Medical Center

University & Woodland Ave.
Philadelphia PA 19104

030-14526

Veterans Administration

JUN 1 1989

In Reply Refer To:
642/11R

U.S. Nuclear Regulatory Commission
Region I
475 Allendale Road
King of Prussia, PA 19406

RE: License NO. 37-00062-07

Dear Sir:

Please amend our by-product material license to include the following:

A possession limit of 1 mCi of C-14 labelled d-xylose for human use for the diagnosis of gastrointestinal bacterial overgrowth. FDA approval has been obtained (see enclosed IND 32,777). Enclosed for your review is a brief description of the procedure and the protocol, which has been approved by both the Radiation Safety Committee our facility's Research and Development Committee.

If you have any questions concerning this request, please contact the Radiation Safety Officer at (215) 823-5859. No amendment fee is required, as we are a Federal facility.

Sincerely,

"For and in the absence of"
ROBERT F. STOTT
Director

6/6/89
JAMES W. FLETCHER, M.D.
Director, Nuclear Medicine Service (115)
Veterans Administration
Washington, DC 20420

Enclosures

8912060094 890816
REG1 LIC30
37-00062-07 PDR

FEE EXEMPT

RECEIVED-REGION 1
89 JUN -9 P2:37

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JUN 09 1989

"America is #1—Thanks to our Veterans"

OFFICIAL RECORD COPY M10

CARBON-14

Chemical and/or Physical Form:	D-xylose
Possession Limit:	1 mCi
Description:	For diagnosis in humans of gastrointestinal bacterial overgrowth in the small bowel.
Patients:	To be used as an on-going diagnostic test in our facility's Nuclear Medicine Service on patients 18 years of age or older. Informed Consent will be received.
Dose:	Approximately 10 microcuries of Carbon-14 labelled D-xylose will be be orally administered to the patient.
Authorized User:	Radioactive material will be administered under the supervision of Dr. John Hansell. (Approved by Radiation Safety Committee, certified by the American Board of Nuclear Medicine, 1974).
Brief Description:	The patient will arrive fasting. Following, obtaining pre-test Expiratory Air Sample, the patient will receive an oral dose containing 10 microcuries of Carbon-14 labelled D-xylose and 1 gram of D-xylose in 250 ml of water. Following this administration, the patient will submit Expiratory Air Samples at 1/2, 1 and 2 hours. The samples will be calculated via scintillation counting as percent dose/mmol CO_2.

NOTICE FOR CLAIMED INVESTIGATIONAL EXEMPTION

FOR A NEW DRUG

FORM 1571

Name of Investigator: John R. Hansell, M.D.

Institution Name: Veteran Medical Administration Medical Center

Address: University and Woodland Avenues

Philadelphia, PA 19104

Date: March 27, 1987

I. The best descriptive name of the drug(s) is:
Carbon-14 D-xylose.

II. Complete list of components:

1. D-xylose
2. Carbon-14 D-xylose
3. Water

III. Final Quantitative Composition of drug:

1. 10 uCi of Carbon-14 D-xylose
2. 1 gm D-xylose

IV. Description of the Source Components of the New Drug

1. Carbon-14 D-xylose

Amersham Corporation
2636 Clearbrook Drive
Arlington Heights, IL 60005

2. D-xylose

Sigma Chemical Company
P.O. Box 14508
Saint Louis, MO 63178

V. Methods, Facilities, and Controls used for Synthesis, Processing of the New Drug

1. Method of Synthesis

Preparations are received from manufacturer with the specifications of 200 uCi of ^{14}C D-xylose/ml, 587.5 uCi/mg. Aliquots of this material are prepared by diluting with water such that each ml contains 10 uCi ^{14}C D-xylose (17 mcg).

The orally administered dose is prepared by adding to the aliquot (containing 10 uCi ^{14}C D-xylose), 1 gm of D-xylose.

The resultant mixture is diluted with water to a total volume of 250 ml. Unused aliquots are stored at -20 C until subsequently needed.

2. Facilities and Equipment

The preparation will be in the radiopharmaceutical preparative room of the Nuclear Medicine Service; Philadelphia VAMC, University and Woodland Avenues, Philadelphia, PA 19104.

The work will be under the supervision of investigator. Sterile precautions are unnecessary for the preparation of the oral dose.

a) Mettler Analytic Balance
b) Packard Tricarb Liquid Scintilliation Counter
c) Miscellaneous - piquettes, volumetric flasks, gloves.

