. Davis
Sponsoring Physician

Committee on Clinical Investigations and
Uses of Radioisotopes

Approval recommended ✓ Date FEB 25 1966

Disapproval _____ Date _____

V. P. Bond

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

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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)
Inulin-carboxyl- C^{14}
2. Physical characteristics: (Physical half-life; decay scheme (or type, energy and relative frequency of major emissions)
 β -decay - 5,000 years
3. Source: (BNL reactor, cyclotron, hot lab.), commercial supplier, etc.)
New England Nuclear Corp., Boston, Mass.
4. Preparation: (Target material, quantity, special problems)
Commercial product
5. Specific activity and isotopic purity of administered material:
1 - 3 m C/g
6. Radioassay and calibration procedures: (Include validation to be performed at BNL prior to use)
Factory specifications
7. Vehicle and route of administration:
Aqueous solution Intravenous
8. Procedures for control of sterility and pyrogenicity: (Or note that commercially supplied isotopes are certified as ready for administration to human beings.)
Delivered in sterile, pyrogen free aqueous solution.
9. Extraneous effects, if pertinent: (Such as pharmacological or toxic actions of the parent compound or vehicle, etc.) None expected.
Occasional fever from pyrogens in solution.

B. Radiation Dosage

1. Biological half-life or half-lives, including slow components:
2 hours
2. Organ, cellular, or subcellular localization: (Should account for the effects of special drugs or agents on altering the natural distribution of the radioisotope)
 - a. Critical or "target" organ(s): Kidney, Bladder
 - b. Gonadal exposure: Same as whole body

Inulin is not metabolized. Excreted in urine. Effective half value time 2 hrs. or less in normal subjects.

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

Ref. ~~Veall and Vetter~~ ^{Veall, N. and Vetter, H. Radioisotope techniques in clinical research and diagnosis. Butterworth, London, 1958}
 14 C - absorbed dose rate: 0.10 millirad/hr for 1 $\mu\text{Ci}/\text{kg}$

Total dose, calculated as if all activity were initially distributed in

Kidney:	$\frac{50 \mu\text{c}}{0.6}$	0.1 .2 1.44	=	<u>24 mrad</u>
Bladder:			=	<u>150 mrad</u>
Whole body:			=	<u>0.5 mrad</u>

C. Radiological Health Aspects

- Hazards to other patients and to personnel from external or internal radiation: None
- Monitoring procedures, if necessary: None
- Special procedures for handling waste products, excreta, biological samples, etc., where indicated: All activity is excreted in urine over 24 hrs.
- Plan for isotope accountability, if required:

Injected dose will be measured and compared to total excretion.