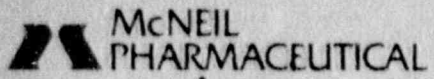


030-06212

X



McNEIL
PHARMACEUTICAL

SPRING HOUSE, PA 19477-0776 (215)628-5000

May 23, 1988

U. S. Nuclear Regulatory Commission
Region 1
Nuclear Materials Safety Section B
475 Allendale Road
King of Prussia, PA 19406

Re: Byproduct Materials License No. 37-09743-01

Gentlemen:

McNeil Pharmaceutical is submitting, in duplicate, a request to renew the above Byproduct Materials License. The license is currently due to expire on June 30, 1988. This submission is accompanied by a check for \$460.00 as the fee for renewal under Category 3(M) - Possession and Use of Byproduct Material for Research and Development.

The last application for renewal was dated May 18, 1983. The letters and applications that have been submitted since that date have been reviewed. We submit that application; the letter dated July 15, 1983 supplying additional information; the applications dated April 12, 1984, May 31, 1984 and June 12, 1987, together with the letter of understanding dated November 16, 1987 as reflecting the current state of the McNeil Pharmaceutical radiation safety program, with the following changes:

Section 7

The following people are to be removed from the list of those who use, or supervise, the use of radioactive materials:

- C. A. Janicki, Ph.D.
- T. Kiorpes, Ph.D.
- J. Plostnieks, Ph.D.

License Fee Information
on Application

1988 MAY 25 PM 2:34
RECEIVED-REGION 1

9001160351 881129
REQ1 LIC30
37-09743-01 PDR

108958
5-25-88

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Page Two
Byproduct Materials License No. 37-09743-01
May 23, 1988

Please add the following names to the list of persons using, or supervising, the use of radioisotopes:

J. A. Buben, Ph.D.
M. L. Holland, Ph.D.
E. S. Kimball, Ph.D.
S. P. Sit, Ph.D.
W. Nan Wu, Ph.D.

The training and history of radioisotope usage for these people is attached in Appendix 1.

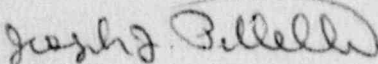
Section 9

The instruments for measuring radiation are listed in Appendix 2. This list supercedes the lists given in the May 18, 1983 application, and prior letters.

Finally, the change in reporting mentioned in the November 16, 1987 letter of understanding, has taken place. Some of the people listed as supervisors of radioisotope usage are now members of the Janssen Research Foundation. All safety and radiation safety programs for that group are under the aegis of McNeil Pharmaceutical personnel. This means that McNeil Pharmaceutical is responsible for developing and administering the radiation safety programs, monitoring, training, auditing and procedures for this group, in addition to the rest of McNeil Pharmaceutical operations. All radioisotope usage continues to be located at the Spring House site, only.

Should you have any questions regarding this application, please contact the Radiation Safety Officer, Brian E. Reynolds, Ph.D., C.I.H., at (215) 628-5858.

Sincerely,



Joseph J. Pittelli, M.D.
Vice President, Scientific Affairs

JJP:ma
Enclosure

APPLICATION FOR MATERIAL LICENSE

030-06212

INSTRUCTIONS: SEE THE APPROPRIATE LICENSE APPLICATION GUIDE FOR DETAILED INSTRUCTIONS FOR COMPLETING APPLICATION. SEND TWO COPIES OF THE ENTIRE COMPLETED APPLICATION TO THE NRC OFFICE SPECIFIED BELOW.

APPLICATIONS FOR DISTRIBUTION OF EXEMPT PRODUCTS FILE APPLICATIONS WITH:

U.S. NUCLEAR REGULATORY COMMISSION
DIVISION OF FUEL CYCLE AND MATERIAL SAFETY, NMSS
WASHINGTON, DC 20545

ALL OTHER PERSONS FILE APPLICATIONS AS FOLLOWS. IF YOU ARE LOCATED IN:

CONNECTICUT, DELAWARE, DISTRICT OF COLUMBIA, MAINE, MARYLAND, MASSACHUSETTS, NEW HAMPSHIRE, NEW JERSEY, NEW YORK, PENNSYLVANIA, RHODE ISLAND, OR VERMONT, SEND APPLICATIONS TO:

U.S. NUCLEAR REGULATORY COMMISSION, REGION I
NUCLEAR MATERIALS SAFETY SECTION B
475 ALLENDALE ROAD
KING OF PRUSSIA, PA 19406

