A11/4

BUMED-7146:JS
RR 62 05 60
21 Mar 1958

SECOND ENDORSEMENT on NAVRADLDEFLAB ltr 730-37 WJF:sms of 17 Feb 1958 to SECNAV, via BUSHIPS and BUMED

From: Chief, Bureau of Medicine and Surgery
To: Secretary of the Navy

Subj: Authorization for use of radioisotopes in human volunteers; request for

1. Forwarded.

2. The U. S. Naval Radiological Defense Laboratory proposes to use radioisotopes K^{42}, Br^{82} and H^3 in human volunteers for the purpose of determining total exchangeable potassium, total exchangeable chloride and total body water content of healthy adult males and females. The simultaneous administration of the above radioisotopes in the proposed dosage would result in a total dose of approximately 0.183 rads. This represents no more hasard than that which occurs following radioisotopes administered in many present day medical procedures. Accurate dosage records would be maintained of the subjects.

3. It is recommended that the basic proposal be approved.

4. Upon approval and upon return of basic proposal and its enclosures to this office, the Chief, Bureau of Medicine and Surgery will further process the application forms (AEC-313 and AEC-313a), as required by Isotopes Extension, Division of Civilian Application, U. S. Atomic Energy Commission, for utilization of radioisotopes in the human.

D. L. YARBOROUGH
Assistant Chief for Research and Military Medical Specialties

3 APR 1958

Copy to:
Chief, BuShips
CO&DIR, USNRDL

Approved
RICHARD JACKSON
Assistant Secretary of the Navy

RETURNED TO ORIGINATOR FOR ~~MAILING~~ THIS DATE 4-4
/s/

OFFICIAL FILE
SECNAV

CLEARED TRACER DESK
Date 4/4/58 Init

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FIRST ENDORSEMENT on NAVRADLDEFLAB ltr 730-37 WJF:ams of 17 Feb 58
to SECNAV, via BUSHIPS and BUMED

28 FEB 1958

From: Chief, Bureau of Ships
To: Secretary of the Navy
Via: Chief, Bureau of Medicine and Surgery

Subj: Authorization for use of radioisotopes in human volunteers; request for

1. Forwarded.

2. In view of the intent for using radioisotopes in human volunteers, it is requested that the Bureau of Medicine and Surgery process the application forms, AEC-313 and AEC-313a. Reference (b) of the basic correspondence does not apply when it is planned to use radioisotopes in humans.

F. B. Owen

Copy to:
NAVRADLDEFLAB

F. B. OWEN
By Direction

A11/M
1/58
6-1

U. S. NAVAL RADIOLOGICAL DEFENSE LABORATORY
SAN FRANCISCO 24, CALIFORNIA

IN REPLY REFER TO FILE:
730-37
WJF:ems

17 FEB 1958

AIR MAIL

From: Commanding Officer and Director
To: Secretary of the Navy
Via: (1) Chief, Bureau of Ships (Code 348)
(2) Chief, Bureau of Medicine and Surgery (Code 74)

Subj: Authorization for use of radioisotopes in human volunteers; request for

Ref: (a) NavMed P-1325 (Rev 1951), Chapter 7-1
(b) BuShips ltr J-3/2(348) Ser 348-128 of 7 June 1956
(c) NavMed P-117 (1952) Chapter 1-17

Encl: (1) Three copies of application forms AEC-313 and 313a with Supplement 1

1. In accordance with references (a) and (b), request is made for authorization to use the radioisotopes Potassium 42, Bromine 82, and Tritium (Hydrogen 3) in a proposed research experiment entitled "Measurement of Total Exchangeable Potassium, Total Exchangeable Chloride, and Total Body Water Simultaneously in Healthy Adult Men and Women." This work will be accomplished under Subtask 13 of Bureau of Medicine and Surgery Task Number MR62 03 60. It is proposed to use volunteer naval and civilian personnel as subjects in this study, in accordance with provisions set forth in reference (c).

2. The complete details of isotope use are given in enclosure (1). It is pointed out that the experiment will be conducted by a trained physician who is experienced in the use of radioisotopes, and who has had previous experience with this same type of work with human subjects. It is further pointed out that, due to the use of improved techniques, the total body radiation dose received by any given subject will be less than 0.2 rad.