3. Process Control

a) Quantity of radioactivity will be verified by using liquid scintillation counting using commercially available standards of carbon-14 (Packard Company) correcting for relative efficiency of counting system.

b) The specifications of the components used are as follows:

1. D-(U-^{14}C] xylose

Amersham Company
(Typical Shipment)
Specific Activity: 89.9 mCi/mMol
587.5 uCi/mg

Molecular Weight: 153

Radioactive concentration: 200 uCi/ml
Radiochemical purity:
by paper chromatography in
a) n - butanol: ethanol: water (52:33:15) 99%
b) n - butanol: pyridine: water (1:1:1) 99%
c) ethyl acetate: acetic acid: 2% phenol boronic acid (9:2:2) 99%

2. D-xylose

Sigma Chemical Company
X1500
Sigma Grade: 99-100% (pfs)
White Crystals

4. Dispensing and Processing

a) Those doses will be prepared by the Nuclear Medicine Service, Philadelphia VAMC as described in Section V, 2.

b) Dispensing and processing will be done by the investigator.

c) Records will be kept to insure identity of reagents, preparation sequence, and the individual performing the study.

d) It will be the responsibility of the investigator or his designee to obtain informed consent of the subject undergoing the procedure (Appendix).

e) Packaging and labeling: Individual doses will be prepared at initiation of each procedure. The dose will be administered in same room dose that the dose is prepared.

VI. Preclinical and Clinical Investigations to Establish the Safety and Efficiency of D-xylose absorption studies.

Chemical Investigation

a) D-xylose, an aldopentose, is absorbed by the proximal small intestine wherein small amounts of the absorbed sugar are oxidized in the liver and other tissues.

Though the sugar is not found in significant quantities in the human body, doses of 25 gm of d-xylose may result in serum levels of approximately 35 mg/dL one to two hours following oral administration.

About 40 percent of the absorbed dose is excreted in the urine and approximately 20 percent in the breath. The use of stable d-xylose and its chemical quantititation in urine has been used as a measurement of gastrointestinal carbohydrate absorption.

b) Radiolabeled d-xylose is also absorbed in the same manner as its stable form. The degree to which its major metabolite, $^{14}CO_2$, appears in the breath of an individual receiving this substance is indicative of both mucosal absorption and celluar metabolism of the sugar as well as its oxidation by bacteria within the gastrointestinal tract. The degree to which $^{14}CO_2$ is eliminated in the breath above normal levels is a means to detect small intestinal bacterial overgrowth.

Individuals with mucosal absorption abnormalities, however, may mask positive findings associated with bacterial colonization of the small bowel. Among the major prerequisites of the study are the choice of the dose which has an optimum specific activity and the specific times at which breath samples are procured to produce the most clinically significant findings. King, et al., have found that reduction of carrier d-xylose to 1 gram results in an increased radioconcentration in the small intestine and a lowered osmotic-related passage of the substance into the colon, thus increasing the study's specificity and sensitivity. False positive and negative studies are lessened by the simultaneous administration of technetium - 99m sulfur colloid or diethylenetriaminepentacetic acid (DTPA) in the test dose. The adequate and timely gastric emptying as well as the premature presence of the dose within the colon, at the time of sampling can be verified.

Breath samples are procured prior to the administration of

an oral dose of 10 uCi of xylose as well as 1/2, 1 and 2 hours afterward. Later sampling may be necessary if delayed gastric emptying observed on the scintigrams.

King et al., also have found with the oral administration of 10 uCi of ^{14}C d-xylose and 1 gm d-xylose was significantly elevated in patients with small intestinal bacterial overgrowth as compared to controls ($P<0.05$ at 30 min. $P<0.01$ thereafter). No false negative or positive studies were observed in their series of 14 abnormal patients and 8 normal. Their work was further supported in subsequent review articles. *(1,2,3,4)

We wish to use this study to diagnose bacterial overgrowth.

The drug has not been marketed outside the United States.

c) Drug is not a part of a previously investigated preparation.

d) Radiation Dose Estimates:

** See next page **

Dose (rad) = 73.8 x E x T 1/2

E = 0.155 MeV
Conc = 10 uCi/70,000 g

35% excreted in urine
20% oxidized
45% fecal

T 1/2 blood act = 90 min = 0.0625 days
= 0.77%/min

Assume worse scenario T 1/2 = 1 day for WB (Allowable Radiation)

Dose (whole body) = $73.8 \times \frac{10}{70{,}000} \times 0.155 \times 1 = 1.60$ m Rad (5 Rem)

Dose (kidney) = $73.8 \times \frac{10 \times .35}{310} \times 0.155 \times 6/24 = 32.2$ m Rad (15 Rem)

Dose (small bowel) = $73.8 \times \frac{(10 \times .45)}{(640\ gm)} \times 0.155 \times 4/24 = 13.4$ m Rad (15)

Dose (upper large int.) = $73.8 \times \frac{(10 \times .40)}{(210)} \times 0.155 \times 8/24 = 7216$ m Rad (15)

Dose (lower large int.) = $73.8 \times \frac{(10 \times .40)}{(160)} \times 0.155 \times 18/24 = 214$ m Rad (15)

Dose (lungs) = $73.8 \times \frac{(10 \times .40)}{(1000)} \times 0.155 \times 1/24 = 1.9$ m Rad (15)

Seltzer RA, Keriebkes JB, Sainger EL: Radiation Exposure from Radiorsotopis in Pediatrics: NEJM 271; 84, 1964

MIRD Pamphlet #4, SNM, 1969.