ALABAMA, FLORIDA, GEORGIA, KENTUCKY, MISSISSIPPI, NORTH CAROLINA, PUERTO RICO, SOUTH CAROLINA, TENNESSEE, VIRGINIA, VIRGIN ISLANDS, OR WEST VIRGINIA, SEND APPLICATIONS TO:

U.S. NUCLEAR REGULATORY COMMISSION, REGION II
NUCLEAR MATERIALS SAFETY SECTION
101 MARIETTA STREET, SUITE 2800
ATLANTA, GA 30323

IF YOU ARE LOCATED IN:

ILLINOIS, INDIANA, IOWA, MICHIGAN, MINNESOTA, MISSOURI, OHIO, OR WISCONSIN, SEND APPLICATIONS TO:

U.S. NUCLEAR REGULATORY COMMISSION, REGION III
MATERIALS LICENSING SECTION
799 ROOSEVELT ROAD
GLEN ELLYN, IL 60137

ARKANSAS, COLORADO, IDAHO, KANSAS, LOUISIANA, MONTANA, NEBRASKA, NEW MEXICO, NORTH DAKOTA, OKLAHOMA, SOUTH DAKOTA, TEXAS, UTAH, OR WYOMING, SEND APPLICATIONS TO:

U.S. NUCLEAR REGULATORY COMMISSION, REGION IV
MATERIAL RADIATION PROTECTION SECTION
611 RYAN PLAZA DRIVE, SUITE 1000
ARLINGTON, TX 76011

ALASKA, ARIZONA, CALIFORNIA, HAWAII, NEVADA, OREGON, WASHINGTON, AND U.S. TERRITORIES AND POSSESSIONS IN THE PACIFIC, SEND APPLICATIONS TO:

U.S. NUCLEAR REGULATORY COMMISSION, REGION V
NUCLEAR MATERIALS SAFETY SECTION
1480 MARIA LANE, SUITE 210
WALNUT CREEK, CA 94698

PERSONS LOCATED IN AGREEMENT STATES SEND APPLICATIONS TO THE U.S. NUCLEAR REGULATORY COMMISSION ONLY IF THEY WISH TO POSSESS AND USE LICENSED MATERIAL IN STATES SUBJECT TO U.S. NUCLEAR REGULATORY COMMISSION JURISDICTION.

1. THIS IS AN APPLICATION FOR (Check appropriate item)

- A. NEW LICENSE
- B. AMENDMENT TO LICENSE NUMBER _____
- C. RENEWAL OF LICENSE NUMBER 37-09743-01

2. NAME AND MAILING ADDRESS OF APPLICANT (Include Zip Code)

McNeil Pharmaceutical
Welsh and McKean Roads
Spring House, PA 19477

3. ADDRESS(ES) WHERE LICENSED MATERIAL WILL BE USED OR POSSESSED.

McNeil Pharmaceutical
Welsh and McKean Roads
Spring House, PA 19477

4. NAME OF PERSON TO BE CONTACTED ABOUT THIS APPLICATION
Brian E. Reynolds, Ph.D., C.I.H.

TELEPHONE NUMBER
215-628-5858

SUBMIT ITEMS 5 THROUGH 11 ON 8 1/2 x 11" PAPER. THE TYPE AND SCOPE OF INFORMATION TO BE PROVIDED IS DESCRIBED IN THE LICENSE APPLICATION GUIDE.

5. RADIOACTIVE MATERIAL
a. Element and mass number, b. chemical and/or physical form, and c. maximum amount which will be possessed at any one time.

6. PURPOSE(S) FOR WHICH LICENSED MATERIAL WILL BE USED.

7. INDIVIDUAL(S) RESPONSIBLE FOR RADIATION SAFETY PROGRAM AND THEIR TRAINING AND EXPERIENCE.

8. TRAINING FOR INDIVIDUALS WORKING IN OR FREQUENTING RESTRICTED AREAS.

9. FACILITIES AND EQUIPMENT.

10. RADIATION SAFETY PROGRAM.

11. WASTE MANAGEMENT.

12. LICENSEE FEES (See 10 CFR 170 and Section 170.31)
FEE CATEGORY 3(M) AMOUNT ENCLOSED \$460.00

13. CERTIFICATION. (Must be completed by applicant) THE APPLICANT UNDERSTANDS THAT ALL STATEMENTS AND REPRESENTATIONS MADE IN THIS APPLICATION ARE BINDING UPON THE APPLICANT.

