VOID SHEET

03034350

TO: License Fee Management Branch

FROM: Region I

SUBJECT: VOIDED APPLICATION

Control Number: 124166

Applicant: Nemapharm, Inc.

Date Voided: 3/11/97

Reason for Void: Massachusetts becoming a new agreement state. Action to be sent to Massachusetts for processing. After review. License No. New Application (030-34350).

M. A. Perkins 3/11/97
Signature Date

Attachment:
Official Record Copy of
Voided Action

FOR LFMB USE ONLY

Final Review of VOID Completed:

Refund Authorized and processed

No Refund Due

Fee Exempt or Fee Not Required

Comments: After Review

Log completed

Processed by: BB

OFFICIAL RECORD COPY

ML 10

March 11 1997

MEMORANDUM FOR: John D. Kinneman, Chief
Nuclear Materials Safety Branch 2

FROM: Sattar Lodhi

SUBJECT: License Application of NemaPharm, Inc.
Mail Control No. 124166

Approximately 60% of the review of the application is complete. A 14-item deficiency letter was sent to the applicant on February 25, 1997. As of March 10, 1997, a response to the deficiency letter had not been received.

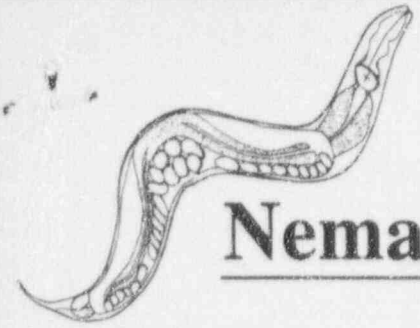
The applicant was called on March 10, 1997, to respond to the deficiency letter, but as of 3:00 p.m. on March 10, 1997, no response was received from the applicant.

The applicant faxed their response around 4:00 p.m. The response was reviewed and still certain items needed to be clarified.

It is recommended that this action be voided because the review can not be completed before the licenses are transferred to the Commonwealth of Massachusetts.

OFFICIAL RECORD COPY

ML 10



NemaPharm, Inc.

26 Landsdowne Street
Suite 470
Cambridge, MA 02139
tel: (617) 494-8701
fax: (617) 494-5101

March 10, 1997

M516
Q-2

John D. Kinneman
Nuclear Materials Safety Branch 2
US Nuclear Regulatory Commission
475 Allendale Road
King of Prussia, PA 19406-1415

Dear Dr. Kinneman:

In reply to your letter, docket number 030-34350, Control number 124166, dated February 25, 1997, the following response is submitted.

1. Appendix I of the Radiation Safety Guide will be amended to confirm that an amendment to the license will be procured **prior** to allowing an individuals to work as authorized users of licensed material. We are submitting 7 completed forms requesting authorized user status and the résumé's for those individuals.

2. The following table identifies each individual and their level of responsibility

Employee name	level of responsibility
Lin Sun, PhD	Radiation Safety Officer
Michael Basson, PhD	supervisor
Ralph Clover, PhD	independent researcher
Carl Johnson, PhD	independent researcher
Jill Spoerke, MS	independent researcher
Leo Liu, MD	supervisor
Beth Westlund, PhD	independent researcher

3. The individual designated as the Radiation Safety officer will be Dr. Lin Sun, not Robert Johnson. Robert is an outside consultant who will provide training and answer technical questions. At the time of our application, Dr. Sun was not yet an employee of the company and we listed Dr. Johnson, VP of Research as an interim RSO. The Radiation Safety Guide and all other pertinent materials have been changed to reflect Dr. Sun as the RSO.

4. As RSO, Dr. Sun will ensure that only authorized individuals use licensed materials, will perform routine inspections and will maintain all required records.

5. Personnel will be trained prior to the use of radioactive materials and in accordance with 10-CFR-19.12 will receive training if frequenting any area where radioactivity is used or stored and when there is a significant change in duties.

124166

OFFICIAL RECORD COPY ML 10

MAR 11 1997
MAR 10 1997

FAX REC'D

6. Backup survey meters will be used when the primary meter is being serviced or is unavailable.

7. Our meters will be calibrated by a commercial firm authorized to perform calibrations such as Rockland Instrument & Calibration service in Rockland, Massachusetts.

8. Individual surveys will be conducted several times per day and in the case of skin contamination, decontamination will be affected immediately. The resulting dose can be calculated based on the procedures in the textbook, Radiation Protection, A Guide for Scientists and Physicians, pages 59-61, 3rd edition, by Dr. Jacob Shapiro.

9. The dose limits on page 15 should reflect the institutional commitment to ALARA which determines that any exposure which exceeds 10% of the permissible levels be investigated for determination of the cause and actions taken to prevent a recurrence. For example, any whole body dose exceeding 125 mrem/quarter or any skin dose exceeding 1,250 mrem/quarter will be evaluated.

10. The action limits for restricted area provide that any dose be reduced to 2 mrem/hr and for any unrestricted the dose be <2 mrem/hr providing that any exposed individual could not receive more than 0.1 Rem/year. (reference section 20-1301 parts a and b) Contamination levels must be reduced to less than 2,200 d/m (1E-3 uCi) in a restricted area and $<$ 220 d/m (1E-4 uCi) in an unrestricted are. If a survey determines that these levels have been exceeded, the individuals will be immediately notified, monitored for contamination, and decontamination procedures immediately instituted. The dose rates will be minimized by appropriate shielding in addition to decontamination.

11. All discharges of liquids via the sanitary sewerage system must be readily dispersible and soluble biological material. We will assure that our releases meet solubility criterion in 10 CFR 20.2003(a)(1) by determining the chemical form and thus the solubility class. This method will be taken from appropriate scientific literature (reference Information notice 94-07 dated 1/28/94)

12. Please refer to question #3 - Dr. Sun is the radiation safety officer.

13. Unfortunately, this number slipped through in the editing process. The correct reference is 10-CFR 20.1906 (a-f).

14. The radiation protection program will be reviewed annually by senior management, the RSO and the safety consultant. This review process may be described thusly:

a) A representative of senior management will meet quarterly with the safety personnel to review any changes in the federal regulations, provisions of the license and the compliance status.

b) A review of the radiation safety office and staff performance will be made by a senior scientist who has received radiation safety training and

has the authorization to implement changes. This will be carried out in coordination with senior management.

c) the use of radioactive materials will be audited quarterly by the radiation safety officer and staff to include inventories, survey records, procedures, performance of independent work area surveys, signs and labels, familiarization of the personnel with regulations, potential items of non-compliance, proper use of film badges and finger rings, compliance with requirements for Bio-assays, and the use of impervious plastic gloves, lab coats, eyeglasses and solid-toe shoes.

I believe the above answers will adequately address deficiencies identified in NemaPharm's application for a Nuclear Regulatory license. If there are additional questions, please don't hesitate to reach either of the individuals listed below or Dr. Sun. Thank you for your consideration.

Sincerely,

Carl Johnson, Ph.D.
Vice President, Research

P. Yasemin vanBeuzekom, MPH
Director, Business Operations

enclosures

will supervise use of Materials

NemaPharm, Inc.

AUTHORIZATION TO USE RADIOACTIVE MATERIALS

Instructions. *Complete this form and submit to Radiation Safety Officer. Authorization for use requires signed approval of Radiation Safety Officer.*

Name of Applicant

Leo Liu M.D.

Social Security Number

280467865

Department & Supervisor

Biology no supervison required

Location where Isotopes will be used/stored

on premises; room #417

Radioactive material(s):
(List chemical symbol and mass number of each)

P^{33}, P^{32}, S^{35}

Form of Material
(Chemical and/or Physical)

any form

Training and Education

Subject Covered	Date (MP) Course	On-Job Training Yes/No	Hours	Instit	date
A. Principles and Practices of Radiation Protection		Yes		Beth Israel Hospital	1987
B. Measurements and Monitoring Techniques					1990
C. Mathematical principles for Calculating Activity					1993
					1996
D. Biological Effects of Radiation					

Experience (actual use of radioactive materials)

Isotope	Maximum Activity	Where Used?	Duration of Use	Type of Use
^{32}P, ^{33}P	100 mCi	Beth Israel Hospital	1990-1996	sequencing labeling screening
^{35}S	1 mCi	" " "		
^{3}H, ^{12}C		" " "	1987-1992	

I have read, understand, and agree to abide by NemaPharm's Radiation Safety Program.

Applicant Signature: Leo Liu Date: 3/10/97

RSO Signature (Approval): [signature] Date: 3/10/97

Start 9/96

CURRICULUM VITAE

Date prepared: 6/96

NAME: Leo X. Liu, MD, DTMH

ADDRESS: 88 Rockport Road, Weston, MA 02193

TELEPHONE: 617 667-2322 (work); 617 237-7158 (home)
617 667-5541 (fax)

E-MAIL: lliu@bih.harvard.edu

PLACE OF BIRTH: New York, NY

DATE OF BIRTH: May 31, 1957

MARITAL STATUS: married to Dr. Pendred E. Noyce; 3 children

EDUCATION:

1978 B.A.	Ohio State University
1983 M.D.	Stanford University School of Medicine

POSTDOCTORAL TRAINING:

1983-86	Intern and Resident in Medicine, Beth Israel Hospital, Boston, MA
1986-87	Clinical Fellow, Harvard Medical School Combined Infectious Disease Program, Beth Israel and Brigham & Women's Hospitals, Dana Farber Cancer Institute, Boston
1987-89	Research Fellow, Harvard Medical School Combined Infectious Disease Program
1990	Biology of Parasitism intensive course, Marine Biological Laboratory, Woods Hole, MA
1992-93	Fellow, Wellcome Research Centre for Parasitic Infections, Imperial College of Science, Technology and Medicine, London, UK

LICENSURE AND CERTIFICATION:

1986	Massachusetts medical licensure
1986	Diplomate, American Board of Internal Medicine
1988	Diplomate, subspecialty of Infectious Diseases, American Board of Internal Medicine
1993	Diploma in Tropical Medicine and Hygiene, Royal College of Physicians (London)

ACADEMIC APPOINTMENTS:

1983-89	Fellow in Medicine, Harvard University
1989-93	Instructor in Medicine, Harvard Medical School
1993-	Assistant Professor of Medicine, Harvard Medical School

HOSPITAL APPOINTMENTS:

1986-89	Fellow, Department of Medicine, Beth Israel and Brigham & Women's Hospitals
1989-	Associate in Medicine, Beth Israel Hospital

OTHER PROFESSIONAL POSITIONS AND MAJOR VISITING APPOINTMENTS:

1981-82	Visiting Instructor, Nanjing Medical College, Nanjing, China
1985	Visiting Physician, Tibetan Delek Hospital, Dharmsala, H.P., India
1992-93	Visiting Scientist, Department of Biology, Imperial College of Science, Technology and Medicine, London, UK
1992-	Consultant, Nemapharm, Inc., Cambridge, MA.
1995-	Consultant, Biomedisyn, Inc., Woodbridge, CT

AWARDS AND HONORS:

1974-77	Rasor Mathematics Prize, Lorbach Research Scholar, Phi Kappa Phi Award, Phi Beta Kappa
1989	Maxwell Finland Young Investigator Award for outstanding research fellow at Harvard Medical School, Massachusetts Infectious Diseases Society
1989-90	Young Investigator Award, National Foundation for Infectious Diseases
1990-92	Charles A. King Trust Fellow, The Medical Foundation, Inc., Boston, MA.
1990-95	Physician Scientist Award, National Institute of Allergy and Infectious Diseases
1994	Milton Fund Award, Harvard University

COMMITTEE ASSIGNMENTS:

1980-81	Admissions panel, Stanford Medical School
1983-85	Housestaff committee, Beth Israel Hospital
1989-92	Internship Selection Committee, Department of Medicine, Beth Israel Hospital
1993	Special Review Committee, National Institute of Allergy and Infectious Diseases

MEMBERSHIPS IN PROFESSIONAL SOCIETIES:

1985	American College of Physicians
1986	American Association for the Advancement of Science
1987	American Society of Tropical Medicine and Hygiene
1988	Infectious Diseases Society of America
1988	American Federation for Clinical Research
1992	Royal Society of Tropical Medicine and Hygiene, fellow
1992	British Society for Parasitology
1993	American Society of Parasitologists
1993	Society of Nematologists
1993	American Society of Microbiology

Journal reviewer for: New England Journal of Medicine, Clinical Infectious Diseases, Mayo Clinic Proceedings, Southern Medical Journal, Molecular and Biochemical Parasitology

MAJOR RESEARCH INTERESTS:

1. Molecular biology of parasitic nematodes
2. Comparative genomics and molecular phylogenetics
3. Tropical medicine and travelers' diseases

RESEARCH FUNDING:

1989-90 National Foundation for Infectious Diseases (PI)
Filarial prostaglandins: biosynthesis and cellular actions

1989-91 NIAID, individual NRSA (PI)
Biology of filarial arachidonate metabolism

1990-92 The Medical Foundation, Inc. (PI)
Biosynthesis & cellular actions of filarial parasite-derived eicosanoids

1991-96 NIAID, K11 AI00965 (PI)
Filarial eicosanoids: biosynthesis and cellular actions

1993-97 World Health Organization, TDR (Co-investigator)
Characterization of filarial cyclooxygenase

1994-95 William F. Milton Fund, Harvard University (PI)
Chemoreceptors in Parasitic Nematodes

1996- NIH AI40399-01 (consultant)
Toxocara canis Immunodiagnostic Test

1996- NIH AI40720-01 (consultant)
Strongyloidiasis Immunodiagnostic Kit

1996- NIH AI38940-01 (PI)
Mechanisms of *Toxocara* larval activation

1996- DOD SBIR (Co-investigator)
PCR Detection of *Strongyloides stercoralis*

PRINCIPAL CLINICAL AND HOSPITAL SERVICE RESPONSIBILITIES:

1989 - Attending Physician, Department of Medicine, Beth Israel Hospital
1990 - Attending Physician, Infectious Diseases Service, Beth Israel Hospital

TEACHING EXPERIENCE:

Harvard Medical School

1988-present Infectious Diseases [Medicine 513M.J]
Section Leader and Lecturer, helminthic infections
10 medical students (sections); 40-60 medical students (lectures)

1989-94 Mechanisms of Microbial Pathogenesis [HST 040]
Lecturer, helminthic infections
35 medical students (Health Sciences and Technology Program)

1996 Immunology and Infectious Diseases
Section leader

Beth Israel Hospital

1989-present General Medicine Service, Department of Medicine

Attending physician, Basic Medicine clerkship [Medicine 500M.1] (1 month/year)
1-3 medical students, 0-2 subinterns, 2 residents

1990-present Infectious Diseases Consulation Service
Consult attending physician (1-2 months/year)
1-2 medical students, 1-2 residents, 1-2 infectious diseases fellows

1995-96 Infectious Diseases Consulation Service
teaching attending (2 months/year)

1986-87 Thorndike lecture series, Department of Medicine
"Medicine among the Tibetans"

1989 Primary Care Seminar, Department of Medicine
"Approach to the International Traveler"

1990 Thorndike lecture series, Department of Medicine
"Advice for Travelers"

1992 Primary Care Seminar, Department of Medicine
"Evaluation of Immigrants and Travelers"

1994 Thorndike lecture series, Department of Medicine
"Travel Medicine"

1995 Morbidity and Mortality conference, Department of Medicine
"Schistosomiasis and portal vein thrombosis"

1995 Intensive Review of Internal Medicine course, Department of Medicine
"Travel Medicine: Imported Infections and Their Prophylaxis"