VII. The study wherein radiocarbon labeled d-xylose is administered orally for the detection of bacterial overgrowth has been widely published. * (1,2,3,4)

Other than radiation to the patient, which is within acceptable levels, there is no known contraindications, hazards, or side-effects of the drug.

VIII. The sponsor should be knowledgeable of the methodology of gastro-intestinal absorption measurement with competence in the use of by product material in the laboratory and its administration to human beings.

IX. Curriculum vitae of principal investigator is submitted. There are no other investigators.

X. Chemical Evaluation of radiocarbon-labeled d-xylose for the Dectection of Small Intestinal Bacterial Overgrowth.

a) Name and Address of Investigator

John R. Hansell, M.D.
Veterans Administration Medical Center
University and Woodland Avenues
Philadelphia, PA 19104

b) Objective of Rational:

The procedure is performed to define the presence or absence of bacterial overgrowth in the small bowel. The presence of bacteria will result in increased intestinal absorption and resultant oxidation and elimination in breath. The presence of increased

activity of radiocarbon dioxide at 2 hours following dosage is indicative of the presence of bacterial decomposition of the x-ylose. The results are reported as percent of administered dose per millimole of reopued CO_2.

c) Patient Selection

Individuals to be studied will be 18 years of age or older and non-pregnant who will exhibit signs and symptoms compatible with intestinal bacterial overgrowth.

The patient will be advised as to why the procedure is being done, what the study does and what is required of the patient. The patient consent form will be presented and signed by the patient prior to the beginning of the study.

d) Methods

The patient will arrive fasting and in a state approximating that of basal metabolism. Following obtaining a pretest expiratory air sample, the patient will receive a dose containing 10 microcurees of carbon-14 labeled d-xylose and 1 gm of d-xylose in 250 ml water. following the oral administration of this dose, the patient will submit expiratory air samples at 1/2, 1, and 2 hours. The response will be calculated as percent dose/ mmol CO_2.

e) Criteria for Efficacy

Findings will be correlated will clinical symptoms and signs, radiologic procedures of the small intestine,

procurement of intestinal biopsy or culture where indicated, or comparison to values obtained with this test following antibiotic therapy.

f) Observations and/or Measurements for Safety Determination

Untoward reactions, if they were to occur, will be recorded in clinical report.

g) Case Report Form

A standard clinical evaluation/information form will be completed for each study (see Appendix).

Principle Investigator

John R. Hansell, M.D.
Chief, Nuclear Medicine
VAMC
University and Woodland Avenues
Philadelphia, PA 19104

References

1. King CE, Toskis PP, Spivey JC, Lorenz E, and Wilkos S: Detection of Small Intestine Bacterial Overgrowth by Means of a 14C-D-xylose Breath Test, Gastroenterology 77: 75-82, 1979.

2. King CE, and Toskis PP: Breath Tests in the Diagnosis of Small Intestine Bacterial Overgrowth Critical Reviews, Chemical Laboratory Sciences 21: 269, 1985.

3. Fromm H, and Saroa R: Tests of Intestinal Absorption Using Carbon-14-Labeled Isotupes, Nuclear Medicine: Quantitative Procedures, ed. Wahner HW, Little Brown, 1983,

4. Caspary W: Breath Tests, Clinical, Gastroenterology 7: 351-374, 1978.

CLINICAL CASE REPORT FORM

CARBON-14 D-XYLOSE ABSORPTION STUDY

I. This is to verify that all needed referrals and review have been made to accept their patient into this clinical study. The patient has been instructed regarding this study, and has completed and signed an informed consent form.