3. The following named trained physicians are members of the Laboratory Staff and will be available at all times for consultation:

Capt. A.R. BEHNKE, Jr., MC USN, a physician trained in internal medicine; has wide experience in physiological research.

ROBERT R. NEMKLL, M.D., Emeritus Professor of Radiology, Stanford University Medical School.

LCDR J.S. ARNOLD, MC, USNR, a physician trained in pathology.

730-37
WJF:mm

4. After review by cognizant Bureaus and if the request is approved, it is requested that enclosure (1) be forwarded to the Atomic Energy Commission, Isotopes Branch, Division of Licensing and Regulations, 1717-H Street, N.W., Washington 25, D.C., for the purpose of obtaining AEC approval of this proposed use of the subject radioisotopes.

5. Since the physician who will conduct the experimental work is a Navy Reserve Officer with limited obligated service remaining, it would be appreciated if this request is expedited.

J.H. McQUILKIN

Form AEC-313 (2-57)	ATOMIC ENERGY COMMISSION **APPLICATION FOR BYPRODUCT MATERIAL LICENSE**	Form approved. Budget Bureau No. 38-R02

INSTRUCTIONS.—Complete items 1 through 16 if this is an initial application. If application is for renewal of a license, comple only items 1 through 7 and indicate new information or changes in the program as requested in items 8 through 15. Use supp mental sheets where necessary. Item 16 must be completed on all applications. Mail two copies to: U. S. Atomic Ener Commission, P. O. Box E, Oak Ridge, Tenn. Attention: Isotopes Extension, Division of Civilian Application. Upon approval of t application, the applicant will receive an AEC Byproduct Material License. An AEC Byproduct Material License is issued in accor ance with the general requirements contained in Title 10, Code of Federal Regulations, Part 30 and the licensee is subject to Title Code of Federal Regulations, Part 20.

1. (a) NAME AND STREET ADDRESS OF APPLICANT. *(Institution, firm, hospital, person, etc.)*

A.L. Baistti
Chairman, Radioisotope Committee
U.S. Naval Radiological Defense Laboratory
San Francisco 24, California

(b) STREET ADDRESS(ES) AT WHICH BYPRODUCT MATERIAL WILL BE USED. *(If different from 1 (a).)*

2. DEPARTMENT TO USE BYPRODUCT MATERIAL

Scientific Department
Biological & Medical Sciences Division
Biochemistry Branch

3. PREVIOUS LICENSE NUMBER(S). *(If this is an application for renewal o license, please indicate and give number.)*

License No. 4-487-3 (Expires 1/31/59)

4. INDIVIDUAL USER(S). *(Name and title of individual(s) who will use or directly supervise use of byproduct material. Give training and experience in items 8 and 9.)*

Elden A. Baling, MD
LT (MC) USNR

5. RADIATION PROTECTION OFFICER *(Name of person designated as radiation tection officer if other than individual user. Attach resume of his training and perience as in items 8 and 9.)*

A.L. Baistti
Chairman, Radioisotope Committee
(Ref: Ltr 3-730-267 ALBaistti of 4 Dec 19 w/att Form AEC-313 and supplements).

6. (a) BYPRODUCT MATERIAL. *(Elements and mass number of each.)*	(b) CHEMICAL AND/OR PHYSICAL FORM AND MAXIMUM NUMBER OF MILLICURIES OF EACH CHEMICAL AND/OR PHYSICAL FORM THAT YOU WILL POSSESS AT ANY ONE TIME. *(If sealed source(s), also state name of manufacturer, number, number of sources and maximum activity per source.)*	
Hydrogen 3	Hydrogen 3 - Tritiated Water (HTO)	50 millicuries
Potassium 42	Potassium chloride solution	3 millicuries
Bromine 82	Ammonium bromide solution	9 millicuries

7. DESCRIBE PURPOSE FOR WHICH BYPRODUCT MATERIAL WILL BE USED. *(If byproduct material is for "human use," supplement A (Form AEC-313a) must be completed in lieu of this item. If byproduct material is in the form of a sealed source, include the make and model number of the storage container and/or device in which the source will be stored and/or used.)*

Supplement 1 (AEC-313A) is attached.