Brigham & Women's Hospital

1990 Intensive Review of Internal Medicine course, Department of Medicine
Lecturer, parasitic infections

1994 Morbidity and Mortality conference, Department of Medicine
"A 37 year-old Laotian man with fever and hepatitis"

Other

1981 - 82 Nanjing Medical College, China
Course developer and director, Medical English

Invited presentations

1990 Medical Grand Rounds, Maine Medical Center, Portland, ME
"Health Advice for International Travel"

1990 Tropical Public Health Seminar, Harvard School of Public Health, Boston, MA
"Arachidonic Acid Metabolism in Filarial Parasites"

1991 Wellcome Research Centre Seminar Programme, Imperial College, London
"Prostaglandin Formation by Filarial Parasites"

1992 Department of Immunology Seminar, University of Glasgow, Glasgow, Scotland, UK
"Lipid Mediators of an Intravascular Parasitic Nematode"

1993 Kenya Medical Research Institute, Nairobi, Kenya
"Immunobiology of Filarial Infections"

1995 Molecular Epidemiology Seminar, Harvard School of Public Health, Boston, MA
"A molecular phylogeny of parasitic nematodes"

1996 CLS/CNE annual meeting, Marlborough, MA
"Emerging and Imported Infectious Diseases"

1996 MetroWest Medical Center, Framingham Union Campus, Framingham, MA
"Imported Infectious Diseases"

Advising and supervisory responsibilities

Postdoctoral fellow advisor
1-2 postdoctoral fellows in laboratory/year

Tutor in Biochemical Sciences, Dept. of Molecular and Cellualr Biology, Harvard University
2-3 thesis or independent research students/year

Former trainees:
André Lopez, MD; Medical Resident, UC Irvine
Alberto Iaia, MD; Radiology Resident, Massachusetts General Hospital
Janet Buhlmann, BA; PhD student, Biochemistry, Dartmouth
Sandy Ryeom, PhD; Postdoctoral fellow, Cell Biology, Harvard Medical School
Han Xu, MD, PhD; Pathology Resident, Cleveland Clinic
Guangyuan Hong, PhD; Dept of Microbiology, Cornell Medical College, New York
Pinki Gupta, PhD; National Institute of Immunology, New Delhi, India
Indranil Debnath, BA; Medical student, University of Tennessee

PUBLICATIONS:

1. Liu LX, Seward SJ, Crumpacker CS. Intravenous trimethoprim- sulfamethoxazole and ataxia. *Annals of Internal Medicine* 1986; 104: 448.

2. Liu LX, Rustgi A. Cardiac myonecrosis in hypertensive crisis associated with monoamine oxidase inhibitor therapy in a young woman. *American Journal of Medicine* 1987; 82: 1060-1064.

3. McIntosh KM, Liu LX. Infectious Disease Rounds: Fever and Rash in a Pregnant Woman from the Ivory Coast. *Reviews of Infectious Diseases* 1987; 9: 1175-79.

4. Liu LX, Weller PF. *Brugia malayi*: microfilarial polyunsaturated fatty acid composition and formation. *Experimental Parasitology*, 1989; 69: 198-203.

5. Weller PF, Liu LX. Bancroftian filariasis and ivermectin. *New England Journal of Medicine* 1990; 332: 1153-54.

6. Liu LX, Serhan CN, Weller PF. Intravascular filarial parasites elaborate cyclooxygenase- derived eicosanoids. *Journal of Experimental Medicine* 1990; 172: 993-96.

7. Liu LX, Weller PF. Intestinal nematodes. In: VK Rustgi, ed., *Gastrointestinal Infections in the Tropics*, Basel: S. Karger. 1990; 145-169.

8. Liu LX, Weller PF. Intestinal tapeworms and flukes. In: VK Rustgi, ed., *Gastrointestinal Infections the Tropics*, Basel: S. Karger. 1990; 170-181.

9. Liu LX, Weller PF. Minireview: arachidonic acid metabolism by intravascular filarial parasites. *Experimental Parasitology* 1990; 71: 496-501.

10. Liu LX, Serhan CN, Weller PF. Formation of cyclooxygenase-derived eicosanoids by a parasitic intravascular nematode. In: Samuelsson B, Paoletti R, Ramwell P, eds. *Advances in Prostaglandin, Thromboxane, and Leukotriene Research.* Vol. 21. Prostaglandins and related compounds. New York: Raven Press. 1990; 509-512.

11. Liu LX, Weller PF. Evaluation of the febrile traveler returning from Southeast Asia and Oceania. In: Remington JS, Swartz MN, eds. *Current Clinical Topics in Infectious Diseases*; vol.12. Cambridge: Blackwell Scientific Publications. 1992: 138-163.

12. Liu LX. Basic Laboratory Methods in Medical Parasitology (review). *Gastroenterology* 1992; 103: 714.

13. Liu LX, Weller PF. Intravascular filarial parasites inhibit platelet aggregation. Role of parasite-derived prostanoids. *Journal of Clinical Investigation* 1992; 89: 1113-1120.

14. Liu LX, Buhlmann JE, Weller PF. Release of prostaglandin E_2 by microfilariae of *Wuchereria bancrofti* and *Brugia malayi*. *American Journal of Tropical Medicine and Hygiene* 1992; 46: 520-523.

15. Liu LX. Spinal and cerebral schistosomiasis. *Seminars in Neurology* 1993; 13:189-200.

16. Weller PF, Liu LX. Eosinophilic meningitis. *Seminars in Neurology* 1993; 13: 161-168.

17. Liu LX, Weller PF. Strongyloidiasis and other intestinal nematode infections. *Infectious Disease Clinics of North America* 1993; 7: 655-682.

18. Liu LX. Travel medicine, part 1: traveler's advice and immunizations. *Infections in Medicine* 1993; 10: 58-67.

19. Liu LX. Travel medicine, part 2: malaria, traveler's diarrhea, and other problems. *Infections in Medicine* 1993; 11: 24-28.

20. David JR, Liu LX. Molecular biology and immunology of parasitic infections. Chapter 170. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, eds. *Harrison's Principles of Internal Medicine.* 13th ed. New York: McGraw-Hill. 1994: 865-871.

21. Liu LX, Weller PF. Therapy of Parasitic Infections. Chapter 172. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, eds. *Harrison's Principles of Internal Medicine.* 13th ed. New York: McGraw-Hill. 1994: 878-882.

22. Liu LX, Weller PF. Trichinosis and Tissue Nematodes. Chapter 180. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, eds. *Harrison's Principles of Internal Medicine.* 13th ed. New York: McGraw-Hill. 1994: 914-916.

23. Liu LX, Weller PF. Intestinal Nematodes. Chapter 181. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, eds. *Harrison's Principles of Internal Medicine.* 13th ed. New York: McGraw-Hill. 1994: 916-920.

24. Rynkiewicz DL, Liu LX. Human ehrlichiosis in New England (letter). *New England Journal of Medicine* 1994, 330: 292-293.

25. Rynkiewicz DL, Liu LX. Human ehrlichiosis in New England (letter). *New England Journal of Medicine* 1994, 330: 1760-1761.

26. Liu LX. Travel medicine, part 3: infections in returned travelers. *Infections in Medicine* 1995; 12: 233-243.

27. Liu LX, Chi JY, Upton MP, Ash LR. Eosinophilic enterocolitis associated with larvae of the pinworm *Enterobius vermicularis*. *Lancet* 1995; 346: 410-412.

28. Surmont I, Liu LX. Enteritis, eosinophilia, and *Enterobius vermicularis* (letter). *Lancet* 1995; 346: 1167.

29. Weller PF, Liu LX. Trichinellosis. In: Rakel RE, ed. *Conn's Current Therapy*. Philadelphia: W.B. Saunders. 1996, pp.160-161.

30. Liu LX, Compton CC. A 40-year-old woman with the rapid onset of flaccid paraplegia. Case records of the Massachusetts General Hospital (Case 4 - 1996). *New England Journal of Medicine* 1996, 334: 382-389.

31. Liu LX, Weller PF. Drug Therapy: Antiparasitic drugs. *New England Journal of Medicine* 1996, 334: 1178-1184.

32. Liu LX. Paralysis due to schistosomiasis (letter). *New England Journal of Medicine* 1996, 334: 1548-1549.

33. Blaxter ML, Liu LX. Nematode spliced leaders - ubiquity, evolution, and utility. *International Journal for Parasitology* 1996, in press.

34. Liu LX, Xu H, Weller PF, Shi A, Debnath I. Structure and expression of a novel nematode gene for glia maturation factor. *Gene* 1996, in press.

35. Allen JE, Liu LX. Immunity to parasitic and fungal infections. In: Pier GB, ed. *Immunology, Infection, and Immunity*. American Society for Microbiology Press 1996, in press.

36. Liu LX, Harinasuta KT. Liver and intestinal flukes. *Clinics of Gastroenterology* 1996, in press.

37. Liu LX, Weller PF. Therapy of Parasitic Infections. Chapter 172. In: Fauci AS, Braunwald E, Isselbacher KJ, Martin JB, Kasper DL, Wilson JD, Hauser SL, Longo DL, eds. *Harrison's Principles of Internal Medicine*. 14th ed. New York: McGraw-Hill. 1996, in press.

38. Liu LX, Weller PF. Trichinosis and Tissue Nematodes. Chapter 180. In: Fauci AS, Braunwald E, Isselbacher KJ, Martin JB, Kasper DL, Wilson JD, Hauser SL, Longo DL, eds. *Harrison's Principles of Internal Medicine*. 14th ed. New York: McGraw-Hill. 1996, in press.

39. Liu LX, Weller PF. Intestinal Nematodes. In: Fauci AS, Braunwald E, Isselbacher KJ, Martin JB, Kasper DL, Wilson JD, Hauser SL, Longo DL, eds. *Harrison's Principles of Internal Medicine*. 14th ed. New York: McGraw-Hill. 1996, in press.

40. Liu LX, Blaxter ML, Shi A. The 5S RNA intergenic region of nematodes: variation in size and presence of SL1 RNA. Manuscript in preparation.

ABSTRACTS:

1. Liu LX, Weller PF. Lipoxygenase pathway metabolism of arachidonic acid by filarial parasites. AFCR/ASCI/AAP national meeting, Washington, D.C. May 1, 1988. *Clinical Research* 1988;36:461A.

2. Liu LX, Weller PF. Eicosanoid formation from arachidonic acid by microfilariae of *Brugia malayi*. 37th annual meeting of the American Society for Tropical Medicine and Hygiene, Washington, D.C. December 7, 1988.

3. Liu LX, Weller PF. Eicosanoid production by human filarial parasites. 1989 Winter Prostaglandin Conference, Keystone, CO. January 16-20, 1989.

4. Liu LX, Weller PF. Human filarial parasites synthesize prostaglandins. AFCR/ASCI/AAP national meeting, Washington, D.C. May 1, 1989.

5. Liu LX, Weller PF. Formation of prostanoids by filarial parasites. Gordon Research Conference on Molecular and Immunological Aspects of Parasitology, Colby-Sawyer College, NH. August 7-11, 1989.

6. Liu LX, Weller PF. Human filarial parasites synthesize prostaglandins. 38th annual meeting of the American Society for Tropical Medicine and Hygiene, Washington, D.C. December 10-14, 1989.

7. Liu LX, Weller PF. Intravascular filarial parasites elaborate cyclooxygenase-derived eicosanoids. 7th International Conference on Prostaglandins and Related Compounds, Florence, Italy. May 28-June 1, 1990.

8. Liu LX, Weller PF. Intravascular filarial parasites inhibit platelet aggregation. Role of parasite-derived prostanoids. 39th annual meeting of the American Society for Tropical Medicine and Hygiene, New Orleans, LA. November 4-8, 1990.

9. Liu LX, Weller PF. Intravascular filarial parasites inhibit platelet aggregation. Gordon Research Conference on Molecular and Immunological Aspects of Parasitology, Colby-Sawyer College, NH. August 5-9, 1991.

10. Liu LX, Weller PF. Human filarial parasites elaborate prostaglandins active on human host cells. 8th International Conference on Prostaglandins and Related Compounds, Montreal, Canada. July 26-31, 1992.

11. Liu LX. A family of putative chemosensory receptors in free-living and parasitic nematodes. Keystone Symposium on Molecular Helminthology, Tamarron, CO. February 10-17, 1993. *Journal of Cellular Biochemistry* 1993; 17C: 116.

12. Xu H, Weller PF, Liu LX. Filarial prostaglandin H synthase (cyclooxygenase). British Society for Parasitology annual meeting, University of Leeds, England. April 4-7, 1993.

13. Weller PF, Liu LX, Kim J. *Brugia malayi*: costimulation and modulation of human T lymphocyte responses. American Society for Tropical Medicine and Hygiene annual meeting, Atlanta, GA. October 31-November 4, 1993.

14. Liu LX. Molecular phylogeny of some free-living and parasitic nematodes based on the 28S ribosomal RNA gene. American Society of Parasitologists annual meeting, Pittsburg, PA. July 6-10, 1995.

15. Liu LX, Chi JY, Upton MP, Ash LR. Molecular identification of *Enterobius vermicularis* larvae as a cause of human eosinophilic ileocolitis. American Society of Parasitologists annual meeting, Pittsburg, PA. July 6-10, 1995.

16. Liu LX. Molecular phylogeny of parasitic nematodes: speciation of an unidentified nematode associated with eosinophilic enterocolitis. Infectious Diseases Society of America annual meeting, San Francisco, CA September 16-18, 1995.

17. Liu LX, Chi JY, Upton MP, Ash LR. Molecular identification of *Enterobius vermicularis* larvae as a cause of human eosinophilic ileocolitis. American Society for Tropical Medicine and Hygiene annual meeting, San Antonio, November 17-21, 1995.

18. Liu LX. Molecular phylogenetics of nematodes based on the 28S ribosomal RNA D1 domain. Keystone Symposium on Molecular Helminthology, Santa Fe, NM. February 18-24, 1996.

19. Debnath I, Xu H, Weller PF, Shi A, Liu LX. Structure and expression of a novel filarial gene for glia maturation factor. Keystone Symposium on Molecular Helminthology, Santa Fe, NM. February 18-24, 1996.

20. Blaxter ML, De Ley P, Garey JG, Liu LX, Thomas WK, Ried A, Schideman P, Vanfleteren J. Phylogenetic relationships of nematodes as deduced from 18S rRNA sequence analysis. Third International Nematology Congress, Guadelupe, West Indies. July 7-12, 1996.

21. Blaxter ML, De Ley P, Garey JG, Liu LX. Origins of zooparasitic nematodes inferred from ribosomal RNA molecular phylogeny. Molecular Parasitology Meeting, Marine Biological Laboratory, Woods Hole, MA. September 15-19, 1996.

22. Liu LX. A novel host-activated cysteine-rich secreted protein from the parasitic nematode *Toxocara canis*. Molecular Parasitology Meeting, Marine Biological Laboratory, Woods Hole, MA. September 15-19, 1996.