_____

Principle Investigator's Signature Date

II. Patient Information

Name: _____

SS: _____

Referring Patient: _____

Age: _____ Sex: _____ Weight: _____ Height: _____

Patient History _____

_____

_____

_____

III. Chemical Data

Reason for study: _____

Diarrhea: _____

Vomiting: _____

Abdominal Pain (Cramps): _____

Stool Character: _____

Therapeutic Regimen: _____

Radiologic Findings: _____

Bacterial Cultures: _____

IV. Stuc, Specifications

Standard Activity: _____

Standard Dilution: _____

Background Sample: _____

1/2 hour sample activity

1 hour sample activity

2 hour sample activity

Percent dose/m mol CO_2

1/2 hr _____

1 hr _____

2 hrs _____

V. Dose Specification

1) Quantity (uCi): _____

2) Lot# (Amersham): _____

3) Date Of Preparation and Study: _____

VI. Interpretation

Negative: _____

Consistent with Bacterial Overgrowth: _____

_____

Consistent with Treatment In Bacterial Overgrowth:

_____

_____

INFORMED CONSENT FORM

1) I, _____, voluntarily consent to participate in an investigation entitled: Detection of Bacterial Overgrowth using Radioactive-14 Labeled d-xylose.

2) I understand that I will receive a liquid dose containing 10 microcuries of carbon-14 labeled d-xylose, a sugar, and a small quantity (1 gram) of non-radioactive sugar in water. Immediately, prior to the study, I will offer an expiratory breath sample (by blowing into a tube for 4-5 minutes, and at 1/2, 1, and 2 hours after I receive the dose.

3) The sugar I ingest will be absorbed by my intestine and excreted in my bowel movements, urine, and breath. In those conditions which are characterized by the presence of bacteria in my small intestine, the sugar will be eliminated primarily in my breath. By measuring the radioactivity in my breath, and observing a higher elimination rate of the sugar, my doctor may predict the presence of bacteria in my small intestine.

4) This procedure is an easy method to diagnose the presence of abnormal amounts of bacteria in my intestine. While this dose present a small amount of radiation to my body, it is rapidly eliminated, and the amount of radiation is minimal compared to many studies done using x-ray. Though, we cannot guarantee no reaction to the ingested sugar, there have been no such cases known at this time.

5) Alternative methods to diagnose this entity would be to have inserted a tube through my mouth to the small intestine for sampling. This procedure does not require this.

6) Though, this study has technically been referred as a research procedure, it is being done for the clinical diagnosis of your condition.

7) As a part of this agreement to participate in this study, I acknowledge to have read or explained to me the agreement entitled, " Part 1: Agreement to Participate in Research by or under the Direction of the Veterans' Administration", VA Form 10-1086, and that this form is a part of that agreement.

8) If I sustain any physical injury related to my participation in this study, I understand that I will be entitled to medical care and treatment, and in some circumstances, compensation may also be payable under USC 351 or under the Federal Tort Claims Act.

9) If I need information in addition to that which is provided, I may contact the VA Medical Center Patient's representative, Mr. Eugene Montgomery at 382-2400 X6622.

Amersham

Radiochemical Batch Analysis Results

D-[U-^{14}C]XYLOSE
Code CFB.59
Batch 32

Batch analysis sheet C/2550

D-[U-^{14}C]Glucose is prepared photosynthetically from [^{14}C]carbon dioxide and converted into 1,2-O-isopropylidene-D-[U-^{14}C]glucose which is oxidised with periodate. The oxidation product is reduced and then hydrolysed to give D-[U-^{14}C]xylose which is purified by paper chromatography.

BATCH TECHNICAL DATA

Specific activity	:	39.9	mCi/mmol	(3.33 GBq/mmol)
		587.5	uCi/mg	(21.74 MBq/mg)
Molecular weight	:	153	(at this specific activity)	
Radioactive concentration	:	200	uCi/ml	(7.40 MBq/ml)

Radiochemical purity

by paper chromatography in

(a) n-butanol:ethanol:water (52:33:15) (system 102)	:	99%
(b) n-butanol:pyridine:water (1:1:1) (system 55)	:	99%
(c) ethyl acetate:acetic acid:2% phenyl boronic acid (9:2:2) (system 98)	:	99%

Analysed 4th February 1982

Packaging and Storage

D-[U-^{14}C]Xylose is supplied in aqueous solution containing 3% ethanol. The solution is sterilized by 'Millipore' filtration to minimise loss by microbiological action, but is not offered as suitable for injection. The material is dispensed under aseptic conditions in borosilicate multidose vials with additional screw cap ("Duoseal" vial).

Under the influence of its own radiation this material is likely to decompose to an extent of about 1% per year at -20°C, the temperature at which it has been stored between preparation and the time of despatch. At room temperature in the unopened tube the annual rate of decomposition may rise to 2-3%.

To ensure that our products are always of the highest standard, each batch of this compound is analysed by our Quality Control Department at intervals based on our experience of the stability of previous batches.