(Continued on reverse side)

Form AEC-313 (2/57) Page

TRAINING AND EXPERIENCE OF EACH INDIVIDUAL NAMED IN ITEM 4 *(Use supplemental sheets if necessary)*

8. TYPE OF TRAINING	WHERE TRAINED	DURATION OF TRAINING	ON THE JOB (Circle answer)	FORMAL COU (Circle answ
a. Principles and practices of radiation protection	Peter Bent Brigham Hospital Boston, Massachusetts	2 yrs	(Yes) No	Yes (N
b. Radioactivity measurement standardization and monitoring techniques and instruments	Same	2 yrs	(Yes) No	Yes (N
c. Mathematics and calculations basic to the use and measurement of radioactivity	Same	2 yrs	(Yes) No	Yes (N
d. Biological effects of radiation	Same, also U.S. Naval Radiological Defense Lab., S.F. Calif.	2yrs-9 mo.	(Yes) No	Yes (N

9. EXPERIENCE WITH RADIATION. *(Actual use of radioisotopes or equivalent experience.)*

ISOTOPE	MAXIMUM AMOUNT	WHERE EXPERIENCE WAS GAINED	DURATION OF EXPERIENCE	TYPE OF USE
C-42	3 mc	Peter Bent Brigham Hospital	2yrs	Measuring body com-
Na-24	3 mc	"	2 yrs	position in adult
Br-82	9 mc	"	1 yr	human beings by
H^3	5. mc	NHDL	9 months	isotope dilution & In vitro.

10. RADIATION DETECTION INSTRUMENTS. *(Use supplemental sheets if necessary.)*

TYPE OF INSTRUMENTS (Include make and model number of each)	NUMBER AVAILABLE	RADIATION DETECTED	SENSITIVITY RANGE (mr/hr)	WINDOW THICKNESS (mg/cm^2)	USE (Monitoring, surveying, measuri
1) Plastic well scintillation counter	1	Beta	See attached sheet 313A		Measuring
2) Naiffi well scintillation counter	1	Gamma	"		Measuring
3) Packard Tri-Carb Spectrometer	1	Beta	"		Measuring

11. METHOD, FREQUENCY, AND STANDARDS USED IN CALIBRATING INSTRUMENTS LISTED ABOVE.

Standard solutions of long-life isotopes

12. FILM BADGES, DOSIMETERS, AND BIO-ASSAY PROCEDURES USED. *(For film badges, specify method of calibrating and processing, or name of supplier.)*

Film badges calibrated against radium and/or cobalt 60, changed monthly. 0-200 mr pocket dosimeters used during handling of large quantities. Facilities for radio-analysis of urine available.

INFORMATION TO BE SUBMITTED ON ADDITIONAL SHEETS

13. FACILITIES AND EQUIPMENT. Describe laboratory facilities and remote handling equipment, storage containers, shielding, fume hoods, etc. Explanatory sketch of facility is attached. (Circle answer) Yes No

14. RADIATION PROTECTION PROGRAM. Describe the radiation protection program including control measures. If application covers sealed sources, submit leak testing procedures where applicable, name, training, and experience of person to perform leak tests, and arrangements for performing initial radiation survey, servicing, maintenance and repair of the source.

15. WASTE DISPOSAL. If a commercial waste disposal service is employed, specify name of company. Otherwise, submit detailed description of methods which will be used for disposing of radioactive wastes and estimates of the type and amount of activity involved.

CERTIFICATE (This item must be completed by applicant)

16. THE APPLICANT AND ANY OFFICIAL EXECUTING THIS CERTIFICATE ON BEHALF OF THE APPLICANT NAMED IN ITEM 1, CERTIFY THAT THIS APPLICATION IS PREPARED IN CONFORMITY WITH TITLE 10, CODE OF FEDERAL REGULATIONS, PART 30, AND THAT ALL INFORMATION CONTAINED HEREIN, INCLUDING ANY SUPPLEMENTS ATTACHED HERETO, IS TRUE AND CORRECT TO THE BEST OF OUR KNOWLEDGE AND BELIEF.