REFERENCES:

Robert M. Glickman, MD	Herrman M. Blumgart Professor of Medicine, Harvard Medical School Physician-in-Chief, Beth Israel Hospital, Boston, MA
Rick M. Maizels, PhD	Professor of Zoology, Institute of Cell, Animal, and Population Biology, Univeristy of Edinburgh, UK. formerly Director, Wellcome Research Centre for Parasitic Infections, Dept of Biology, Imperial College of Science, Technology, & Medicine, London, UK
Peter F. Weller, MD	Professor of Medicine, Chief, Infectious Disease Division, Beth Israel Hospital, Boston, MA
Dennis L. Kasper, MD	William Ellery Channing Professor of Medicine, Harvard Medical School Co-Director, Channing Laboratory and Co-chief, Infectious Diseases, Brigham and Women's Hospital, Boston, MA
Carl D. Johnson, PhD	President and Director of Research, Nemapharm, Inc., Cambridge, MA
Gerhard A. Schad, PhD	Professor of Parasitology, Department of Pathobiology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA
Peter J. Hotez, MD, PhD	Associate Professor of Pediatrics and Epidemiology, Director, Medical Helminthology Laboratory, Yale University School of Medicine, New Haven, CT

Will Supervise use of Materials

NemaPharm, Inc.

AUTHORIZATION TO USE RADIOACTIVE MATERIALS

Instructions. *Complete this form and submit to Radiation Safety Officer. Authorization for use requires signed approval of Radiation Safety Officer.*

Name of Applicant
MICHAEL BASSON

Social Security Number
122-44-1917

Department & Supervisor
BIOLOGY
no supervisor required

Location where Isotopes will be used/stored
On premises
Room 417

Radioactive material(s):
(List chemical symbol and mass number of each)
32 P
33 P
35 S

Form of Material
(Chemical and/or Physical)
any form

Training and Education

Subject Covered	Date (NB) Course	On-Job Training Yes/No	Hours	Instit	date
A. Principles and Practices of Radiation Protection	TRAINING at				
B. Measurements and Monitoring Techniques	UC Berkeley				1983
C. Mathematical principles for Calculating Activity	MIT				1988
D. Biological Effects of Radiation					

Experience (actual use of radioactive materials)

Isotope	Maximum Activity	Where Used?	Duration of Use	Type of Use
32 P	1 mCi	MIT	1988-1995	Screening DNA labeling for probes sequencing
35 S	2 mCi	MIT	1988-1995	
32 P	10 mCi	UC Berkeley	1983-1988	DNA labeling for probes sequencing in vivo labeling

I have read, understand, and agree to abide by NemaPharm's Radiation Safety Program.

Applicant Signature: Michael Basson Date: 3-10-97

RSO Signature (Approval): [signature] Date: 3/10/97

Curriculum Vita and Bibliography

Michael Basson
Biology Department 68-422
Massachusetts Institute of Technology
77 Massachusetts Avenue
Cambridge, MA 02139
phone: 617-253-5820
fax: 617-253-8126
email: basson@mit.edu

Personal Data

Born: November 12, 1960
Place: New York, N.Y.
Citizenship: United States
Marital status: Single
Address:
96 Porter Street #1
Somerville, MA 02143
Phone: (617) 625-7076

Education

Yale College
September 1978 - May 1982
B.S. in Chemistry, May 1982
Honors: Summa cum laude, Phi Beta Kappa

U.C. Berkeley
September 1982-March 1988
Ph.D. in Biochemistry, June 1988
University of California Regents Fellowship, 1983-1985

Research Experience

National Science Foundation Undergraduate Research Participant
Advisor: Dr. Alan Waggoner
Topic: Mechanism of the interaction of oxonol dyes with a membrane
Amherst College, June 1981 - August 1981

Undergraduate Thesis Research
Advisor: Dr. Stephen Sligar
Topic: The stereochemistry of P450 LM_2-catalyzed hydroxylation of a chiral substrate
Yale College, September 1981 - May 1982

Graduate Research
Advisor: Dr. Jasper Rine
Topic: Regulation of the sterol biosynthetic pathway in *Saccharomyces cerevisiae*
U.C. Berkeley, September 1982 - March 1988

Postdoctoral Research
Sponsor: Dr. H. Robert Horvitz
Topic: Regulation of neuronal differentiation in *Caenorhabditis elegans*
Massachusetts Institute of Technology, March 1988 - present

Postdoctoral Fellow of the Jane Coffin Childs Fund for Medical Research
March 1988 - March 1991

Postdoctoral Fellow of the Howard Hughes Medical Institute
March 1991 - September 1991

Postdoctoral Fellow of the Medical Foundation
October 1991 - September 1993

Postdoctoral Fellow of the Lucille P. Markey Fellowship
October 1993 - September 1994

Postdoctoral Associate
Massachusetts Institute of Technology
October 1994 - December 1995

Bibliography

Basson, M. and H. R. Horvitz. The *C. elegans* gene *sem-4* controls neuronal and mesodermal cell development and encodes a zinc-finger protein. Manuscript submitted for publication.

Basson, M. and H. R. Horvitz. The *C. elegans* gene *egl-45* is required for serotonergic motor neuron differentiation and encodes an evolutionarily-conserved protein. Manuscript in preparation.

Hsier, L., M.E. Basson and J. Rine. *ERG10* from *Saccharomyces cerevisiae* encodes acetoacetyl-CoA thiolase. (1994) J. Biol. Chem. **269**:31383-31389.

Basson, M.E., M. Thorsness, J. Finer-Moore, R. Stroud and J. Rine. Structural and functional conservation between yeast and human 3-hydroxy-3-methylglutaryl coenzyme A reductases, the rate-limiting enzyme of sterol biosynthesis. (1988) Mol. Cell. Biol. 8:3797-3808.

Wright, R., M. Basson, L. D'Ari and J. Rine. Increased amounts of HMG-CoA reductase induce "karmellae": A proliferation of stacked membrane pairs surrounding the yeast nucleus. (1988) J. Cell Biol. **107**:101-114.

George, E.B., P. Nyirjesy, M. Basson, L.A. Ernst, P.R. Pratap, J.C. Freedman and A.S. Waggoner. Impermeant potential-sensitive oxonol dyes. I. Evidence for an "on-off" mechanism. (1988) J. Membr. Biol. **103**:245-253.

Nyirjesy, P.,E.B. George, R.K. Gupta, M. Basson, P.R. Pratap, J.C. Freedman, K. Raman, and A.S. Waggoner. Impermeant potential-sensitive oxonol dyes: II. The dependence of the absorption signal on the length of alkyl substituents attached to the dye. (1988) J. Membr. Biol. **105**:45-53.

Basson, M.E., R.L. Moore, J. O'Rear and J. Rine. Identifying mutations in duplicated functions in *Saccharomyces cerevisiae*: Recessive mutations in HMG-CoA reductase genes. (1987) Genetics **117**:645-655.

Basson, M.E., M. Thorsness and J. Rine. *Saccharomyces cerevisiae* contains two functional genes encoding 3-hydroxy-3-methylglutaryl coenzyme A reductase. (1986) Proc. Natl. Acad. Sci. USA **83**:5563-5567.

Talks

Basson, M. and H. R. Horvitz, Control of the timing and execution of HSN neuron differentiation. (1993) International Meeting on *C. elegans*, Madison, Wisconsin.

Basson, M. and H. R. Horvitz, Differentiation of the HSN neurons is temporally regulated and requires two transcription factors. (1992) East Coast Regional Meeting on *C. elegans*, New York, New York.

Basson, M. and H. R. Horvitz, Differentiation of the HSN neurons in *C. elegans* is temporally regulated and requires two transcription factors. (1992) Northeast Regional Developmental Biology Conference, Woods Hole, Massachusetts.

Basson, M. and H. R. Horvitz, Mutants defective in the onset of HSN differentiation. (1990) East Coast Regional Meeting on *C. elegans*, Cambridge, Massachusetts.

Basson, M., M. Thorsness, R. L. Moore, and J. Rine. The yeast genes for HMG-CoA reductase: sequence, protein structure and regulation. (1986) International Meeting on Yeast Genetics and Molecular Biology, Champaign-Urbana, Illinois.

NemaPharm, Inc.

AUTHORIZATION TO USE RADIOACTIVE MATERIALS

Instructions. *Complete this form and submit to Radiation Safety Officer. Authorization for use requires signed approval of Radiation Safety Officer.*

Name of Applicant

Jill Spoerke

Social Security Number

109-70-5298

Department & Supervisor

Biology - Michael Bassen, PhD

Location where Isotopes will be used/stored

on premises room #417

Radioactive material(s):
(List chemical symbol and mass number of each)

P^{33}, P^{32}, S^{35}

Form of Material
(Chemical and/or Physical)

any form

Training and Education

Subject Covered	Date (MM) Course	On-Job Training Yes|No	Hours	Instit	date
A. Principles and Practices of Radiation Protection	3/13/97 and 3/20/97				
B. Measurements and Monitoring Techniques					
C. Mathematical principles for Calculating Activity					
D. Biological Effects of Radiation					

Experience (actual use of radioactive materials)

Isotope	Maximum Activity	Where Used?	Duration of Use	Type of Use
none				

I have read, understand, and agree to abide by NemaPharm's Radiation Safety Program.

Applicant Signature: Jill Spoerke Date: 3/10/97

RSO Signature (Approval): [signature] Date: 3/10/97

Start: 7/96

JILL M. SPOERKE

108 College Place
Department of Biological Sciences
Syracuse University
Syracuse, NY 13244
315-443-9169 (Office), 437-5292 (Home)

OBJECTIVE A challenging research position at a molecular biology or genetics laboratory

EDUCATION

1992 - 1994 M.A. in Biology, State University of New York at Binghamton

1988 - 1992 B.S. in Biology, State University of New York at Binghamton

RESEARCH EXPERIENCE

1994 - present **Research Assistant: Developmental Genetics of *C. elegans***
Dr. Eleanor M. Maine, Syracuse University
- Investigated genes in signal transduction pathway for germline development: mutagenesis, genetic characterization, detailed microscopic analysis of phenotypes
- Experienced in molecular biology techniques: DNA preparation, Southern analysis, DNA subcloning, PCR, library screening
- Responsible for lab management: supervised laboratory assistants, maintained supplies and chemicals, trained students and designed experiments for undergraduate projects
- Familiar with Macintosh computer systems
- Presented work at local and national conferences
- Stained and photographed specimens, developed and printed micrographs

1992 - 1994 **Master's Thesis: Microbial Population Genetics of *Bradyrhizobium***
Dr. Matthew A. Parker, SUNY Binghamton
- Isolated *Bradyrhizobium* from soil bacteria and maintained cultures
- Optimized and utilized protein extraction procedures
- Performed starch gel electrophoresis

1991 - 1992 **Honor's Thesis: Physiological Ecology of *L. esculentum***
Dr. Nancy E. Stamp, SUNY Binghamton
- Developed and utilized a chemical analysis for leaf alkaloid content
- Maintained greenhouse plants
- Analyzed leaf nitrogen content

PUBLICATIONS

Spoerke, J.M., H.H. Wilkinson, and M.A. Parker. 1996. Nonrandom genotypic associations in a Legume-*Bradyrhizobium* mutualism. **Evolution** 50:146-154.

Wilkinson, H.H., J.M. Spoerke, and M.A. Parker. 1996. Divergence in symbiotic compatibility in a Legume-*Bradyrhizobium* mutualism. **Evolution** (in press).

Wilkens, R.T., J.M. Spoerke, and N.E. Stamp. 1996. Differential responses of growth and two soluble phenolics of tomato to resource availability. **Ecology** 77:247-258.

Spoerke, J.M., S.C. Stacey, E.M. Maine. 1996. The *ego-6* gene interacts with the *glp-1* signaling pathway and is involved in maintenance of proper mitotic and meiotic zones in the *C. elegans* germline. **Genes and Development** (in prep.).

REFERENCES Available upon request

NemaPharm, Inc.

AUTHORIZATION TO USE RADIOACTIVE MATERIALS

Instructions. *Complete this form and submit to Radiation Safety Officer. Authorization for use requires signed approval of Radiation Safety Officer.*

Name of Applicant

Bethany Westlund

Social Security Number

469-92-1540

Department & Supervisor

Biology no supervision required

Location where Isotopes will be used/stored

on premises - Rm #417

Radioactive material(s):
(List chemical symbol and mass number of each)

P^{33}, P^{32}, S^{35}

Form of Material
(Chemical and/or Physical)

any form

Training and Education

Subject Covered	Date (MM/YY) Course	On-Job Training Yes/No	Hours	Instit	date
A. Principles and Practices of Radiation Protection	1987	yes	1h/year	Washington University	1987-1993
B. Measurements and Monitoring Techniques	1987	yes	"	"	"
C. Mathematical principles for Calculating Activity	1987	yes	"	"	"
D. Biological Effects of Radiation	1987	no	"	"	"

Experience (actual use of radioactive materials)

Isotope	Maximum activity	Where Used?	Duration of Use	Type of Use
^{3}H	0.6mCi	Washington University	1993	pulse labeling of tissue culture cells
^{32}P	[illegible] ?	"	1987-1993	Northern blots, DNA sequencing
^{35}S	2mCi	"	1987-1993	pulse labeling of tissue culture cells
^{125}I	[illegible] 0.5mCi	"	1987-1992	iodination of proteins

I have read, understand, and agree to abide by NemaPharm's Radiation Safety Program.

Applicant Signature: Bethany Westlund Date: 3/10/97

RSO Signature (Approval): [signature] Date: 3/10/97

Start 10/96

Curriculum Vitae

Bethany Marie Westlund

Personal

Date of Birth:	October 21, 1963; St. Paul, Minnesota
Married:	Alan Cantor, M.D. Ph.D., May 30, 1993
Address:	Washington University School of Medicine Department of Genetics Box 8232 4566 Scott Avenue St. Louis, MO 63110
Telephone:	(314) 362-6164
FAX:	(314) 362-~~4187~~ 2255
email:	westlund@genetics.wustl.edu

Education

Undergraduate Education at St. Olaf College (1982-1986), B.A. in Biology

Graduate Education at Washington University School of Medicine, Division of Biology and Biomedical Sciences (1986-1993), Ph.D.

Postdoctoral research at Washington University School of Medicine, Department of Genetics, (September 1993-present)

Awards/Fellowships

Minnesota Mining and Manufacturing Special Scholarship, (1982-1986)

Lucille Markey Special Emphasis Pathway in Pathobiology postdoctoral fellowship, (September, 1993-August, 1995)

NIH postdoctoral fellowship F32 HD08103-01 (March, 1996-funding approved for two years)

Teaching Experience

Teaching Assistant, St. Olaf College, 2/85-5/85 and 2/86-5/86

Teaching Assistant, Washington University, 1/88-5/88

Research Experience

I. *Thesis research* in the laboratory of Stuart Kornfeld, M.D., Department of Medicine, Washington University Medical School. The focus of my research was intracellular protein targeting to two organelles, lysosomes and secretory granules.

Lysosomal enzyme targeting. Phosphorylated lysosomal enzymes are high affinity ligands for two mannose 6-phosphate (Man-6-P) receptors. One of these, the cation-independent Man-6-P receptor (CI-MPR), contains fifteen homologous extracellular repeating units, but binds just two moles of Man-6-P. The two ligand binding sites were found to be comprised within domains 1-3 and 7-11.

1)Westlund, B., Dahms, N. M., and Kornfeld, S. (1991) The Bovine Mannose 6-Phosphate/Insulin-like Growth Factor II Receptor: Localization of Mannose 6-Phosphate Binding Sites to Domains 1-3 and 7-11 of the Extracytoplasmic Region. *J. Biol.Chem.* **266**, 23233-23239.