PART II - AGREEMENT OF SUBJECT'S REPRESENTATIVE TO ALLOW SUBJECT TO PARTICIPATE IN RESEARCH BY OR UNDER THE DIRECTION OF VETERANS ADMINISTRATION

DATE

1. I, _____ (Type or print name of subject's representative) an authorized to give consent

_____ (Type or print subject's name) by virtue of _____ (Relationship, legal appointment, etc.)

I voluntarily consent for this person to participate as a subject in the investigation entitled _____ (Title of study)

2. I have signed one or more information sheets with this title to show that I have read the description including the purpose and nature of the investigation, the procedures to be used, the risks, inconveniences, side effects, and benefits to be expected, as well as other courses of action open to me and my right to withdraw the subject from the investigation at any time. Each of these items has been explained to me by the investigator in the presence of a witness. The investigator has answered my questions concerning the investigation and I believe that I understand what is intended.

3. I understand that no guarantees or assurances have been given me since the results and risks of an investigation are not always known beforehand. I have been told this investigation has been carefully plannned, that the plan has been reviewed by knowledgeable people, and that every reasonable precaution will be taken to protect the well-being of the subject.

4. In the event the subject sustains physical injury as a result of participation in this investigation, if the subject is eligible for medical care as a veteran, all necessary and appropriate care will be provided. If the subject is not eligible for medical care as a veteran, humanitarian emergency care will nevertheless be provided.

5. I realize I have not released this institution from liability for negligence. Compensation may or may not be payable, in the event of physical injury arising from such research, under applicable federal laws.

6. I understand that all information obtained about the subject during the course of this study will be made available only to doctors who are taking care of the subject and to qualified investigators and their assistants where their access to this information is appropriate and authorized. They will be bound by the same requirements to maintain the subject's privacy and anonymity as apply to all medical personnel within the Veterans Administration.

7. I further understand that, where required by law, the appropriate federal officer or agency will have free access to information obtained in this study should it become necessary. Generally, I may expect the same respect for the subject's privacy and anonymity from these agencies as is afforded by the Veterans Administration and its employees. The provisions of the Privacy Act apply to all agencies.

8. In the event that research in which the subject participates involves certain new drugs, information concerning the subject's response to the drug(s) will be supplied to the sponsoring pharmaceutical house(s) that made the drug(s) available. This information will be given to them in such a way that the subject cannot be identified.

I _____
NAME OF SUBJECT'S REPRESENTATIVE

HAVE READ THIS CONSENT FORM. ALL MY QUESTIONS HAVE BEEN ANSWERED, AND I FREELY AND VOLUNTARILY CHOOSE THAT THE SUBJECT PARTICIPATE. I UNDERSTAND THAT THE SUBJECT'S RIGHTS AND PRIVACY WILL BE MAINTAINED. I AGREE TO THE SUBJECT'S PARTICIPATION AS A VOLUNTEER IN THIS PROGRAM.

9. Nevertheless, my consent for the subject's participation in the investigation is limited as follows:

ADDRESS OF SUBJECT'S REPRESENTATIVE (Print or type)	SIGNATURE OF SUBJECT'S REPRESENTATIVE
WITNESS'S NAME AND ADDRESS (Print or type)	WITNESS'S SIGNATURE
SUBJECT'S NAME (Print or type)	SUBJECT IS NOW A PATIENT AT (Name - VA Facility)
INVESTIGATOR'S NAME (Print or type)	INVESTIGATOR'S SIGNATURE

☐ Signed information sheets attached. ☐ Signed information sheets available at

SUBJECT'S IDENTIFICATION (I.D. plate or print name - last, first, middle)	SUBJECT'S I.D. NO.	AGE	WARD

AGREEMENT BY SUBJECT'S REPRESENTATIVE TO PARTICIPATE IN RESEARCH BY OR UNDER THE DIRECTION OF THE VETERANS ADMINISTRATION

☆ U.S. Government Printing Office: 1981—341-488/4219

Curriculum Vitae

Date: February 17, 1987

John Royer Hansell

Home Address: 2051 Berks Road
Lansdale, Pennsylvania 19446

Office Address: Nuclear Medicine Service
Veterans Administration Medical Center
University and Woodland Avenues
Philadelphia, PA 19104

Social Security Number: 144-30-7526

Education:

1949-53	A.B.	University of Pennsylvania
1953-57	M.D.	Jefferson Medical College

Postgraduate Training and Fellowship Appointments:

1957-58	Rotating Intern, Germantown Hospital and Dispensary, Philadelphia
1958-61	Pathology Resident, Germantown Hospital and Dispensary, Philadelphia
1961-62	Pathology Resident, Bryn Mawr Hospital, Bryn Mawr
1962-63	American Cancer Society Pathology Fellow, New England Deaconess Hospital, Boston
1966-67	Pathology Fellow (Nuclear Medicine) Mayo Foundation, Rochester

Military Service:

1963-65	Laboratory Director, USPHS Indian Hospital, Gallop
1965-66	Staff Pathologist, USPHS, Armed Forces Institute of Pathology, Washington