Date 2/13/58

Applicant named in item 1

By: Eugene Cronkite

Acting Chairman, Radioisotope Committee

Title of certifying official

WARNING.—18 U. S. C., Section 1001; Act of June 25, 1948; 62 Stat. 749; makes it a criminal offense to make a willfully false statement or representation to any department or agency of the United States as to any matter within its jurisdiction.

U. S. GOVERNMENT PRINTING OFFICE 1957 O-F—426006

Form AEC 313a
(3/56)

ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

SUPPLEMENT A—HUMAN USE—PAGE 1

Form approved.
Budget Bureau No. 38-R027.3.

If byproduct material is for "human use" (internal administration of byproduct material or the radiation therefrom to human beings), complete this supplement and attach to the application for byproduct material license.

1(a) Using physician's name

Eldon A. Boling, MD
LT (MC) USNR
U.S. Naval Radiological Defense Lab.
San Francisco 24, California

(b) Name & address of applicant (if different from 1(a))

A.L. Brietti
Chairman, Radioisotope Committee
U.S. Naval Radiological Defense Laboratory
San Francisco 24, California

	CIRCLE ANSWER		
2. The using physician indicated above is licensed to dispense drugs in the practice of medicine by a state or territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico.		(Yes)	No
3. A Supplement A—Human Use—Page 3 (statement of using physician's clinical radioisotope experience) is submitted in support of this application. If answer is NO, use reverse side of this page to explain or refer to other application or related documents on which this information appears.	CIRCLE ANSWER	(Yes)	No

PROPOSED DIAGNOSIS OR TREATMENT

4. (a) Describe purpose for which byproduct material will be used including specific conditions or diseases to be diagnosed or treated: (Use reverse side if necessary).

Measurement of total exchangeable Potassium, total exchangeable chloride, and total body water simultaneously in healthy adult men and women.

(b) Chemical form administered: 1) Potassium chloride
2) Ammonium bromide
3) Enriched tritiated water

(c) Describe procedures which will be observed to minimize hazard from handling, storage, and disposal of the byproduct material:

1) Handling will be done by trained personnel using NRDL equipment.
2) Storage will be in 2 inch lead shielding.
3) K^{42} and Br^{82} will decay away. H^3 wastes will consist only of counting solutions

	CIRCLE ANSWER		
(d) Description and sketches of special devices to be used for administering byproduct material to human beings are (1) Attached (Literature references will suffice).		(Yes)	No
(2) On file with the Isotopes Extension. Refer to Application No: ---------- See remarks(over)	CIRCLE ANSWER	Yes	No

PROPOSED DOSAGE SCHEDULE

5. (a) In millicuries for internally administered byproduct material other than discrete fixed source; and in roentgens or rads, as appropriate, for internal or external irradiation from discrete fixed sources (gold seeds, cobalt needles, etc.;) state separately for each condition or disease (use reverse side if necessary).

Potassium 42: 0.050 millicuries
Bromide 82: 0.010 millicuries
Hydrogen 3: 1.0 millicuries

} To be given as one single dose. (See 5b).

For total dose (rad) see 5(b) supplement.

	CIRCLE ANSWER		
(b) Investigative proposal for experimental, new or unusual human uses is attached. (Attachment should include outline of conditions to be evaluated, including data from animal studies and/or abstract of literature reference, if any, and number and type of patients (i.e., age group, moribund, etc.).) See Suppl.	CIRCLE ANSWER	(Yes)	No

6. If byproduct material will not be obtained in precalibrated form for oral administration or in precalibrated and sterilized form for parenteral administration, describe identification, processing, and standardization procedures:

These will be carried out as follows: See reverse of page

	CIRCLE ANSWER		
7. The proposed use of byproduct material has been, or will be, approved by the medical isotope committee.	CIRCLE ANSWER	(Yes)	No

HOSPITAL FACILITIES FOR INDIVIDUAL PRACTICE USE ONLY

	CIRCLE ANSWER		
8. (a) The applicant has completed arrangements for a hospital to admit radioactive patients whenever advisable.	CIRCLE ANSWER	Yes	No
(b) A copy of instructions to be furnished to the hospital as to radiological safety precautions to be taken and available radiation instrumentation is attached.	CIRCLE ANSWER	Yes	No

Item 4(d): [redacted] will be administered to the human subjects by means of [redacted] sterile glass syringes in volume of 20 ml, using [redacted] sodium chloride solution as diluent.