Trafficking of lysosomal enzymes to lysosomes is mediated in part by two Golgi enzymes that act sequentially to generate Man-6-P residues on newly synthesized lysosomal hydrolases. Recognition of the lysosomal enzyme cathepsin H by the first enzyme, UDP-*N* -acetylglucosamine: lysosomal enzyme *N* -acetylglucosamine-1-phosphotransferase (phosphotransferase) was examined *in vivo* and *in vitro*. Man-6-P receptor affinity column chromatography in conjunction with oligosaccharide analysis indicates that human cathepsin H acquires phosphomannosyl residues when transiently expressed in both *Xenopus laevis* oocytes and COS-1 cells. In contrast, barley aleurain, a nonlysosomal thiol protease that is highly homologous to cathepsin H, does not acquire phosphomannosyl residues when expressed in either system. A chimera generated between cathepsin H and aleurain that contains the aleurain propiece and first 35 amino acids of the mature protein fused to the remaining mature cathepsin H polypeptide (85% of the mature cathepsin H sequence) also fails to acquire Man-6-P residues when expressed in *X. laevis* oocytes. In addition, procathepsin H is an acceptor in an *in vitro* phosphotransferase assay, but mature cathepsin H is not. These data are consistent with at least a portion of the cathepsin H phosphotransferase recognition marker residing within the propiece.(Westlund, B. and Kornfeld S., unpublished data)

Regulated secretion. Human renin, an aspartyl protease, enters the regulated secretory pathway when expressed in the murine neuroendocrine cell line AtT-20. An attempt was made to identify a second aspartyl protease that is not secreted in a regulated manner from AtT-20 cells, with the intent of generating chimeras between the two proteins and mapping the regulated secretion trafficking marker. I examined human renin, human pepsinogen, yeast proteinase A, and human cathepsin D/human pepsinogen chimeras using

a secretagogue assay. All of them were found to enter the regulated secretory pathway, albeit extremely inefficiently.

In the course of the above studies, a human immunoglobulin lambda chain (hλA) was identified that enters the regulated secretory pathway in AtT-20 cells more efficiently than any of the aspartyl proteases. Confirmation of HλA's presence in secretory granules was obtained by subcellular fractionation and immunofluorescence studies. A second human lambda chain (hλB) differing from hλA by just 23 amino acids dispersed throughout the variable domain was subsequently shown not to enter the regulated secretory pathway in AtT-20 cells. Chimeras generated between hλA and hλB reveal that one or more amino acids within the hλA hypervariable loops are necessary for optimal sorting. The differential sorting of hλA and hλB is maintained in a second cell line capable of regulated secretion (the rat insulinoma line RIN-5F), indicating that the targeting mechanism is conserved. Recently, others have defined an amphipathic loop structure that may be the regulated secretion sorting signal (Cool, D.R., *et al.*, (1995) *J. Biol. Chem.* 270(15):8723-9). Initial modeling results suggest that hλA contains a similar loop structure, but hλB does not. Currently, this is being tested more stringently taking advantage of previously solved immunoglobulin lambda chain crystal structures.

2)Westlund, B., and Kornfeld, S. Differential Sorting of Two Highly Homologous Human Immunoglobulin Lambda Chains into the Regulated and Constitutive Secretory Pathways. Manuscript in preparation.

II. *Postdoctoral research* in the laboratory of Tim Schedl, Ph.D., Department of Genetics, Washington University Medical School. I have been studying germ cell tumor formation in the nematode *C. elegans*.

Laura Wilson Berry has identified a gain-of-function allele of *glp-1* that has semi-dominant tumorous germline and multivulva phenotypes. I engineered the *glp-1(oz112gf)* molecular lesion *in vitro* and expressed it in wild type hermaphrodites. The transgene was shown to recapitulate the somatic *glp-1(gf)* multivulva phenotype.

3)Berry, L.W., Westlund, B., and Schedl, T. Germline tumor formation and somatic cell fate alteration caused by a novel gain-of-function mutation in *glp-1*, a member of the *Notch* family of receptors. Manuscript in preparation.

Work in progress. Most of my efforts have been focused on *oz36*, which was isolated previously in the Schedl lab as a transient dominant suppressor of *fem-1(hc17)*. Interestingly, *oz36* hermaphrodites and males display an incompletely penetrant cold-sensitive late-onset tumorous germline phenotype. The distal-to-proximal polarity normally found within *C. elegans* germlines is established appropriately. However, with time the mitotically active stem cell population, usually confined to the most distal region of the gonad, expands

and in extreme cases fills the entire gonad arm. In addition, *oz36* hermaphrodites display a maternal effect sterile (as yet not well-characterized but not tumorous) phenotype at 25°C and males appear to be slightly feminized both in the soma and the germline. I mapped *oz36* to a 200 kb region between *stP127* and *mua-3* on chromosome III and showed that it represents a new allele of the previously identified gene *let-42*. The only other known allele of *let-42*, *g38*, exhibits the same temperature sensitive maternal effect sterility as *oz36* but is not tumorous. Based on behavior over a deficiency, neither *g38* nor *oz36* appears to be a null allele and *oz36* may be a gain-of-function. I have cloned *let-42* by transformation rescue. It is predicted to encode a 495 amino acid protein whose only significant homology to date is with a human aorta expressed sequence tag. The *g38* and *oz36* molecular lesions have been identified as missense and nonsense mutations, respectively. In *C. elegans*, mRNAs containing nonsense mutations are thought to be degraded by products of the *smg* genes. The tumorous phenotype of *oz36* was found to be enhanced in a *smg-1* background, consistent with it being the result of a gain-of-function. Due to similarities between the tumorous germline phenotypes of the *glp-1(gf)* allele mentioned above and *oz36*, I have begun to examine whether *oz36* interacts with the *glp-1* signalling pathway. *oz36* suppresses *glp-1(q231)*, a temperature sensitive partial loss-of-function, but does not suppress the null allele *(q175)*. My current efforts are focused on trying to dissect further the interaction between *oz36* and the *glp-1* signalling pathway. In addition, I hope to embark on a series of expression studies and am in the process of generating antisera against *let-42*.

NemaPharm, Inc.

AUTHORIZATION TO USE RADIOACTIVE MATERIALS

Instructions. *Complete this form and submit to Radiation Safety Officer. Authorization for use requires signed approval of Radiation Safety Officer.*

Name of Applicant

Ralph Clover

Social Security Number

185-44-5507

Department & Supervisor

Screening Department

Location where Isotopes will be used/stored

on site Room 417

Radioactive material(s):
(List chemical symbol and mass number of each)

P^{32}, P^{33}, S^{35}

Form of Material
(Chemical and/or Physical)

any form

Training and Education

Subject Covered	Date (MO/YR) Course	On-Job Training Yes/No	Hours	Instit	date
A. Principles and Practices of Radiation Protection	3/13/97 + 3/20/97		4 hrs total		
B. Measurements and Monitoring Techniques					
C. Mathematical principles for Calculating Activity					
D. Biological Effects of Radiation					

Experience (actual use of radioactive materials)

Isotope	Maximum Activity	Where Used?	Duration of Use	Type of Use
none				

I have read, understand, and agree to abide by NemaPharm's Radiation Safety Program.

Applicant Signature: Ralph Clover Date: 3/10/97

RSO Signature (Approval): _____ Date: _____

start date: 10/92

Ralph Clover, PhD
9 Adams Terrace
Cambridge, MA 02138
home phone: (617) 492-2669

EDUCATION:

Massachusetts Institute of Technology, Cambridge, MA
PhD in Microbiology May 1989
Thesis advisor: E.R Signer
Lipopolysaccharide in Symbiosis of *Rhizobium meliloti*

Purdue University, Ft. Wayne, IN
BS in Biology May 1982
Graduated with highest distinction (6.0/6.0)
Completed 2-semester research project in maize genetics

Pennsylvania State University, State College, PA
September 1969 - December 1971

SCIENTIFIC WORK EXPERIENCE

October 1992 - present
Staff Scientist, NemaPharm, Inc., Cambridge, MA

1988 - 1991
Postdoctoral Associate, Northeastern University, Boston, MA
studied chemotaxis of *Rhizobium meliloti* to sites on the roots of their alfalfa host

1983 - 1988
teaching Assistant for various MIT biology courses

January 1983 - August 1983
Research Intern, Argonne National Laboratory, Argonne, IL
studied effects of toxins on circadian rhythms of rats

PUBLICATIONS

Klein, S, K Lohman, R Clover, GC Walker and ER Signer (1982) A directional, high-frequency chromosomal mobilization system for genetic mapping of *Rhizobium meliloti*. Journal of Bacteriology. 174:324-326.

Clover, RH, J Kieber and ER Signer (1989) Lipopolysaccharide mutants of *Rhizobium meliloti* are not defective in symbiosis. Journal of Bacteriology. 171:3961-3967.

Kieber, J, R Clover, TM Finan and ER Signer (1987) "Surface properties of *Rhizobium meliloti* associated with symbiosis" in Molecular Genetics of Plant-Microbe Interactions. DPS Verma and N. Brisson eds. Martinus Nijhoff Publishers, pp 182-184.

Radiation Safety Officer

NemaPharm, Inc.

AUTHORIZATION TO USE RADIOACTIVE MATERIALS

Instructions. *Complete this form and submit to Radiation Safety Officer. Authorization for use requires signed approval of Radiation Safety Officer.*

Name of Applicant

Lin Sun

Social Security Number

552-91-1607

Department & Supervisor

Biology no supervisor required

Location where Isotopes will be used/stored

Radioactive material(s):
(List chemical symbol and mass number of each)

Form of Material
(Chemical and/or Physical)

α-^{32}P-dATP , ~ 580

^{35}S - methionine ~ 149

^{33}P

Training and Education

Subject Covered	Date (~~RSP~~) Course	On-Job Training Yes/No	Hours	Instit	date
A. Principles and Practices of Radiation Protection	1987, 1993	Yes		UCLA	1987
B. Measurements and Monitoring Techniques	1987, 1993	Yes		UCLA	1987
C. Mathematical principles for Calculating Activity	1987, 1993	Yes		UCLA	1987
D. Biological Effects of Radiation	1987, 1993	Yes		UCLA	1987

Experience (actual use of radioactive materials)

Isotope	Maximum Activity	Where Used?	Duration of Use	Type of Use
^{32}P		UCLA + MGH	10 years	labeling probes
^{35}S		UCLA + MGH	10 years	sequencing

I have read, understand, and agree to abide by NemaPharm's Radiation Safety Program.

Applicant Signature: Lin L Date: 3/10/97

RSO Signature (Approval): Lin L Date: 3/10/97

call Lisa 12/96

Resume

Name: Lin Sun

Date of Birth: April 27, 1959

Citizenship: Chinese, permanent resident of U.S.A.

Sex: Male

Institution Address: Department of Genetics, Harvard Medical School and Department of Molecular Biology, Massachusetts General Hospital, Boston, MA 02114, USA

Home Address: 453 Washington St., #1, Brookline, MA 02146, USA

Telephone Numbers: (617)726-5942 (work); (617)738-6059 (home).

Fax: (617)726-6893

E-Mail: sun@frodo.mgh.harvard.edu

Education

Postdoctoral fellow	Department of Genetics, Harvard Medical School and Department of Molecular Biology, Massachusetts General Hospital, March 1993-present.
Ph.D.	Department of Biology, University of California at Los Angeles, 1993
M.Sc.	Biology Department, Harbin Normal University and Biophysics Institute, Chinese Academy of Sciences, 1985
B.Sc.	Biology Department, Nanchong Teacher's College, 1982

Research and Working Experience

March 1993-present, Postdoctoral research fellow in the laboratory of Dr. Howard Goodman, Department of Genetics, Harvard Medical School and Department of Molecular Biology, Massachusetts General Hospital. Research intersts included isolation and functional analysis of new genes important for plant development and gene targeting in plants

Jan. 1987-March 1993 , In Dr. Tobin's laboratory at UCLA, involved in studying light-regulated cab gene expression in *Arabidopsis thaliana*. Ph.D. thesis: "Light-regulated gene expression: protein interacting with a phytochrome-responsive promoter in *Arabidopsis thaliana*".

April 1987-July 1987; April 1989-July 1989; April 1991-July 1991: Teaching assistant, Biology Dept., UCLA, Courses taught: Molecular Biology (Bio 144), Introduction to Principles of Genetics (Bio 8), and Principles of Biology (Bio 2);

Sept. 1986-Jan. 1987: Lab rotation in Dr. Dan S. Ray's laboratory, Biology Department, UCLA, working on minicircle DNA replication in the kinetoplast of *Trypanosome*.

Feb. 1985-June 1986: Associate in the Academy of Food and Fermentation Industries, Sichuan, China. Involved in discussions with the Miles Laboratories, Inc. for establishing a joint-venture project.

Sept. 1983-Nov. 1984: M. Sc. studies, Harbin Normal University and Institute of Biophysics, Chinese Academy of Sciences. M. Sc. thesis: " Isolation and Characterization of Chloroplast DNA from *Lycopersicon esculentum*".

April 1984-Sept. 1984: participated in the compilatory work on "An English-Japanese-Chinese Industrial Dictionary", National Defense Industry Press, Beijing, China.

Publications:

1. Sun, L and Goodman, H.M. (1995) Antisense prohibitin expression interferes with early development in transgenic *Arabidopsis*, in preparation.

2. cCA-1 encodes a transcription factor specifically involved in the phytochrome regulation of an Arabidopsis Lhcb gene, in preparation.

3. Sun, L., Doxsee. R.A., Harel, E. and Tobin, E.M. (1993) CA-1, a novel phosphoprotein, interacts with the promoter of the *cal* 140 gene in *Arabidopsis* and is undetectable in *det1* mutant seedlings. Plant Cell, 5, 109-121.

4. Sun,L and Tobin,E.M. (1990). Phytochrome-regulated expression of genes encoding light-harvesting chlorophyll a/b-protein in two long hypocotyl mutants and wild type plants of *Arabidopsis thaliana*. Photochem. Photobiol., 52, 51-56.

5. Tobin,E.M., Brusslan,J.A., Buzby,J.S., Karlin-Neumann,G.A., Kehoe,D.M., Okubara,P.A., Rolfe, S.A., Sun,L., and Yamada,T (1990). Phytochrome regulation of transcription: genetic and biochemical approaches. In Thomas,B(ed.) Phytochrome Properties and Biological Action, ASI Cell Biology Series, Springer-Verlag, New York;

6. Tobin,E.M., Brusslan,J.A., Buzby,J.S., Karlin-Neumann,G.A., Kehoe,D.M., Okubara,P.A., Rolfe, S.A., Sun,L. (1990). Approaches to understanding phytochrome regulation of transcription in Lemna gibba and Arabidopsis thaliana. In Herrmann,R. (ed.) Plant Molecular Biology, NATO/ASI Series, Plenum Press, New York;

7. Karlin-Neumann,G.A., Sun,L. and Tobin, E.M. (1988). Expression of light-harvesting chlorophyll a/b-protein genes is phytochrome-regulated in etiolated Arabidopsis thaliana seedlings. Plant Physiol., 88, 1323-1331.

8. Cheng,Z-Q, Sun,L, Huang,Y-F, Wang,Q-Y, and Wang,H-T.(1985). Isolation and initial characterization of chloroplast DNA from Lycopersicon esculentum. J. Biochemistry (Chinese) 1, 1-6.

9. Tang,Z-S, Deng,C-X and Sun,L. (1981). Chromosomal variations in barley mutants induced by 60Co irradiation. Acta Nanchong Teachers College.