Faculty Appointments:

1967-70	Assistant Professor of Radiology, Womens Medical College of Pennsylvania
1970-73	Assistant Professor of Radiology, Medical School of the University of Pennsylvania
1973-	Associate Professor of Radiology, Medical School of the University of Pennsylvania

Hospital and Administrative Appointments:

1967-	Chief, Nuclear Medicine Service Veterans Administration Medical Center Philadelphia

Specialty Certification:

1963	American Board of Pathology, Anatomic Pathology
1965	American Board of Pathology, Clinical Pathology
1974	American Board of Pathology, Radioisotopic Pathology
1974	American Board of Nuclear Medicine

Licensure: Pennsylvania

Awards, Honors and Membership in Honorary Societies:

NA

Memberships in Professional and Scientific Societies

National Societies:

National Council for Clinical Laboratory Standards from Society of Nuclear Medicine (Liaison Member, 1978-)
Council for Clinical Laboratory Standards (Member)
Survey Committee, College of American Pathologists (Member)
Ligand Assay Resource Committee, College of American Pathologists (Chairman, 1972-80; member 1980-)
Ligand Assay Task Force, National Council for Clinical Laboratory Standards (Member, 1980-82)
Task Force 18B, National Committee for Radiation Measurement and Protection (Member)
American Board of Pathology (Examination Committee, 1974-84)
American Board of Science in Nuclear Medicine (Examination Committee, 1978)
Certification and Competence Committee, Society of Nuclear Medicine (Member, 1976-85)
Self-Assessment Examination Committee, Society of Nuclear Medicine (Member)
American Board of Nuclear Medicine (Member, 1984-89; Vice-Chairman, 1986-87)
Nuclear Medicine Resource Committee, Society of Nuclear Medicine (Chairman, 1972-75, 1982-83; liaison member, 1986-)
Federated Council of Nuclear Medicine Organizations (Treasurer, Secretary, 1976-86)
Joint Review Committee on Educational Programs in Nuclear Medicine Technology (Member, 1980-87)

Editorial Positions:

1976- Advisory Board, Critical Reviews in Clinical Laboratory Services (Member)

Principal Investigator of Grants:

NA

Academic Committees at the University of Pennsylvania:

NA

Major Teaching and Clinical Responsibilities at the University of Pennsylvania:

NA

Lectures by Invitation:

NA

Bibliography:

Original Papers

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Hansell, J.: Invitation paper X Triennial World Congress of Pathology, Rio De Janeiro, 1978.

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Hansell, J.: An evaluation of thyroxine kits, 1979. Pathologist 33:590-592, 1979.

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Alavi, J. B., Hansell,J. R.: Labeled cells in the investigation of hematologic disorders. Semin Nucl Med 14:208-225, 1984.

Lluberas-Acosta, G., Hansell, J. R., Schumacher, H. R.: Paget's disease of bone in patients with gout. Arch Intern Med 146:2389,2392, 1986.

Abstract

NA

Editorials, Reviews, Chapters:

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In-Vitro Procedures in Quality Assurance in Nuclear Medicine, p 61-7. HHS Publication FDA 84-8224

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

INSTRUCTIONS: Complete all items for each application. Items may be completed by referring to earlier applications made on this form which are on file in the Radiation Safety Office. (Items 1, 2, 3, 4, 5, 6(a), 6(c), 7, 8(a), 10(b), 12, 13, 15, 16, 17, 18, appear on AEC application form 313.)

1. (a) NAME AND SHIPPING ADDRESS OF APPLICANT (Institution, firm, hospital, person, etc.)	(b) ADDRESS(ES) AT WHICH BYPRODUCT MATERIAL WILL BE USED (If different from shipping address)
John R. Hansell, M.D. Nuclear Medicine Service, VAMC University & Woodland Ave., Philadelphia, PA 19104	

2. DEPARTMENT TO USE BYPRODUCT MATERIAL

Nuclear Medicine Service

3. INDIVIDUAL USER (Name and title of individual(s) who will use or directly supervise use of byproduct material)

John R. Hansell, Chief, Nuclear Medicine Service

4. RADIOLOGICAL SAFETY OFFICER (Name of person qualified in radiological safety, if other than individual user)

Diana Snyder, H.P.

5. PREVIOUS LICENSE OR AUTHORIZATION NUMBER (If this is an application for renewal of a license for byproduct material obtained under a prior license or authorization for radioisotope procurement)

Currently authorized to use byproduct material on VAMC license.