THE APPLICANT AND ANY OFFICIAL EXECUTING THIS CERTIFICATION ON BEHALF OF THE APPLICANT, NAMED IN ITEM 2, CERTIFY THAT THIS APPLICATION IS PREPARED IN CONFORMITY WITH TITLE 10, CODE OF FEDERAL REGULATIONS, PARTS 30, 32, 33, 34, 35, AND 40 AND THAT ALL INFORMATION CONTAINED HEREIN, IS TRUE AND CORRECT TO THE BEST OF THEIR KNOWLEDGE AND BELIEF.

WARNING: 18 U.S.C. SECTION 1001 ACT OF JUNE 25, 1949, 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.

SIGNATURE—CERTIFYING OFFICER 	TYPED/PRINTED NAME Joseph J. Pittelli, M.D.	TITLE Vice President Scientific Affairs	DATE 5/23/88
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FOR NRC USE ONLY

TYPE OF FEE REN	FEE LOG Jun. 4 th	FEE CATEGORY 3M	COMMENTS	APPROVED BY
AMOUNT RECEIVED \$460	CHECK NUMBER 051912			DATE Jun. 4 th

"OFFICIAL RECORD COPY"

MLT

108958

Appendix 1

Training and experience of the new additions to Section 7

J. A. Buben, Ph.D. (Drug Metabolism)

Training

- 1976 **University of Cincinnati, Cincinnati, OH**
Principles of Radiation and Safe Practices
- 1983 **University of Kansas**
Minicourse in Radiation Safety and the Use of Open Sources
Biophysics 701 - Quantitative Radiation Safety
- 1985 **McNeil Pharmaceutical**
Ionizing Radiation; the McNeil Pharmaceutical Radiation
Safety Program
In-house radiation safety seminars

Experience

- 1976-77 In vitro tracer studies (microcurie amounts); maintained
laboratory radioisotope inventory - **University of Cincinnati**
- 1983-84 Synthesis of tritium labeled compounds (25-50 mCi/synthesis);
set up radiosynthesis laboratory - **University of Kansas**
- 1983-85 In vitro metabolism experiments with tritium, carbon-14
(microcurie amounts) - **University of Kansas**
- 1984 In vivo metabolism studies with tritium and carbon-14 dual
label (100 microcuries/animal) - **University of Kansas**
- 1985 -
Present In vivo metabolism and distribution studies with carbon-14
and tritium (approximately 50 microcuries/animal, up to
1 millicurie/experiment) - **McNeil Pharmaceutical**

* * *

M. L. Holland, Ph.D. (Drug Metabolism)

Training

- 1978 **Anderson College**
Radioisotope techniques; independent study project
on X-Ray fluorescence.
- 1983 **McNeil Pharmaceutical**
Ionizing Radiation; the McNeil Pharmaceutical Radiation
Safety Program
In-house radiation safety seminars

M. L. Holland, Ph.D. (Drug Metabolism) [Cont'd]

Experience

1983 -

Present Metabolism and extraction efficiency studies with carbon-14 (up to 1 millicurie/experiment) -
McNeil Pharmaceutical

* * *

E. S. Kimball, Ph.D.

Training

1978

N.I.H., Bethesda, MD

Effects of radiation, user protection, measurement techniques, monitoring techniques, storage and appropriate uses of radioisotopes

1985

Ayerst Laboratories, Princeton, NJ

Use of small animal irradiators, personnel monitoring, personnel protection

1986

McNeil Pharmaceutical

McNeil Pharmaceutical Radiation Safety Program
In-house radiation safety seminars

Experience

1977-84

Protein labelling (iodine-125 2mCi/experiment; tritium and carbon-14, 10 mCi/experiment) - **N.I.H., Bethesda, MD**
Biosynthetic labelling of tumor cells (tritium, 30 mCi/experiment; sulfur-35, 10 mCi; phosphorous-32, 1 mCi and carbon-14, 2 mCi/experiment) - **N.I.H., Bethesda, MD**
Cell surface labelling (chromium - 51, 5 mCi/experiment)
Incorporation of DNA precursors into proliferating cells (tritium 1-5 mCi/experiment) - **NIH, Bethesda and Frederick, MD**

1984-86

Tritiated thymidine incorporation (1-5 mCi handled) -
Ayerst Laboratories Research, Inc.