Scientific Awards:

Dean's Graduate Fellowship, Biology Dept., UCLA, Oct. 1989-Dec. 1989, April 1990-June 1990, and Oct. 1990-March 1991;

McKnight Foundation Fellowship, Biology Dept., UCLA, May 1987-May 1989;

University Fellowship, UCLA, Oct. 1986-March 1987.

Outstanding Student Fellowship, Nanchong Teachers College Feb. 1978-Feb. 1982.

NemaPharm, Inc.

AUTHORIZATION TO USE RADIOACTIVE MATERIALS

Instructions. *Complete this form and submit to Radiation Safety Officer. Authorization for use requires signed approval of Radiation Safety Officer.*

Name of Applicant

Carl D. Johnson — VP Research, NemaPharm, Inc.

Social Security Number

345-42-3589

Department & Supervisor

Biology

Location where Isotopes will be used/stored

On premises: room #417

Radioactive material(s):
(List chemical symbol and mass number of each)

P^{33}, P^{32}, S^{35}

Form of Material
(Chemical and/or Physical)

Chemical or Physical

Training and Education

Subject Covered	Date ([redacted]) Course	On-Job Training Yes/No	Hours	Instit	date
A. Principles and Practices of Radiation Protection B. Measurements and Monitoring Techniques C. Mathematical principles for Calculating Activity D. Biological Effects of Radiation	Complete training in courses @ Cambridge NeuroScience, Inc 1988 @ University of Wisconsin 1977				

Experience (actual use of radioactive materials)

Isotope	Maximum Activity	Where Used?	Duration of Use	Type of Use
^{32}P	5 mCi	Cambridge NeuroScience	2 yr.	Molecular Biology/Sequencing
^{3}H	0.2 mCi	"	"	
^{3}H	15.0 mCi	Univ. of Wisconsin	8 yr.	Biochemistry Assays.
^{125}I	2 mCi	"	"	Labelling

I have read, understand, and agree to abide by NemaPharm's Radiation Safety Program.

Applicant Signature: [signature] Date: 3/10/97

RSO Signature (Approval): [signature] Date: 3/10/97

not updated

CURRICULUM VITAE

NAME: Carl Douglas Johnson

DATE OF BIRTH: May 7, 1948

PLACE OF BIRTH: Joliet, Illinois

CURRENT POSITION: President and Director of Research
NemaPharm, Incorporated
565 Science Dr.
Madison, WI 53711
phone -- (608) 233-2404
FAX -- (608) 238-5120

EDUCATION:

1966-1970 University of Chicago, Chicago, IL
B.S. in Chemistry with Honors.
Research advisor: Paul B. Sigler
Thesis: The Purification of Formylmethionine Transfer RNA from Baker's Yeast.

1970-1976 California Institute of Technology, Pasadena, CA
Ph.D. in Biology (Biochemistry and Genetics)
Research advisor: Richard L. Russell
Thesis: Multiple Molecular Forms of Cholinesterase from Elongated Animals (Electric Eel and Nematode)

PROFESSIONAL EXPERIENCE:

1976 NIH Post-doctoral Trainee/Division of Biology
California Institute of Technology

1977-1986 Post-doctoral Fellow, Assistant Scientist, Associate Scientist
Laboratory of Antony O.W. Stretton
Department of Zoology/University of Wisconsin

1987-1991 Director of Genetics
Cambridge NeuroScience Research/Cambridge, MA

1990 - President
NemaPharm, Inc.

1991- Visiting Scientist
Massachusetts Institute of Technology

RESEARCH SUPPORT -- GRANTS

1977-1979 Muscular Dystrophy Association Post-doctoral Fellowship: Neurotransmitter Functions in the Nematode Ascaris.

1979-1982 NIH Research Grant: Acetylcholine Function in the Nematode Ascaris.

1982-1986 NIH Research Grant: Monoclonal Antibodies to Neural Antigens of the Nematode Ascaris.

NIH Small Business Innovation Research (SBIR) Grant: Novel, Nematode-Specific Anthelmintics and Nematicides.

1988 Phase I ($50,000/6 months)

1989-1991 Phase II ($500,000/2 years)

RESEARCH SUPPORT -- CONTRACTS

American Cyanamid Contract Research: Phase II -- Biochemical Studies of Ivermectin Resistant Mutants; Phase III -- Molecular Cloning avr-15: a Putative Avermectins Receptor Structural Gene

1989 Phase II ($120,000/6 months)

1989-1990 Phase III ($240,000/1 year)

PATENT

"NemaScreen™: A Method for Screening and Classifying Compounds" -- Pending: U.S. Patent Application No. 305,835, Filed Feb. 3, 1989; CIP Filed Feb. 2, 1990.

PROFESSIONAL SOCIETIES

Genetics Society of America
Society for Neuroscience
Society for Developmental Biology
The Society of Nematologists
American Society of Parasitologists

PUBLICATIONS: ARTICLES

Johnson, C. D., K. Adolph, J. J. Rosa, M. D. Hall, and P. B. Sigler (1970): Crystallographic study of formylmethionine tRNA from baker's yeast. Nature 266:1246-1247.

Johnson, C. D., and R. L. Russell (1975): A rapid, simple radiometric assay for cholinesterase, suitable for multiple determinations. Anal. Biochem. 64:229-238.

Johnson, C. D., S. P. Smith, and R. L. Russell (1976): Separation and selective collagenase modification of Electrophorus electricus acetylcholinesterase. J. Neurochem. 28:617-624.

Russell, R. L., C. D. Johnson, J. B. Rand, S. Scherer, and M. S. Zwass (1977): Mutants of acetylcholine metabolism in the nematode Caenorhabditis elegans. J. Supramol. Struct. VIII:359-371.

Johnson, C. D. and A. O. W. Stretton (1980): Neural control of locomotion in Ascaris: anatomy, physiology and biochemistry. "Nematodes as model biological systems." ed. B.M. Zuckerman, Academic Press, N.Y. pp. 159-196.

Johnson, C. D., J. G. Duckett, J. G. Culotti, R. K. Herman, P. N. Meneely, and R. L. Russell (1981): An acetylcholinesterase-deficient mutant of the nematode Caenorhabditis elegans. Genetics 97:261-279.

Emmerling, M. R., C. D. Johnson, D. F. Mosher, B. H. Lipton, and J.E. Lilien (1981): Cross-linking and binding of fibronectin with asymmetric acetylcholinesterase. Biochemistry 20:3242-3247.

Rand, J. B. and C. D. Johnson (1981): A single-vial biphasic liquid extraction assay for choline acetyltransferase using [^{3}H]-choline. Anal. Biochem. 116:361-371.

Johnson, C. D. and R. L. Russell (1983): Multiple molecular forms of acetylcholinesterase from the nematode Caenorhabditis elegans. J. Neurochem. 41:30-46.

Johnson, C. D. and A. O. W. Stretton (1985): Localization of choline acetyltransferase within single motor neurons of the nematode Ascaris. J. Neurosci. 5:1984-1992.

Stretton, A. O. W., R. E. Davis, J. D. Angstadt, J. E. Donmoyer, and C. D. Johnson (1985): Neural control of behavior in Ascaris. Trends in Neuroscience 8:294-300.

Millar, T. J., I. Ishimoto, C. D. Johnson, M. L. Epstein, I. W. Chubb, and I G. Morgan (1985): Cholinergic and acetylcholinesterase containing neurons in the chicken retina. Neurosci. Letts. 8:311-316.

Johnson, C. D. and M. L. Epstein (1986): Monoclonal antibodies and polyvalent antiserum to chicken choline acetyltransferase. J. Neurochem. 46:968-976.

Tumosa, N., W. K. Stell, C. D. Johnson, and M. L. Epstein (1986): Putative cholinergic interneurons in the optic tectum of goldfish. Brain Research 370:365-370.

Ganetsky, B. and C. D. Johnson (1986): Invertebrate neurogenetics: physiological and neurochemical aspects. in "Encyclopedia of Neurosciences". eds. Edelman, et al., Springer-Verlag, New York.

Johnson, C. D. and A. O. W. Stretton (1987): GABA-immunoreactivity in

inhibitory motor neurons of the nematode Ascaris. J. Neurosci. 7:223-235.

Millar, T. J., I. Ishimoto, I. W. Chubb, M. L. Epstein, C. D. Johnson, and I. G. Morgan (1987): Cholinergic amacrine cells of the chicken retina: a light and electron microscope immunocytochemical study. Neuroscience 21:725-743.

Spira, A. W., Millar, T. J., I. Ishimoto, M. L. Epstein, C. D. Johnson, J. L. Dahl, and I. G. Morgan (1987): Localization of choline acetyltransferase-like immunoreactivity in the embryonic chick retina.J. Comp. Neurol. 260:526-538.

Millar, T. J., I. Ishimoto, M. Boelen, M. L. Epstein, C. D. Johnson, and I. G. Morgan (1987): The toxic effects of ethylene mustard aziridinium ion on cholinergic cells in the chicken retina. J. Neurosci. 7:343-356.

Johnson, C. D., J. B. Rand, R. K. Herman, B. D. Stern and R. L. Russell (1988): The acetylcholinesterase gene family of C. elegans: identification of a third gene (ace-3) and mosaic mapping of a synthetic lethal phenotype. Neuron 1:165-173

Johnson, C. D. (1989) The nematode Caenorhabditis elegans: a Model of the Human Nervous System

Erickson-Lamy, K. A., C. D. Johnson, B. True-Gabelt, and P. Kaufman (1990) Exp. Eye. Res. Ciliary muscle choline acetyltransferase and acetylcholinesterase after ciliary ganglionectomy.

Johnson, C. D. (1991) Nematode acetylcholinesterases: diversity and functions. In "Cholinesterases: Structure, Function, Catalytic Mechanism, Genetics and Cell Biology". ed. J. Massoulie, et. al., Conference Proceedings Series, American Chemical Society Press, Washington, D.C., pp. 136-140.

Guastella, J., C. D. Johnson, and A. O. W. Stretton (1991) J. Comp. Neurol. (in press) GABA immunoreactive neurons in the nematode Ascaris.

Sithigorngul, P., A. O. W. Stretton, and C. D. Johnson (manuscript) Monoclonal antibodies to Ascaris neural antigens generated by a specific immunosuppression method.

MNSB TELEPHONE CONVERSATION RECORD

Person Called: P. Yasemin VanBeuzekom, Director **Phone No.:** (617) 494 8701

Person Calling: Sattar Lodhi **Date:** 3-10-97

Facility Name: NemaPharm, Inc. Cambridge, MA **Time:** 11:15 a.m.

License No. New License **Docket No.** 030-34350

Subject: Response to Deficiency Letter

Summary: I called Ms. VanBeuzekom to remind her that we have not received their response to our letter dated February 28, 1997, and that because of Massachusetts becoming Agreement State on March 21, 1997, if we do not receive their response by today, we may not be able to process their application.

I cautioned her that if their response is inadequate, the whole package will be transferred to Massachusetts. She stated that their consultant is preparing the response and they should be able to fax it to us today. I gave her the Fax number and my phone number.

Action Required/Taken: Document

Signature: Sattar Lodhi Mail Control No. 124168

OFFICIAL RECORD COPY

DFL 10

FEB 25 1997

Docket No. 030-34350
Control No. 124166

Carl D. Johnson
Vice President of Research
NemaPharm, Inc.
26 Landsdowne Street, Suite 470
Cambridge, MA 02139

Dear Mr. Johnson:

This is in reference to your application dated December 27, 1996, requesting a Nuclear Regulatory Commission License. In order to continue our review, we need the following additional information:

1. Appendix 1 of your Radiation Safety Guide appears to indicate that an individual may use or supervise the use of licensed material if approved by your Radiation Safety Officer (RSO). Please note that holders of specific licenses of limited scope are required to obtain NRC's approval ***prior*** to allowing an individual to work as an authorized user. Please revise Appendix 1 of your Radiation Safety Guide accordingly, and confirm that you will request amendment to your NRC license ***prior*** to allowing individual(s) to work as authorized users of licensed material.

2. Provide a brief résumé of the training and experience of each person who will directly supervise the use of material, who will use material without supervision, or who will have responsibility for radiological safety. The résumé should include the type (on-the-job or formal course work), location, and duration of the training. Training should cover (a) principles and practices of radiation protection, (b) radioactivity measurements, standardization, and monitoring techniques and instruments, (c) mathematics and calculations basic to the use and measurement of radioactivity, and (d) biological effects of radiation. The description of the use of licensed materials should include the specific isotopes handled, the maximum quantities of materials handled, where the experience was gained, the duration of experience, and the type of use.

3. You have requested that Mr. Robert U. Johnson be named RSO on your license. It appears that this individual may be an outside consultant\contractor. If this is so, in support of this request, please address the following:

   a. Describe the control over the radiation safety program that will be delegated so that the consultant-RSO will be able to exercise authority

over authorized users when confronted with radiation safety problems that require implementation of corrective actions.

b. Describe the relationship that will exist between the consultant-RSO and your institutional management regarding expenditure of funds to facilitate the objectives of your radiation safety program and related regulatory requirements.

c. Identify other commitments of the consultant-RSO for other NRC or Agreement State licensed facilities, along with a description of how the consultant-RSO will allocate time to permit the performance of the duties of the RSO as described in the regulations. State the consultant-RSO's minimum amount of on-site time (hours per week).

d. Appoint an in-house representative who will serve as the point of contact during the RSO's absence. This person may be allowed to assist the consultant RSO with limited authority.

e. Describe the overall availability of the consultant-RSO to respond to questions or operational issues that arise during the conduct of your radiation safety program and related regulatory requirements. Specify the maximum amount of time it will take the RSO to arrive at the facility in the event of an emergency that requires his presence.

4. Please confirm that the RSO will also be responsible:

a. To ensure that the use of licensed material is by, or under the direct supervision of individuals specifically listed on your NRC license.

b. To perform routine inspections of all laboratories using or storing licensed materials.

c. To ensure that the terms and conditions of your license are met, and that all required records are maintained.

5. Please confirm that personnel will be instructed ***before*** beginning duties with, or in the vicinity of, licensed materials and will be reinstructed whenever there is a significant change in duties, regulations, or the terms of the license.

6. Please confirm that backup instruments will be available to replace instruments off-site for calibration.

7. Your consultant, Mr. Robert U. Johnson does not appear to have a service license to calibrate survey meters for outside clients. You may return the instruments to the manufacturer for calibration or employ the services of a licensed consultant in your area. If you intend to have a consultant calibrate

your survey meters, you should contact the consultant to determine if they are licensed to operate a commercial calibration service with the NRC or an Agreement State. Please submit the name, address, and NRC or Agreement State license number of the consultant or other calibration service you will use.

8. 10 CFR 20.1201 requires, in part, that skin dose be limited to 50 rems per year. 10 CFR 20.2203(b) requires, in part, that each report filed in response to a reportable event include an estimate of each individual's dose. The NRC has observed that programs of your scope have experienced skin contamination incidents. Describe your procedures for assessing dose from skin contamination with licensed material.

9. Please explain the limits for personnel exposure that are described on page 15 of your Radiation Safety Guide. These limits appear to be rather high for use as investigational limits. Please submit your investigational levels for the whole body (TEDE), extremities, and the skin-whole body doses.

10. Specify the action limits for radiation and contamination surveys of the restricted and unrestricted areas, and the actions to be taken when these limits are exceeded. The action limits should be in appropriate units.