(See Supplement 2 for Item 5(b).

Item 6:

I^{131} will be obtained as sterile buffered water.

I^{132} will be obtained as I^{132} in HCl. This will be processed as follows:

1) Shipment will be diluted to total volume of 20 ml/ea, using sterile [redacted] saline as the diluent.
2) 1 N [redacted] will be added using phenol red as indicator to the point of color change.
3) 1.0 ml of this material will be given to two 3 week olds, intraperitoneally, and they will be observed for one hour prior to use of the material.
4) The diluted and neutralized shipment will be sterilized at 15 lbs. pressure for 20 minutes in an autoclave.
5) A sample taken prior to sterilization will be standardized using gold-leaf electroscope and G.M. tube, with reference to primary standards of uranium oxide.
6) The diluted, neutralized, sterilized, standardized solution will be administered with a calibrated sterile glass syringe, in permitted dosage.

I^{132}. This isotope will be received as NaI^{132}, and will be prepared as follows:

1) The shipment, 1.0 gm of NaI^{132}, will be dissolved in 50 ml of 0.1 N [redacted] solution, with agitation.
2) This solution will be filtered, and standardized using a gas-flow proportional counter, against uranium oxide primary standards.
3) Using this figure as a guide, the above solution will be diluted with [redacted] sodium chloride solution so that each 20 ml will contain 20 microcuries of I^{132}. This will provide a standard dose of 2 mg of NaI^{132} equivalent.
4) Phenol red will be added as indicator.
5) The material will be sterilized by autoclaving at 15 lbs. for 20 minutes.
6) 20 ml aliquots of the diluted material will be given intravenously using sterile calibrated glass syringes.

Form AEC 313a (3/56)	ATOMIC ENERGY COMMISSION **APPLICATION FOR BYPRODUCT MATERIAL LICENSE** SUPPLEMENT A—HUMAN USE—PAGE 3	Form approved. Budget Bureau No. 38-R027.3.

This page may be completed by the physician's preceptor (if any) in the medical use of radioisotopes. When the information is not furnished by the preceptor, the name and present address of the preceptor (if any) should be shown in Item 12 below.

9. (a) Using physician's name	(b) Name & address of applicant (if different from 9 (a))
[redacted]	[redacted]

10. Clinical Training and Experience of Physician Who Will Use Byproduct Material

A ISOTOPE	B CONDITION(S) DIAGNOSED OR TREATED	C NUMBER OF CASES	D TYPE OF PARTICIPATION FOR ALL CASES IN COLUMN C (circle applicable numbers of items in accordance with key set forth below)
I 131	Diagnosis of thyroid function		1 2 3 4
	Treatment of hyperthyroidism		1 2 3 4
	Treatment of thyroid cancer		1 2 3 4
	Treatment of cardiac conditions		1 2 3 4
	Brain tumor localization		1 2 3 4
	Blood determinations		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
P 32 Soluble	Treatment of polycythemia and leukemia		1 2 3 4
	Brain tumor localization		1 2 3 4
	Treatment of bone metastases		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
P 32 $CrPO_4$	Treatment of prostatic cancer		1 2 3 4
	Treatment of cervical cancer		1 2 3 4
	Treatment of pleural effusions and/or ascites		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
Au 198 Colloid	Treatment of prostatic cancer		1 2 3 4
	Treatment of cervical cancer		1 2 3 4
	Treatment of pleural effusions and/or ascites		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
Cr 51	Blood determinations		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
Other Isotopes			1 2 3 4
			1 2 3 4
			1 2 3 4

Key to above numbers (Column D) — Active Participation and Discussion

1. Examination of patients to determine suitability for radioisotope diagnosis and/or treatment and recommendations on dosage to be prescribed.
2. Collaboration in calibration and administration of dosages including related measurements and plotting of data.
3. Active period of training and experience of sufficient duration to permit follow-up of patients through treatment and post-treatment period including re-evaluation as to effectiveness and complications.
4. Study and discussion of case histories to establish most efficacious diagnostic and/or therapeutic techniques for this radioisotope use.