BYPRODUCT MATERIAL OR IRRADIATION SERVICE DESIRED

6. (a) BYPRODUCT MATERIAL (Element and mass number)	(b) CHEMICAL AND/OR PHYSICAL FORM (Or catalog number)	(c) HALF LIFE
Carbon-14	d-xylose	5730 years

7. IF IRRADIATION SERVICE IS DESIRED, STATE PERTINENT DETAILS SUCH AS: CHEMICAL COMPOSITION AND WEIGHT IN GRAMS OF TARGET MATERIAL, RADIOACTIVITY, IRRADIATION TIME IN DAYS, AND NEUTRON FLUX

N/A

8. (a) MAXIMUM AMOUNT OF BYPRODUCT MATERIAL IN MILLICURIES YOU WILL POSSESS AT ANY ONE TIME

200 uCi

(b) ESTIMATED YEARLY AMOUNT NEEDED

400 uCi

(c) ESTIMATED MAXIMUM AMOUNTS TO BE USED PER EXPERIMENT AND FREQUENCY OF EXPERIMENTS

10 uCi

CERTIFICATE

THE UNDERSIGNED HAS READ "THE RADIATION SAFETY GUIDE, PHILA. V.A. HOSPITAL" AND ACCEPTS HIS RESPONSIBILITIES AS USER OF RADIOISOTOPES AS DESCRIBED THEREIN.

April 24, 1987
(Date)

John R. Hansell
(Signature of applicant)

THE RADIATION SAFETY COMMITTEE APPROVES THIS APPLICATION

DS
(Signature of Committee Chairman or his authorized representative)

PHILADELPHIA VETERANS ADMINISTRATION HOSPITAL

LICENSE NUMBER _____

John R. Hansell
(Signature of Committee Chairman of the PHILADELPHIA VETERANS ADMINISTRATION

	PER DISINTEGRATION	H_2O	Pb or	
0.156	100%	--	--	--

10. (a) DESCRIBE PURPOSE FOR WHICH BYPRODUCT MATERIAL WILL BE USED (Use Supplement A for human use, Supplement B for sealed sources)

Used as an oral agent to estimate presence of small intestinal bacterial overgrowth. Dosage will be monitored using Tri-Carb Liquid Scintillation Counter, determining efficiency with carbon-14 standards.

(b) EVALUATE POTENTIAL HAZARDS FROM HANDLING AND STORAGE OF BYPRODUCT MATERIAL AND DESCRIBE PROCEDURES PLANNED MINIMIZE THEM (Include survey and monitoring plans)

The quantities of radioactiosity are minimal and pose no large irradiational hazard. Nevertheless, precautionary use of gloves, monthly wipe test and biological testing after use of material.

(c) WHAT IS THE RADIOTOXICITY OF THIS MATERIAL? (metabolism, etc.)

No significant toxicity. See radiation estimates in FDA application.

(d) WHAT RADIOACTIVE WASTES ARE EXPECTED IN THIS WORK AND DESCRIBE PROPOSED METHODS OF DISPOSAL

Residual radioactivity will eliminate by patient in respiration, urine and feces.

11. (a) LIST PERSONNEL WHO WILL WORK ON THIS PROJECT AND ESTIMATE AS WELL AS POSSIBLE MAXIMUM LEVEL OF RADIATION EXPOSURE FOR EACH

John R. Hansell - Administer and prepare dose.

B. McGlone)
B. Whiteman) Obtain breath samples
S. Moore)

Minimal non-detectable radiation exposure should be experienced.

TRAINING AND EXPERIENCE WITH RADIOACTIVITY OF INDIVIDUAL USER NAMED IN ITEM 5

If Radiological Safety Officer named in Item 4 is different from individual user, or if there is more than one individual user, use supplementary sheet to provide equivalent information to that requested in Items 12 and 13 for this (these) person(s).

12. TYPE OF TRAINING	WHERE TRAINED	DURATION OF TRAINING	ON THE JOB (Circle answer)	FORMAL (Circle answer)
a. Principles and practices of radiation protection	Certified ABNM, 1974		Yes No	Yes
b. Radioactivity measurement standardization and monitoring techniques and instruments			Yes No	Yes
c. Mathematics and calculations basic to the use and measurement of radioactivity			Yes No	Yes
d. Biological effects of radiation			Yes No	Yes

13. ISOTOPE HANDLING EXPERIENCE Certified ABNM, 1974

ISOTOPE	MAXIMUM AMOUNT	WHERE EXPERIENCE WAS GAINED	DURATION OF EXPERIENCE	TYPE OF USE

PHYSICAL FACILITIES, EQUIPMENT, AND RADIATION INSTRUMENTATION

14. RADIATION DETECTION INSTRUMENTS (Use separate sheet if necessary)

TYPE OF INSTRUMENTS (Include make and model of each)	NUMBER AVAILABLE	RADIATION DETECTED	SENSITIVITY RANGE (mr/hr)	WINDOW THICKNESS (mg/cm^2)	USE (Monitoring, surveying, measuring)

15. FILM BADGES, DOSIMETERS, AND OTHER PERSONNEL MONITORING DEVICES INCLUDING BIO-ASSAY PROCEDURES
Film badges will be worn as part of routine job requirements. Assay of urine of principal investigator following study.