11. 10 CFR 20.2003(a)(1) requires that a licensee may discharge licensed material into sanitary sewerage if the material is readily soluble (or is readily dispersible biological material). Information Notice 94-07 (enclosed) provides methods for determining compliance with this requirement which are acceptable to the NRC.

    Please review this Information Notice and provide specific information as to how you will assure that your releases to the sanitary sewerage system will meet the solubility criteria in 10 CFR 20.2003(a)(1). If you wish, you may indicate that you will use one of the methods described in Information Notice 94-07. Otherwise, describe your alternative methodology including the models, calculations, analytical techniques, and quality control measurements as well as the records that will be maintained.

12. You are requesting Robert U. Johnson to be the RSO. However, your emergency procedures on page 14 of your Radiation Safety Guide, list Dr. Carl Johnson as the RSO who is to be contacted in case of emergencies. Please identify which of these two individuals is the RSO, and confirm that you will include the name of the correct individual in your emergency procedures.

13. Your Radiation Safety Guide references old 10 CFR Part 20 requirements on page 21. Regulations in Part 20 of 10 CFR were revised and are effective since January 1994. Please update your Radiation Safety Guide to reflect the current regulatory requirements.

14. 10 CFR 20.1101(c) requires that the licensee review the radiation protection program content and implementation at least annually. Submit a description of your program for performing the required annual review. It should include the following criteria:

    a. Senior management oversight of the radiation protection program. Specify the mechanisms that will be used by senior management to ensure that they are aware of NRC regulations, the provisions of the license, and the compliance status of the institution's licensed program.

    b. Review of the Radiation Safety Officer and staff performance. Specify the minimum qualifications for an individual who will perform this review, and confirm that the results will be reported to senior management.

    c. Audits by the Radiation Safety Officer and staff to determine user compliance with the requirements of the NRC license and your radiation protection program. Audits should include such topics as: reviews of users' inventory and survey records, evaluation of users' radiation safety procedures through observation and discussion, and performance of independent work area surveys.

We will continue our review upon receipt of this information. Please reply in duplicate to my attention at the Region I Office and refer to Mail Control No. 124166. If you have any technical questions regarding this deficiency letter, please call Dr. Sattar Lodhi at (610) 337-5364.

If we do not receive a reply from you within 30 calendar days from the date of this letter, we shall assume that you do not wish to pursue your application.

Sincerely,

Original Signed By:

John D. Kinneman, Chief
Nuclear Materials Safety Branch 2
Division of Nuclear Materials Safety

Docket No. 030-34350
Control No. 124166

Enclosures:
1. 10 CFR Parts 19, 20, 30
2. Information Notice 94-07

OFFICIAL RECORD COPY

DOCUMENT NAME: R:\WPS\DLTR\L2030371.01

To receive a copy of this document, indicate in the box: "C" = Copy w/o attach/encl "E" = Copy w/ attach/encl "N" = No copy

OFFICE	DNMS/RI	N	DNMS/RI	N				
NAME	SLodhi		JHanneman					
DATE	02/11/97		02/18/97		02/ /97		02/ /97	

OFFICIAL RECORD COPY ML 10

26 Landsdowne Street
Cambridge, MA 02139
tel: (617) 494 8701
fax: (617) 494-5101

NemaPharm, Inc.

U.S. Nuclear Regulatory Commission, Region I
Nuclear Materials Safety Section B
475 Allendale Road
King of Prussia, PA 19406-1416

January 24, 1997

LL 30371
03-34350
03620

To Whom it may concern:

NemaPharm, Inc. is applying for a license to use sources of ionizing radiation in its laboratories in Cambridge, Massachusetts. Our intention is to use small amounts of radioisotopes in support of our program in pharmaceutical research and development. Labeled compounds will be purchased and used as received in assays of biological activity, binding, permeability, etc.

Our laboratory has been designed with the highest regard for chemical, biological and radiological safety. We have been diligent to arrange for secure areas for receipt, use, storage and disposal of radioactive materials.

Radioactive materials will be used in an area of our laboratory that is segregated and well-marked for its purpose. We will use survey meters, liquid scintillation and gamma counters in support of our research and to monitor our facilities. Calibration will be performed by Mr. Robert U. Johnson or another NRC licensed agents. Additional suitable equipment (glassware, pipettes, etc.) will be dedicated and so labeled for use with radioactives and not used outside of the designated area nor for any other purpose. Disposables and chemical wastes will be kept in well marked and segregated storage containers. We will make arrangements with ADCO, Inc. or another suitable qualified vendor to handle our radioactive waste.

Employees not designated to work with radioactive material will be instructed not to enter restricted areas. Others will be trained in the proper procedures for handling radioactive material and monitored for compliance. Our laboratories and employees will be monitored for possible contamination on a routine basis by making arrangements with an outside service such as Landouer, Inc. for routine analysis of film badges.

I would be happy to answer any questions you may have regarding our application. We would very much appreciate your prompt review of our submission. Thank you for your consideration.

Sincerely,

P. Yasemin VanBeuzekom
Director of Business Operations

124166
JAN 28 1997

MIL 10

cc: Don Camponelli, PhD, Cambridge Laboratory Consultants

NRC FORM 313 U. S. NUCLEAR REGULATORY COMMISSION

(7-96)
10 CFR 30, 32, 33
34, 35, 36, 39 and 40

APPROVED OMB NO. 3150-0120 EXPIRES: 7/31/99

Estimated burden per response to comply with this information collection request: 7 hours. Submittal of the application is necessary to determine that the applicant is qualified and that adequate procedures exist to protect the public health and safety. Forward comments regarding burden estimate to the information and Records Management Branch (T-6 F33), U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001, and to the Paperwork Reduction Project (3150-0120), Office of Management and Budget, Washington, DC 20503. NRC may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

APPLICATION FOR MATERIAL LICENSE

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.

APPLICATION FOR DISTRIBUTION OF EXEMPT PRODUCTS FILE APPLICATIONS WITH:

DIVISION OF INDUSTRIAL AND MEDICAL NUCLEAR SAFETY
OFFICE OF NUCLEAR MATERIALS SAFETY AND SAFEGUARDS
U.S. NUCLEAR REGULATORY COMMISSION
WASHINGTON, DC 20555-0001

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:

LICENSING ASSISTANT SECTION
NUCLEAR MATERIALS SAFETY BRANCH
U.S. NUCLEAR REGULATORY COMMISSION, REGION I
475 ALLENDALE ROAD
KING OF PRUSSIA, PA 19406-1415

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

NUCLEAR MATERIALS LICENSING SECTION
U.S. NUCLEAR REGULATORY COMMISSION, REGION II
101 MARIETTA STREET, N.W., SUITE 2900
ATLANTA, GA 30323-0199

IF YOU ARE LOCATED IN:

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

MATERIALS LICENSING SECTION
U.S. NUCLEAR REGULATORY COMMISSION, REGION III
801 WARRENVILLE RD.
LISLE, IL 60532-4351

ALASKA, ARIZONA, ARKANSAS, CALIFORNIA, COLORADO, HAWAII, IDAHO, KANSAS, LOUISIANA, MONTANA, NEBRASKA, NEVADA, NEW MEXICO, NORTH DAKOTA, OKLAHOMA, OREGON, PACIFIC TRUST TERRITORIES, SOUTH DAKOTA, TEXAS, UTAH, WASHINGTON, OR WYOMING, SEND APPLICATIONS TO:

NUCLEAR MATERIALS LICENSING SECTION
U.S. NUCLEAR REGULATORY COMMISSION, REGION IV
611 RYAN PLAZA DRIVE, SUITE 400
ARLINGTON, TX 76011-8064

LL 30371
030-34350
03620

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 JURISDICTIONS.

1. THIS IS AN APPLICATION FOR *(Check appropriate item)*
   - [X] A. NEW LICENSE
   - [ ] B. AMENDMENT TO LICENSE NUMBER _____
   - [ ] C. RENEWAL OF LICENSE NUMBER _____

2. NAME AND MAILING ADDRESS OF APPLICANT *(Include Zip code)*
   NemaPharm, Inc.
   26 Landsdowne St.
   Suite 470
   Cambridge, MA 02139

3. ADDRESS(ES) WHERE LICENSED MATERIAL WILL BE USED OR POSSESSED
   NemaPharm, Inc.
   26 Landsdowne St.
   Suite 470- Room 417
   Cambridge, MA 02139

4. NAME OF PERSON TO BE CONTACTED ABOUT THIS APPLICATION
   Pamela Yasemin vanBeuzekom
   TELEPHONE NUMBER
   (617)494-8701 X234

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
   see text

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

8. TRAINING FOR INDIVIDUALS WORKING IN OR FREQUENTING RESTRICTED AREAS
   see appendix 2

9. FACILITIES AND EQUIPMENT
   see attach floor plan

10. RADIATION SAFETY PROGRAM
    see attach document

11. WASTE MANAGEMENT
    see appendix 4

12. LICENSEE FEES *(See 10 CFR 170 and Section 170.31)*
    FEE CATEGORY 3M
    AMOUNT ENCLOSED $1,500

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, 36, 39 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, 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.

CERTIFYING OFFICER -- TYPED/PRINTED NAME AND TITLE	SIGNATURE	DATE
Carl D. Johnson V, President of Research		12/27/96

FOR NRC USE ONLY

TYPE OF FEE	FEE LOG	FEE CATEGORY	AMOUNT RECEIVED	CHECK NUMBER	COMMENTS
			$		124168

APPROVED BY | DATE

OFFICIAL RECORD COPY ML 10 JAN 28 1997

NRC FORM 313 (7-96) PRINTED ON RECYCLED PAPER

Attachment 1

Item 5. Licensed Material

Element and Mass No.	Chemical/Physical Form	Max Activity to be possessed at one time
Phosphorus - 32	Non-volatile organic and inorganic compounds	100 mCi
Phosphorus -33	Non-volatile organic and inorganic compounds	100 mCi
Sulfur - 35	Organic and inorganic liquid solutions (non-volatile)	100 mCi

The isotopes and amounts are to be used by several persons authorized and trained to use the material.

Item 6. Use of Radionuclides

All radionuclides we expect to use will usually be in microcurie amounts and occasionally millicurie amounts. They will be used in microbiological and biochemical studies as labelled nucleotides for in vitro studies. The P-33 will be used in DNA sequencing reactions. The basic nature of the research involves the use of radionuclides concurrently by our researchers. The S-35 will be used for in vitro translations, DNA sequencing reactions and protien binding assays. The possession limits have been chosen, after consultation with our scientists and Radiation Safety Consultant, to plan for prudent use and growth of the company and allow some latitude to include the activity in the decay storage program. The review by the RSO will preclude any individual using more than their experience and needs entails.

Item 7. Radiation Safety Trainer

see attached CV for Mr. Bob Johnson

Item 8 Training for individuals working in restricted areas.

See Appendix 2

ATTACHMENT I (con.)
Item 7.

CURRICULUM VITAE

ROBERT U. JOHNSON

DATE AND PLACE OF BIRTH: September 26, 1928 in Beverly, Ma.

HOME ADDRESS: 31 Chipman Road, Beverly, Ma. 01915

ACADEMIC TRAINING: B.S. In Chemistry with Minor in Physics From Northeastern University in 1951

MILITARY SERVICE: Korean Veteran, U.S. Army Sergeant 1951 to 1954

POSITIONS HELD:

Assoc. Radiation Protection Officer, Harvard University, 1959 to 1994 (RETIRED)
Assoc. Radiation Protection Officer, Mass. General Hospital 1961 to Present (Part Time)
Acting Radiation Protection officer, Mass. General Hospital 1965-1966
Radiation Protection Officer, Boston Biomedical Research Institute, 1969 to 1975, Consultant 1975 to 1994
Radiochemist, U.S.Atomic Energy Comm. Raw Materials Development Lab,(Nat'l Lead Co.) Winchester, Ma.1954-1959

MISCELLANEOUS CONSULTING:

Cambridge Nuclear Co.	1961 to 1971
Boston University	1971 to Present
Gamma Diagnostic Labs	1974 to 1990
Herley---MDI	1974 to Present (Retired)
Veterans Administration Hospital	1973 to 1994
Millipore and Milligen Cos.	1977 to 1992
Integrated Genetics	1979 to 1989
New England Bio-Labs	1980 to Present
Immulogic Pharmaceutical Corp.	1987 to 1995
Bio-Surface Technology Co	1987 to 1994
International Biotechnology Co.	1987 to 1993
Nissin Pharmaceutical Co.	1988 to 1993
Eisai Research Inst	1988 to Present
Gene-Trak Corp.	1985 to 1992
Ariad Pharmaceutical Corp.	1989 to Present
Leukocyte Inc.	1993 to Present

Occasional training sessions at Center for Blood Reseaarch, Ontogeny, and others.

MEMBER, RADIOISOTOPE COMMITTEE: Beth Israel Hospital, Brigham and Women's Hospital, Eye Research Inst. to 1994, Mass. General Hospital, Mass. Eye & Ear Infirmary to 1994, Children's Hospital 1965 to 1994, Dana Farber Cancer Inst. 1975 to 1994,

PROFESSIONAL SOCIETIES:

Health Physics Society(National and NE Chapters), 1959 to present, New England Roentgen Ray Society Laboratory Instructor 1964 to 1981, Charter Member "Conference on Radiological Health"

Attachment II

Item 9. Facilities

Floor plans of the NemaPharm, Inc. facilities in Cambridge. MA are attached. The laboratory areas in which radioisotopes will be used are indicated, as is the proposed location of the waste storage facility. The laboratories are presently under renovation and will be completed and occupied well before the radiation permit is issued.