1986 -

Present Tritiated thymidine incorporation (1-5 mCi handled) -
McNeil Pharmaceutical

* * *

S. P. Sit, Ph.D. (Biological Research)

Training

- 1976 **Michigan State University, East Lansing, MI**
 Radiobiology course
- 1984 **McNeil Pharmaceutical**
 Ionizing Radiation; the McNeil Radiation Safety Program
 In-house radiation safety seminars

Experience

- 1974-79 Use of radiolabeled microspheres to measure the effect of
 drugs on the regional distribution of blood flow
 (cerium - 141, strontium - 85, scandium - 46) -
 Michigan State University, East Lansing, MI
- 1979-83 Use of radiolabeled microspheres to study blood flow
 characteristics (cerium -141, strontium - 85, scandium - 46,
 niobium - 95)
 Tritiated materials to study glomerular filtration rates -
 Harvard Medical School, Boston, MA
- 1983 -
Present Regional blood flow distribution studies (cerium -141,
 strontium - 85, scandium - 46, niobium - 95) -
 McNeil Pharmaceutical

* * *

W. Nan Wu, Ph.D. (Drug Metabolism)

Training

- The Ohio State University**
- 1967 Radioisotope Methodology
- 1968 Advanced Pharmaceutical Analysis
- 1970-71 General Biochemistry
- 1971 Biosynthesis of Material Products
- 1978 **McNeil Pharmaceutical**
 Radiation Safety Orientation
 In-house radiation safety seminars

W. Nan Wu, Ph.D. (Drug Metabolism) [Cont'd]

Experience

1967-68 Biosynthesis of fungal metabolites using tritium and carbon-14 - **The Ohio State University**

1978 -

Present Biotransformation of drugs using carbon-14 (600 microcurie max) and tritium (1 mCi max) -
McNeil Pharmaceutical

May 20, 1988

Appendix 2

Section 9

Instrumentation used to monitor the use of radioisotopes falls into two categories:

- A. Liquid scintillation and gamma counters.
- B. Equipment used to monitor the environment during radioisotope usage.

A. Liquid scintillation and gamma counters.

This equipment is used primarily for detection purposes. The equipment is periodically calibrated according to procedures outlined by the manufacturers. The equipment is checked using quenched or unquenched standards to determine counting efficiency. The equipment includes:

<u>Make</u>	<u>Model</u>	<u>Purpose</u>
Beckman	LS-68000	Liquid scintillation counter
Packard TriCarb	460CD	Liquid scintillation counter
LKB	1214 Rackbeta	Liquid scintillation counter
Tracor Mark III	Model 6880	Liquid scintillation counter
LKB	1270 Rackgamma II	Gamma counter
Searle Analytic	1195	Gamma counter
Beckman	LS-58000	Liquid scintillation counter
Packard	Auto gamma 800C	Gamma counter
Packard	Auto gamma 5780	Gamma counter
Searle	Isocap/300	Liquid scintillation counter
Packard Tricarb	4530	Liquid scintillation counter

Searle	Mark III	Liquid scintillation counter
Beckman	LS3801	Liquid scintillation counter
IN/US	Ramona-D	On-line scintillation counter (2 units)
Beckman	171	On-line scintillation counter

B. Monitors & Ratemeters

Monitors detect β and γ radiation and are used for detection purposes. Since they are used only to search for contamination, they are not routinely calibrated.

Eberline E-120E and GM tube

Eberline Radiation Monitor RM-15 with low energy gamma detector PG2

Ludlum Model 2 and GM tube

Eberline E-140 and GM tube

Berthold Model LB 1210B Ratemeter

Baird Atomic Model 441A Ratemeter

Baird Atomic Model 443 Ratemeter

Eberline E-120 and GM tube (2 units)

May 20, 1988

(FOR LFMS USE)
INFORMATION FROM LTS

BETWEEN:

LICENSE FEE MANAGEMENT BRANCH, ARM
AND
REGIONAL LICENSING SECTIONS

PROGRAM CODE: 03620
STATUS CODE: 2
FEE CATEGORY: 3M
EXP. DATE: 19880630
FEE COMMENTS:

LICENSE FEE TRANSMITTAL

A. REGION

1. APPLICATION ATTACHED

APPLICANT/LICENSEE: MCNEIL PHARMACEUTICAL
RECEIVED DATE: 880525
DOCKET NO.: 3006212
CONTROL NO.: 108958
LICENSE NO.: 37-09743-01
ACTION TYPE: RENEWAL

2. FEE ATTACHED

AMOUNT: 460.00
CHECK NO.: 051912

3. COMMENTS

SIGNED BP
DATE 6/3/88

B. LICENSE FEE MANAGEMENT BRANCH (CHECK WHEN MILESTONE 03 IS ENTERED 1)

1. FEE CATEGORY AND AMOUNT: 3M \$460

2. CORRECT FEE PAID. APPLICATION MAY BE PROCESSED FOR:

AMENDMENT _____
RENEWAL ✓ _____
LICENSE _____

3. OTHER _____

SIGNED S. Kimberley
DATE 6/9/88