11. Total number of hours of participation in clinical training _____ hours

12. The training and experience indicated above was obtained under the supervision or guidance of

_____ at _____ _____
(Name of physician (preceptor)) (Institution) (Signature)

SUPPLEMENT 1

Item 5(b). Investigative Proposal

A. Background

Moore and co-workers (1,2,3), using isotope dilution methods, have shown that human beings can have gross altered body composition as a result of chronic disease, and that this state can be reversible following correction of the pathologic condition which caused the changes in composition. Moore has emphasized that isotope dilution methods can be used to follow long-term changes in nutrition in human beings in disease and during convalescence.

Data are available giving the results of determinations of total exchangeable sodium, total exchangeable potassium, and total exchangeable chloride in healthy adult human beings. Such values for total body water are also abundantly available. However, there is little information about the correlation of these parameters one with the other.

Recent work indicates that those aspects of body composition which are primarily aqueous, such as total exchangeable sodium, total exchangeable potassium and total exchangeable chloride, should be compared with simultaneously determined values for lean body mass (4-7) or total body water (8-9), in addition to body weight.

Edelman et al (10), studying total exchangeable potassium in edematous human beings, found that an equilibration period of 40 hours resulted in more satisfactory equilibrium than did one of 24 hours in these subjects.

In the light of these facts, there seems a need for additional measurements of total exchangeable chloride, and total exchangeable potassium, done in healthy adult human beings in conjunction with simultaneous measurements of total body water. Equilibrium periods for measurement of exchangeable potassium should be extended to 40 hours.

B. Instrumentation and Radioactivity Dosage

In performing measurements of total exchangeable potassium in human beings, it has been customary to use a radioactivity dose of 250-350 microcuries of K^{42} (11, 12, 13, 14). We have constructed a counter which enables us to reduce this dose to 50 microcuries, and still measure the activity remaining at 40 hours after administration.

This counter is a plastic wall scintillation counter, based on the work of Hine et al (15) and Michal et al (16), but improved so that it accepts a 10 ml volume without loss of efficiency. In liquid samples of this volume, it has an efficiency of 20% for K^{42}. By using spot urines as equilibration samples, and boiling them to 1/4th of their initial volume, we will be able to make satisfactory measurements by using 50 microcuries of K^{42}. Pilot studies justifying this dose reduction have been made with the help of Dr. Isidore S. Edelman, of University of California Medical School, San Francisco.

C. Proposed Experiments

1. Subjects. Twenty healthy adult human males and twenty healthy human females will be used as subjects. The following parameters will be determined at the same time in each subject:

Total exchangeable potassium (K^{42})
Total exchangeable chloride (Br^{82})
Total body water (H^3)

It is important to do these measurements in persons of each sex, in order to outline sex differences.

2. Isotope Doses:

K^{42}	- 50 microcuries	(0.050 rad)
Br^{82}	- 10 microcuries	(0.033 rad)
H^3	- 1 millicurie	(0.100 rad)
TOTAL		(0.183 rad)

Simultaneous administration of the above quantities of isotope will result in a dose of radioactivity within a recommended limit of 0.3 rem/week.

3. Condition for Measurement. Each subject will be in good health, and will be fasting for 12 hours prior to the time of sample collection. The women will not be measured within one week of a menstrual period, as fluid retention is associated with menstruation.

4. Administration of Dose. 20 ml of sterile, isotonic sodium chloride solution, containing the above amounts of radioactivity, will be given by vein under aseptic conditions. The individual isotope solutions will be tested biologically prior to administration.