Features of the laboratory

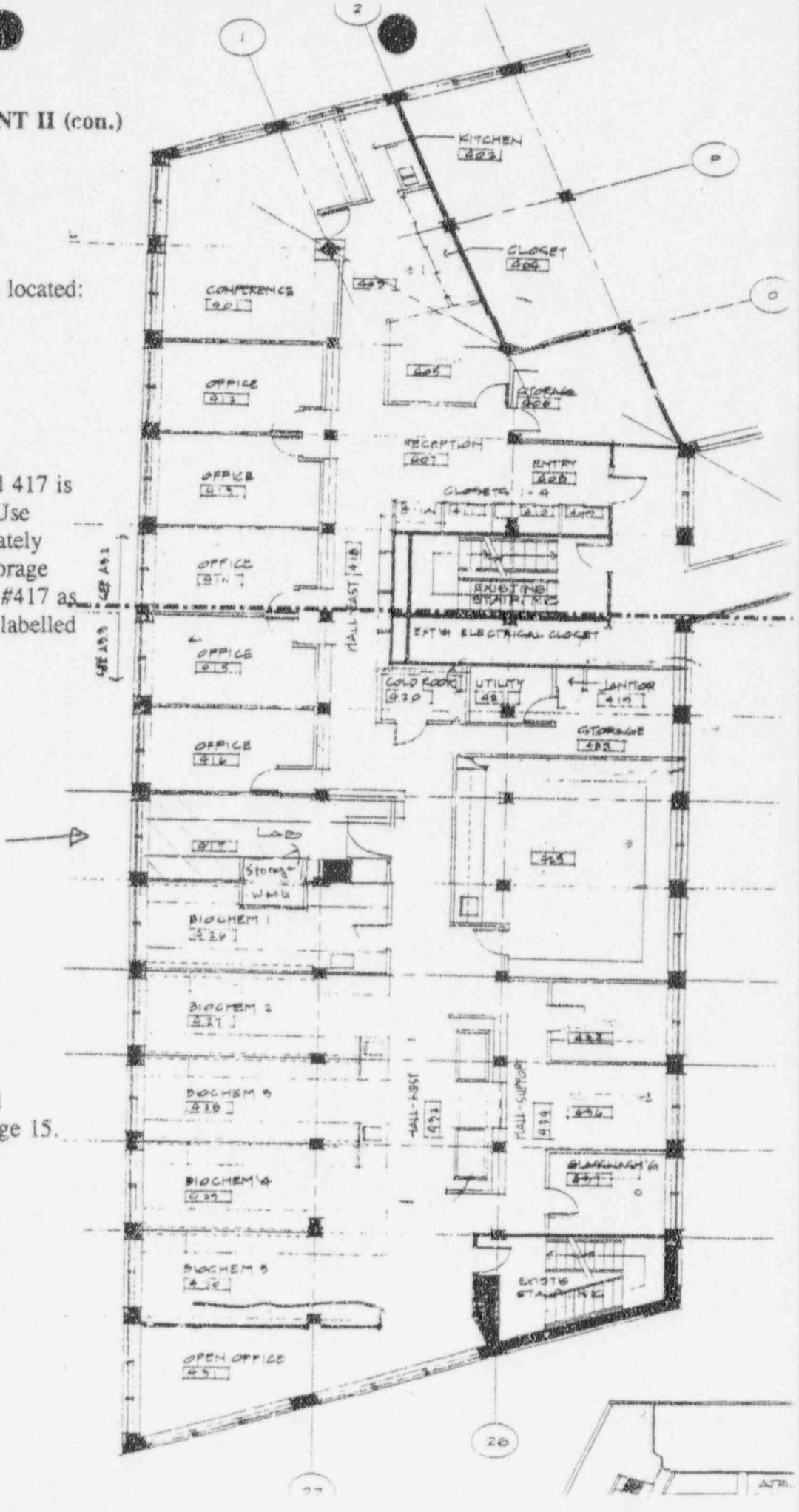
1. Floor covering:	Rolled seamless vinyl and vinyl tile or equivalent.
2. Working surfaces:	Stainless steel, formica, epoxy coated stone or equivalent; absorbent, plastic-backed paper will be used at all times.
3. Hoods:	Impervious surfaces (epoxy or SS); with minimum of 100 linear ft/min air flow across the front of the hood opening with the sashes at normal height (see floor plan).
4. Receiving:	All shipments will be brought to the front Receiving area and the RSO or assistant RSO will be notified. Check-in, radiation survey and logging will be done in the laboratory.
6. Security:	The company facility is secured on a 24 hour basis. During workdays, visitors must sign in with a centrally located security guard. Access, to the building during evening and weekends, is controlled by cardkey and regular key issued to company personnel. Visitors will call from an outside house phone and be escorted into company space. The lab areas are segregated from the office areas and only authorized personnel are allowed into the labs.
7. Waste Storage:	See Attachment V and floor plan.

ATTACHMENT II (con.)

NemaPharm, Inc. facilities located:

26 Landsdowne St
Suite 470
Cambridge, MA 02139

Laboratory room numbered 417 is designated as Radioactive Use Room. Enclosed and separately secure radioactive waste storage room also located in room #417 as depicted on floor plan and labelled "storage waste".



Also see Attachment V and Radiation Safety Guide, page 15.

Attachment III

Item 9. Radiation Detection Equipment and Calibration

Radiation Detection Equipment

Ludlum Model 3 with 44-9 Pancake Detector (Quantity=2)

Use: Monitor the use of 32P and 35S.
Range: 0.025 to 200 mr/hr.
Check: Check source (1 µCi Cs-137).

Liquid Scintillation Counting Spectrometer (Quantity = 1)

Model: Packard 1600TR 3000 or equivalent
Use: Experimental analysis and analysis of contamination smears and urine (bioassay) samples.
Range: 100 cpm/sample to 1,000.000 cpm/sample.
For tritium, 50 dpm/sample detectable limit.
For C-14, I-125, P-32, 100 dpm/sample detectable limit.

Calibration Procedure

Instrument calibration is performed at least annually and following repair by Mr. Robert U. Johnson, Independent Consultant (Harvard University Radiation Safety Officer) retired or at an NRC licensed calibration facility.

1. A calibration label is affixed to the instrument, specifying the ranges that have been calibrated and the date of calibration.

2. A certificate of calibration is provided for each instrument calibrated. Calibration certificates are kept at the company for a minimum of three years.

Attachment IV

Items 8, 10, 11. Radiation Protection Program

The attached Radiation Safety Guide covers all aspects of the company radiation protection program in detail. Please refer to the table of contents for specific items. (Please note that the section on Storage of Radioisotopes describes procedures for 'decay-storage' of certain isotopes which NemaPharm requests to be allowed to do as part of this application as required by Information Notice 90-09)

NemaPharm, Inc.

AUTHORIZATION TO USE RADIOACTIVE MATERIALS

Instructions. Complete this form and submit to Radiation Safety Officer. Authorization for use requires signed approval of Radiation Safety Officer.

Name of Applicant
John Doe

Social Security Number of Applicant
xxx-xx-xxxx

Department & Supervisor
Chemistry, Mary Roe

Location where isotopes will be used / stored
Biochem, Cell Bio, Tissue Culture, Receiving, and Waste Storage Rooms

Radioactive material(s):

List chemical symbol and mass number of each	Form of Material (Chemical and/or Physical)
I-125	NaI, proteins and non-volatile organics
H-3	Non-volatile organics (e.g., peptides)
C-14	Non-volatile organics (e.g., peptides)

Training and Education

Subject Covered	Date of Course	On-Job Training Yes / No	Hours	Institution	Date Completed
A. Principles and Practices		Y		UNU	1985
of Radiation Protection		Y		ARF	1988
B. Measurements and Monitoring Techniques		Y		"	"
C. Mathematical principles for Calculating Activity		Y		"	"
D. Biological Effects of Radiation		Y		"	"

UNU = UnNamed Universtiy; ARF = Another Research Facility

Experience (actual use of radioactive materials)

Isotope	Maximum Activity	Where Used	Duration of Use	Type of Use
H-3	200 mCi/yr	UNU/ARF	1985-8	bindingassays,
S-35	100 mCi/yr	ARF	1985-8	metabolism,
C-14	50 mCi/yr	UNU/ARF	1985-8	membrane perm-
Rb-86	10 mCi/yr	ARF	1985-8	eability studies

I have read, understand, and agree to abide by NemaPharm's Radiation Safety Program.

Applicant Signature _____ Date:_____

RSO Signature (Approval):_____ Date:_____

Attachment V

Item 11. Waste Management

Laboratory waste is collected and stored in containers within the laboratories. Periodically, waste is transported to a larger, secure Waste Storage Room for decay in storage as described in the company manual in fulfillment of Regulatory Guide 90.09. This room (see floor plan) will have a locked door and restricted access. It will be surveyed weekly and the results logged. Ultimately, waste is removed by a licensed vendor, such as ADCO Services, Inc.

NemaPharm, Inc.

RADIATION SAFETY GUIDE

December, 1996

Table of Contents

INTRODUCTION

All uses of radioactive material at NemaPharm, Inc. are controlled by the radiation protection program.

NO WORK WITH SOURCES OF IONIZING RADIATION CAN BE INITIATED UNLESS AUTHORIZATION HAS BEEN OBTAINED FROM THE RADIATION SAFETY OFFICER.

All uses of ionizing radiation (except ultra-violet radiation) in Massachusetts are controlled and regulated by the U. S. Nuclear Regulatory Commission (NRC). NemaPharm has established a radiation safety program to give the necessary assurances to the NRC as well as the company management that all potentially hazardous sources of radiation will be used safely. This guide describes the organization of the program and specifies the regulations, policies and procedures and practices which are to be followed when using radioactive materials.

It is NemaPharm's policy that use of radioactive materials be kept to a minimum and that there be no unwarranted radiation exposure. The prevailing standards for use of radioisotopes requires exposures "as low as reasonably achievable (ALARA)". This means that all possible precautions are to be taken to reduce personnel exposure. Due regard must always be given to the safety and welfare of the radiation workers and the general population, the protection of NemaPharm property and minimization of NemaPharm liability. The NemaPharm operational policy places responsibility on the user and persons who supervise use of radioactive materials. These supervisors can satisfy their responsibilities by adhering to this guide and by requesting assistance from the Radiation Safety Officer (RSO) when there are questions or suspected problems.

NemaPharm will use radioisotopes under a specific license which will be on file with the Radiation Safety Officer (RSO). Only the following isotopes will be used: P-32, P-33 and S-35.

This guide is organized in the following manner:

Section 1	General description of the NemaPharm Radiation Safety Program, Organization and Responsibilities
Section 2	Detailed Procedures and Practices

1. Description of the NemaPharm, Inc. Radiation Safety Program

There are three levels of authority in the radiation safety program:

The Radiation Safety Officer (RSO)

The RSO together with the management of NemaPharm establishes the radiation safety policy such that:

1. Unwarranted radiation safety exposures of NemaPharm employees and general public are avoided.

2. Compliance with all the federal and state regulations is assured.

3. NemaPharm property is protected and liability are minimized.

Specifically, the RSO meets these responsibilities by routinely monitoring all uses of radioactive material to ensure that: (a) each use is by or under the supervision of a properly authorized supervisor, (b) that the appropriate personnel and environmental monitoring equipment is being used and (c) that radioactive material is properly secured against unauthorized removal when not is use.

The Authorized Supervisor (Scientists or Department Manager)

The supervisor has primary responsibility for the radiation safety associated with each source under his/her control. He must ascertain that each person under his supervision using these sources is properly trained and aware of the attendant hazards (see Training Requirements). He must also assure that use of the sources conform to all the safety conditions of this authorization and those of this guide.

The Supervised User

These individuals must use the sources of radiation only under the direction of a supervisor. They must follow those procedures and practices established by the supervisor. All new users are required to attend a Radiation Safety Training Seminar before they begin work with radioactive materials (see Training Requirements).

2. Radiation Regulations, Policies, Procedures and Practices

a. Federal Regulations

The Nuclear Regulatory Commission has established "Standards for Radiation Protection" [10 CFR 20.1001 - 20.2402 (see Appendix for a copy)]. These standards must be strictly adhered to during all uses of by-product material. The NRC also has adopted regulations which assure that workers will be advised of the sources of radiation being used, the hazards, the safety precautions in effect, etc. at the place of employment. These rights are present in "Notice of Instructions and Reports to Workers; Inspections" [10 CFR 19 (see Appendix for a copy)].

b. NemaPharm Policies and Procedures

Management recogniz both the NRC regulations and company policy of preventing unnecessary exposures to radiation as the basic criteria for establishing the radiation safety policies and procedures. The principle means by which the company assures the safe use of sources of radiation are:

1. To require that a person be authorized to use or supervise the use of radiation sources.

2. To require RSO approval for acquisition, receipt and transfer, including disposal of radioisotopes.

Specific procedures and practices have been established for most routine or recurrent situations to assure compliance to the regulations and company policy. For unusual situations, the RSO will interpret the existing regulations, policies and procedures to establish guidelines.

These are the established procedures and practices:

1. Authorization to Use Radioisotopes (Appendix 1)

2. Training of Workers (Appendix 2)

3. Use of Radioisotopes (Appendix 3)

4. Special Procedures (Appendix 4)

5. U.S. Nuclear Regulatory Commission Regulations (Appendix 5)

c. Professional Standards

The RSO also uses as operational guides the published data and recommendations of professionally recognized national and international committees and organizations concerned with health physics or radiation protection, examples of which are:

1. National Council on Radiation Protection (NCRP)

2. International Committee on Radiation Protection (ICRP)

3. International Atomic Energy Agency (IAEA)

4. Health Physics Society (HPS)

APPENDIX 1

Authorization to Use Sources of Radiation

An individual can use or possess radioactive materials only after (s)he has presented evidence of proper training and experience, read the NemaPharm, Inc. Radiation Safety Guide, and received training on the practical aspects of Radiation Protection from the RSO (Section I of Training Outline). Retraining and continuing education occur at least annually by the RSO or an outside consultants (Section I and II of Training Outline). Technique specific training is provided by the supervisor. A company Authorization Use Form must be submitted to the RSO and the RSO must approve the application.

Authorization to use one isotopes does not necessarily authorize the use of all isotopes. The authorization of a Principal Investigator (PI) does not automatically authorize the other personnel in the lab to use a radioisotope.

The Authorization will be reviewed and updated when the company NRC license is submitted for renewal.

A copy of the authorization use form is on the next page.

NemaPharm, Inc.

AUTHORIZATION TO USE RADIOACTIVE MATERIALS

Instructions. *Complete this form and submit to Radiation Safety Officer. Authorization for use requires signed approval of Radiation Safety Officer.*

Name of Applicant **Social Security Number**

Department & Supervisor **Location where Isotopes will be used/stored**

Radioactive material(s):
(List chemical symbol and mass number of each)

Form of Material
(Chemical and/or Physical)

Training and Education

Subject Covered	Date (NP) Course	On-Job Training Yes|No	Hours	Instit	date
A. Principles and Practices of Radiation Protection					
B. Measurements and Monitoring Techniques					
C. Mathematical principles for Calculating Activity					
D. Biological Effects of Radiation					

Experience (actual use of radioactive materials)

Isotope	Maximum Activity	Where Used?	Duration of Use	Type of Use

I have read, understand, and agree to abide by NemaPharm's Radiation Safety Program.

Applicant Signature: _____ Date: _____

RSO Signature (Approval):_____ Date: _____

APPENDIX 2

TRAINING OF WORKERS

Individuals using radioisotopes under an NRC license have certain rights as prescribed in 10 CFR 19 "Notices, Instructions and Reports to Workers; Inspections" (see Appendix 5). In accordance with Part 19, a copy of the NemaPharm license and a copy of the Notice posted in radioisotope areas to advise persons in those areas where work is being done and to describe the documents and regulations pertinent to that work are included in this Appendix.

The RSO is in charge of radiation safety training at NemaPharm. (S)he will either conduct personally the Radiation Safety Training Seminar or have it taught by an independent outside consultant.

NemaPharm has designed its training program to assure that all persons working in or frequenting areas of radioisotope usage are aware of the attendant hazards. All persons using radioisotopes or frequenting areas where radioisotopes are used must attend the Training Seminar which covers the material shown on the following pages. The RSO shall keep records of attendance at these orientations.

Training will also be provided for ancillary personnel (custodial and maintenance), who may frequent areas where radioactive material is stored or used, by the RSO or the Company outside Radiation Safety Consultant. All new staff who work in an area or at a job function where they may encounter radioactive materials must go through safety training.

Annual re-training seminars will be provided for all radiation workers and ancillary staff.

Radiation Safety Training Program Outline

Section I

Responsibility for Training & Radiation Practices

Procedures for Working with Radiation

Units of Radioactivity and Radiation

Safe Handling Techniques

Measurement and Control of Radiation Exposures

Radiation Survey Techniques

Waste Disposal

Waste Minimization

Spills/Accidents

NRC Regulations, NRC Guides, Materials License

Section II

Concepts of Ionizing Radiation

Biological Effects of Radiation

Maximum Permissible Exposures

Update on New Regulations

Update on Low Level Radiation Waste

To NemaPharm Employees

In accordance with the United States Nuclear Regulatory Commission Regulation 10 CFR 19.ll, the following documents relating to the work are available to you from the company.