16. METHOD, FREQUENCY, AND STANDARDS USED IN CALIBRATING INSTRUMENTS LISTED ABOVE (For film badges specify method of calibration and processing, or name supplier)

N/A

17. (a) DESCRIBE BRIEFLY REMOTE HANDLING EQUIPMENT, STORAGE CONTAINERS, SHIELDING, AND LABORATORY FACILITIES (Hoods, special areas, fume hoods, etc.)

Routine use of syringes, needles, vials and paper cups (disposable)
Storage of prepared dose in freezer.

(b) SKETCHES OF SUCH FACILITIES ARE ATTACHED (Circle answer)

INFORMED CONSENT FORM

1. I,_____, voluntarily consent to participate in an investigation entitled: Detection of Bacterial Overgrowth using radioactive Carbon-14 labeled d-xylose. The purpose of this study is to determine whether I have an abnormal amount of bacteria in my small intestine.

2. I understand that I will receive a liquid dose containing a small quantity of a radioactive sugar, 10 microcuries of carbon-14 d-xylose, mixed in water and a larger amount (1 gm) of the non-radioactive form of the sugar. The amount of radiation to my body would be less than that caused by a lower gastrointestinal x-ray.

3. The study will consist of receiving the above described oral dose as well as offering samples of my expired breath. This collection of breath samples will be taken prior to the dose, 1/2, 1 and 2 hours afterwards. The breath samples will be taken by my breathing into a tube for about 4 to 5 minutes.

4. The sugar which I ingest will be absorbed by my intestine and excreted in my bowel movements, urine and breath. In those conditions which are characterized by the presence of bacteria in my small intestine, the sugar will be eliminated more rapidly in my breath. By measuring an increased concentration of radioactivity in my breath, my doctor may predict the presence of bacteria in my small intestine.

5. The alternative method to diagnose this entity would be to have inserted through my mouth a tube for sampling of my intestinal contents. This procedure does not require this.

6. Though, one cannot guarantee no reaction to the ingestion of this sugar, there are no known cases which have produced a demonstrable side-effect.

7. I understand that should I decline to participate in performing this study, my care in this medical facility will not be jeopardized. If I were to sustain any physical injury related to my participation in this study, I understand that I will be entitled to medical care and treatment, and in some circumstances, a compensation may be payable under 38 USC351 or under the Federal Tort Claims Act.

8. Further information concerning this study may be obtained from John R. Hansell, M.D., Chief, Nuclear Medicine Service (215-823-5865). If you feel you have been harmed in any way, you may contact the VA Medical Center Patient's Representative, Mr. Eugene Montgomery (215-382-2400, Extension 6622.

SIGNATURES

1. COUNSELING PHYSICIAN: I have counseled this patient as to the nature of the proposed procedure(s), attendant risks involved, and expected results, as described above.

(Signature of Counseling Physician)

2. PATIENT: I understand the nature of the proposed procedure(s), attendant risks involved, and expected results, as described above, and hereby request such procedure(s) to be performed.

(Signature of Witness) (Signature of Patient) (Date and Time)

MB-10

(FOR LFMS USE)
INFORMATION FROM LTS

PROGRAM CODE: 02110
STATUS CODE: 0
FEE CATEGORY: EX 7B
EXP. DATE: 19910228
FEE COMMENTS: 170.11(A)(5)

BETWEEN:

LICENSE FEE MANAGEMENT BRANCH, ARM
AND
REGIONAL LICENSING SECTIONS

LICENSE FEE TRANSMITTAL

A. REGION

1. APPLICATION ATTACHED
APPLICANT/LICENSEE: V. A. MEDICAL CTR.
RECEIVED DATE: 890609
DOCKET NO: 3014526
CONTROL NO.: 110826
LICENSE NO.: 37-00062-07
ACTION TYPE: AMENDMENT

2. FEE ATTACHED
AMOUNT: ---Ø---
CHECK NO.: ---Ø---

3. COMMENTS

SIGNED EJM
DATE 12 JUN 89

B. LICENSE FEE MANAGEMENT BRANCH (CHECK WHEN MILESTONE 03 IS ENTERED /__/)

1. FEE CATEGORY AND AMOUNT: ----------

2. CORRECT FEE PAID. APPLICATION MAY BE PROCESSED FOR:
AMENDMENT ----------
RENEWAL ----------
LICENSE ----------

3. OTHER ----------

SIGNED ----------
DATE ----------