5. The nude weight of each subject will be taken.

6. Samples:

a. Serum samples will be taken at 2 and 3 hours after administration of the dose for measurement of total body water.

b. All urine from the time of injection up to 40 hours after injection will be collected for measurement of excretion of radioactivity. Analysis will be done for K^{42} and Br^{82} activity.

c. Spot urine will be collected at 40 and 42 hours after administration for measurement of K^{42} specific activity. This will be done by differential gamma and beta counting as outlined by Hine et al (15).

d. Serum will be collected at 40 hours after administration for Br^{82} assay. Correction of the gamma count used for assay will be done by utilizing the potassium specific activity gained from the urine samples.

7. Calculations. The regression of total exchangeable potassium and total exchangeable chloride on body weight and total body water will be compared.

REFERENCES:

1. Moore, F.D., and Ball, M.R.: Metabolic Response to Surgery, Springfield, Charles C. Thomas, 1952.

2. Moore, F.D., Edelman, I.S., Olney, J.M., James, A.A., Brooks, L., and Wilson, G.M.: Body Sodium and Potassium. III. Interrelated Trends in Alimentary, Renal, and Cardiovascular Disease, Lack of Correlation Between Body Stores and Plasma Concentration. Metabolism 3: 334, 1954.

3. Wilson, G.M., I.S. Edelman, L. Brooks, Myrden, J.A., Harken, D.E., and Moore, F.D.: Metabolic Changes Associated With Mitral Valvuloplasty. Circulation 9: 199, 1954.

4. Weir, E.G.: Further Observations on Total Chloride Content. The Relation Between Body Fat and Body Chloride. Am. J. Physiol., 130: 606, 1940.

5. Cheek, D.B., and West, D.D.: An Appraisal of Methods of Tissue Chloride Analysis: The Total Carcass Chloride, Exchangeable Chloride, Potassium and Water of the Rat. J. Clin. Invest. XXXVI, 1744, 1956.

6. Ljunggren, Hakan: Studies on Body Composition With Specific Reference to the Composition of Obesity Tissue and Non-obesity Tissue. Acta Endocrinologica, supplementum 33, 1957.

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8. Anderson, E.C., Schuck, R.L., Perrings, J.D., and Langham, W.H. The Los Alamos Human Counter. Nucleonics, 1956, 14, 14 (No. 1).

9. Boling, E.A., Wilson, G.M., Dudley, H.A.F., and Moore, F.D. The Bromide Space and Total Exchangeable Chlorides: Their Determination With Br^{82} and Their Relationship to the Total Body Water. To be published.

10. O'Meara, M.P., Birkenfeld, L.W., Sotob, F.A., and Edelman, I.S. The Equilibration of Radiosodium (Na^{24}), Radiopotassium (K^{42}), and Deuterium Oxide (D_2O) in Hydropic Human Subjects. J. Clin. Invest. 1957, 36, 784.

REFERENCES (cont.):

11. Arvan, W.L., Vanderlinde, R.E., and Solomon, A.K. II. The Simultaneous Measurement of Exchangeable Body Sodium and Potassium Utilizing Ion Exchange Chromatography. J. Clin. Invest. XXXIII, 1008, 1954.

12. Robinson, C.V., Arvan, W.L., and Solomon, A.K. An Improved Method for Simultaneous Determination of Exchangeable Body Sodium and Potassium. J. Clin. Invest. XXXIV, 134, 1955.

13. Jones, A.H. Brooks, L., Edelman, I.S., Clancy, J.M., and Moore, F.D. Body Sodium and Potassium. I. Simultaneous Measurement of Exchangeable Sodium and Potassium in Man by Isotope Dilution. Metabolism, 1954, 3, 313.

14. Corvo, L., Jr., Clancy, J.M., Jr., Steinberg, E.W., Ball, M.E., and Moore, F.D. The Measurement of Exchangeable Potassium in Man by Isotope Dilution. J. Clin. Invest. 1950, 29, 1260.

15. Hine, G.J., Duncan, R.A., Ajl, L., Pollycove M., Rose, J.F., and Sexton, L.A. Scintillation Counting for Multiple-tracer Studies. Nucleonics, 13: 28, 1955.

16. Nichol, W.D., Brownell, G.L., and Mealey, J., Jr. Designing Sensitive Plastic-wall Counters for Beta Rays. Nucleonics, 14: 96, 1956.