1. 10 CFR 20.1001 - which describes the Nuclear Regulatory Commission Standards for Radiation Protection which must be adhered to in the use of sources of radiation.

2. 10 CFR 19 -which describes the Nuclear Regulatory Commissions Regulations pertaining to notices, instructions, and reports to workers and inspections of radiation activities.

3. Regulatory License and Applications-which specify the special conditions under which radiation work must be carried out.

4. NemaPharm Radiation Safety Guide - which specifies NemaPharm radiation safety policies and procedures.

Ancillary Workers Instructions

What to do About Radioactive Materials

1. Rooms which have the radiation symbol shown on doors or on equipment may contain radioactive materials. You must be careful when working in these rooms. You can sweep, mop, and wax the floors and remove the waste which is not labeled with the radiation symbol, just as in any other room.

2. Any container (box, bottle, carton, etc.) which has radioactive material in it will have the radiation symbol on it. Do not touch these containers. If the contents of these containers are spilled, **DO NOT TOUCH THEM OR ATTEMPT TO CLEAN THEM UP.** Tell your supervisor or the Radiation Safety Officer (RSO).

3. DO NOT empty any waste container which has the radiation symbol on it.

4. DO NOT empty any waste container which has waste material, such as boxes or bottles, with the radiation symbol in it. Tell your supervisor about it.

5. DO NOT eat, drink, smoke or apply cosmetics in any lab or in any room which has the radiation symbol on its door. DO NOT dispose of food/drink, cans/wrappers in laboratory trash

6. Before you work on or around a device or on a piece of equipment with a radiation symbol on it, contact the RSO so the device may be checked for safety.

7. If you think you may have gotten some radioactive material on your skin or clothing, call the RSO immediately. (S)he will assist with proper removal or decontamination.

8. In an emergency, or if you have any questions, ask your supervisor or the RSO for help.

APPENDIX 3

USE OF RADIOISOTOPES

The authorized supervisor is responsible for seeing that the users of radioisotopes under her/his authorization comply with all the governmental regulations, the specific conditions and limitations of her/his authorization, and the procedures and practices outlined in this Appendix. S/he ascertains that all persons who use radioisotopes under the coverage of her/his authorization are supervised, properly trained and experienced, aware of the attendant hazards, and observe the procedures of this guide.

Training and Experience

See Appendix 2 of this guide.

Receipt, Transfer and Disposal of Radioactive Material

All radioisotopes must be shipped to this address:

NemaPharm, Inc.
26 Landsdowne Street
Cambridge, MA 02139
Attn: Radiation Safety Officer

Purchase orders for all radioactive materials must be signed by the RSO or the Assistant RSO. All radioisotopes received will be placed in a holding area. The user will check for contamination and record receipt. (See Appendix 4 for procedures and forms.)

All radioactive material must be disposed of through procedures approved by the RSO. Only those small amounts of liquid radioactive waste allowed by law may be disposed of down the drain of designated sinks. Liquid waste must be placed in a properly labelled plastic container. Solid waste must be placed in a properly labelled container lined with a plastic bag. Liquid scintillation vials must be kept separate. All radioactive waste will be packaged according to the waste vendor's specifications for removal to the disposal site.

Radiation Surveys

Authorized users conduct routine radiation and contamination surveys of their areas. The user must conduct these routine surveys as follows:

RADIATION SURVEYS ARE TO BE MADE BY THE USER AFTER EACH EXPERIMENTAL RUN OR AT THE END OF THE DAY RADIOISOTOPES ARE USED IN ORDER TO DETERMINE THE EXTENT OF RADIOACTIVE CONTAMINATION AND TO ASCERTAIN THAT ALL WASTE AND STOCK MATERIAL HAS BEEN STORED OR PROPERLY DISPOSED OF.

In addition, the RSO, assistant or a designated independent consultant will conduct monthly surveys of all lab areas. All labs are surveyed with an appropriate calibrated survey meter. Wipe tests are taken on all bench tops, hood ledges, sink areas, storage and

waste disposal areas. Surveys will also check for proper labeling, signage, and adherence to rules and regulations by users.

When material is known to have been spilled or become airborne, wipe test surveys of the affected area must be made. Such tests can be made with filter paper or squares of any absorbent paper and the wipes counted with an appropriate counting instrument. The RSO must be called if a researcher has reason to believe his work has resulted in gross contamination or constitutes an emergency situation. (See Emergency Procedures below.)

For example, results from wipe tests must be less than 200 dpm/100 cm2 for P-32, and S-35, and less than 100 dpm/100 cm2 for I-125. If levels are found to be higher than these limits, the area must be decontaminated and re-surveyed until counts fall below these limits.

All radiation survey reports will be maintained by the RSO for inspection by the NRC.

Storage of Radioisotopes

10 CFR 20.1801 requires that licensed material be secured against unauthorized removal from designated storage. In addition 10 CFR 20.1802 requires that NemaPharm control and maintain constant surveillance over materials in unrestricted areas that are not in storage.

Radioisotopes are stored under lock and key to permit access only to authorized users. Each area and room where radioisotopes are stored must be posted with a "Radioactive Material" sign. Radiation levels around storage areas must be measured. If radiation doses could exceed five (5) millirem per hour in an occupiable area, the area must be shielded and also posted with a radiation area sign. Proper signs can be obtained from the RSO or assistant RSO.

NemaPharm will 'decay-in-store' waste from P-32 (T1/2 14 days), P-33 and S-35 (T1/2 87 days). If feasible the waste will be compacted prior to storage. Paper, plastic, and other lab trash expendables are securely stored in covered containers by isotope in a separate, lockable storage room for 10 half lives. The waste is monitored with a survey meter and discarded in the trash only when no radiation above background is detectable. When no radiation is detected, radiation labels are removed prior to placing in the trash.

(See Appendix 4 for Radioisotope Inventory Form.)

Records

A receipt log book will be kept in the radiation holding area to record the receipt of radioactive materials. Log sheets for use and disposal will be kept and posted in appropriate areas. A survey log form will also be used to record the date and results of radiation and contamination surveys, even when the results are negative. Master radioactive material inventory sheets for each isotope will be kept by the RSO based on the information derived from the user logs. See Appendix 4 for examples of these logs.

Other records required by federal law are kept by the RSO or a designated assistant.

Restriction of Radioisotopes Areas

Access to areas where radioisotopes are stored and used must be restricted to those persons cognizant of the associated hazards.

Radioactive Waste

Radioactive waste must be disposed of through procedures approved by the RSO. No waste is to be washed down drains, incinerated, or otherwise disposed without prior clearance from the RSO. A copy of the detailed procedures for waste disposal is given in Appendix 4.

Emergency Procedures

A radiation emergency occurs when a set of circumstances results in hazardous radiation levels, hazardous concentrations of airborne radioisotopes, or gross contamination of property. Examples of radiation emergencies and actions to be taken are:

a. Personnel Contamination
   1) Remove contaminated clothing.
   2) Wash contaminated skin with mild soap and water. Do not use abrasives.
   3) Call the RSO. After hours, refer to the emergency call list.

b. Spill of radioisotope where radioisotope does not become airborne
   1) Wipe up with absorbent paper using a blotting motion so you do not spread contamination.
   2) Dispose of contaminated paper in radioactive waste container.
   3) Call the RSO. After hours, refer to the emergency call list.

c. Volatilization of liquid or dispersal of solid radioisotope outside a ventilated enclosure
   1) If possible, keep contamination localized by closing doors and restricting access to area. (Do NOT shut off hood)
   2) Leave the area.
   3) Call the RSO. After hours, refer to the emergency call list.

d. Fire in radioisotope area.
   1) Treat fire in normal manner.
   2) Call the RSO. After hours, refer to the emergency call list.

ALWAYS USE COMMON SENSE IN HANDLING RADIATION EMERGENCIES AND CALL THE RSO AS SOON AS PRACTICAL. DO NOT TRACK OR OTHERWISE PERMIT RADIOISOTOPES TO BE SPREAD INTO CLEAN AREAS.

NemaPharm Radiation Safety Officer:	Dr. Carl Johnson
Daytime phone:	(617) 494-8701
Weekends & Evenings:	Refer to the emergency call list.

A more detailed procedure can be found on page 17 of this document

Personnel Monitoring

The RSO determines the need for personnel dosimetry during the authorization evaluation or evaluation of amendment requests.

NemaPharm requires all personnel using or routinely exposed to radioisotopes to wear film badges. Badges are supplied and analyzed monthly by R. S. Landauer, Jr. & Co., 39 Milltown Road, East Brunswick, NJ, 08816. Individuals using 1 mCi or more of P-32 are also required to wear a TLD finger ring. Monitoring reports are returned to the RSO, who reviews them to assure that exposures are maintained within acceptable levels.

The authorized supervisor has the responsibility to assure that all persons who use radioisotopes or work in his(her) area wear appropriate radiation dosimeters when required.

Maximum Permissible Dose levels have been set by the National Council on Radiation protection and Measurement. The following limits are in effect at NemaPharm pending further investigation:

Annual (for non pregnant workers)

Whole body- TEDE	2,400 millirems
Extremities	37,500 millirems
Skin- whole body	15,000 millirems

Because of the vulnerability of the fetus, the whole body exposure for pregnant women shall be limited to 500 millirems for the duration of the pregnancy. Employees who suspect they may be pregnant and who work in areas where radioactive materials are used are requested to see the RSO. The Pregnant worker should be made aware of the fact that the fetus is especially vulnerable to the effects of ionizing radiation.

Radioisotope Laboratory Design

The design and furnishings of a laboratory must be commensurate with the hazards presented by the radioisotope and its condition of use. In practical terms, some baseline requirements are that:

a. Bench tops or other surfaces on which radioisotopes will be used must either be made of or be covered with a permanently impervious surface.

b. Floors must be covered with an impervious material; properly waxed, vinyl asbestos tiles are normally acceptable.

c. Walls must have a smooth, crack- and hole-free surface.

d. Proper room ventilation and adequate radioisotope storage must be provided.

Rules for Working with Radioactive Materials

The following pages outline the routine working procedures for handling radioactive materials at NemaPharm.

RULES FOR WORKING WITH RADIOACTIVE MATERIALS
ROUTINE PROCEDURES

Eating, drinking, smoking	Eating, drinking, smoking or using cosmetics is not permitted in this laboratory.
Food	Never keep or store beverages or food in radioisotope labs, refrigerators or freezers with radioisotopes.
Wash hands	Wash hands after handling any radioactive material before going about other work.
Pipetting	Never pipette anything, even water, by mouth.
Eyewear	Always wear safety glasses in the laboratory. See Chemical Hygiene Plan outlining NemaPharm policy.
Protective Clothing	Always use latex gloves when handling radioisotopes. Protective gloves must be removed before leaving the laboratory to avoid contaminating doorknobs and telephones. Lab coats must be worn in the lab and left in the laboratory. Open toe sandals are not allowed in the lab.
Confine the Activity	Always work over trays or on absorbent paper or transparent benchtop covers. Transport radioactive materials doubly contained.
Spills	Notify the Radiation Safety Officer of all spills.
Labeling	Label radioactive material with your name, date, isotope and quantity of isotope.
Signage	Clearly label all containers of radioactive material and post all radiation and storage areas with the standard radiation warning symbol. Placards for posting of radiation and storage areas should bear the legend "Caution -- Radiation Area" or "Caution -- Radioactive Material", respectively.
Disposal of Liquid	Liquid radioactive materials must be stored in plastic containers or in metal containers if the material is incompatible with plastic. The quantity of isotope, the isotope name, date, and the user's name must be recorded in a log kept with the container. A log is also kept of all liquids disposed of at designated sinks.
Disposal of Solid	Solid radioactive waste must be placed in plastic-lined boxes or containers. When filled, the contents are transferred to a drum in the waste storage room.
Hoods	Materials which could become airborne must be stored and used in a hood. All vacuum pumps involved in radioactive work should be vented into a hood. Hood ventilation shall be left "ON" at all times.
Before Leaving	Clean up and monitor your work area and yourself.

RULES FOR WORKING WITH RADIOACTIVE MATERIALS
EMERGENCY PROCEDURES

EXTREME HAZARDS ***Hazards such as high radiation levels (greater than 2200 dpm/) or the possibility of airborne contamination from dry or volatile radioactive materials.***

Evacuate Evacuate the laboratory immediately; close the door and lock it.

Call RSO Call the RSO immediately. If you have to leave the area to do so, remove your shoes if you suspect contamination and do not touch anything unnecessarily.

OTHER HAZARDS ***Hazards such as spills or suspected spills of radioactive material where the material does not become airborne.***

Keep Calm Keep calm, use common sense, protect people, do not spread contamination (always assume you are contaminated until a survey proves otherwise).

Confine Contamination Localize the spill. Right tipped container; drop absorbent material on the spill. Damp down a dry spill.

Do not track contamination about the laboratory. Call, do not go for help, if possible!

Close door, and where possible adjust the ventilation to prevent spread of airborne material.

Check shoes before leaving the area of a cleaned up spill.

Protect Personnel Remove contaminated clothing and wash contaminated parts of the body with detergent. Be especially thorough in flushing out wounds. Care should be taken not to abrade the skin, as this may introduce internal contamination.

Warn other workers.

Decontaminate If thorough washing with detergent does not remove contamination from body, consult the RSO.

You will be expected to perform the major work of decontamination of the area of your spill. The RSO will survey for contamination and advise on procedures and assist as necessary.

All suspected contaminated persons and areas must be monitored after decontamination and before work is resumed.

Submit a complete written record to the RSO of the accident and subsequent remedial protective measures

IN ALL EMERGENCIES, EXCEPT VERY MINOR SPILLS OF RADIOACTIVE MATERIALS, THE RSC MUST BE CALLED AS SOON AS POSSIBLE.

APPENDIX 4

SPECIAL PROCEDURES

Monthly Laboratory Survey Procedure

1. Laboratory contamination surveys shall be done on a monthly basis, either by the RSO, an appointed RSO assistant or an independent consultant.

Surveys must also be done by the researcher using radioactive materials at least daily when radiation is used.

2. A survey data notebook must be kept, containing layouts of the laboratories indicating the points at which the wipes were made and data tables containing the results of the counting of the wipes.

3. Wipes are made using filter paper. Approximately 100 square centimeters of surface should be wiped.

4. Penetrating radiation, e.g., P-32, can be monitored with the solid scintillation probe survey instrument.

Radioactive Material Receipt and Opening Procedure

Package Receipt

1. If the shipment appears to be damaged, ask the carrier to remain and immediately proceed to the 'Package Opening' procedure below.

2. A contamination survey must be made within three (3) hours after receipt of a radioactive material shipment (within 18 hours if the delivery is after hours). Deliveries are accepted only between 9am - 5pm Monday through Friday. No weekend deliveries.

3. Radioactive material shipments must be separated from the non-radioactive shipments upon receipt. The Radiation Safety Officer or RSO assistant must be notified immediately.

Package Opening

1. Wear gloves a lab coat and badge and glasses when opening the package.

2. Wipe the outside shipping container surface and count the wipes to check for contamination. Record the results.

3. Using the G-M survey meter, measure the radiation levels at the surface of the container and if necessary at one meter from the surface. Record the results.

4. Open the package, and take a wipe of the primary vial containing the radioisotope (or the outside of the package if it is sterile wrapped). Count these and record the results. If there are no counts above background, the container may be discarded in regular trash; otherwise the container must be discarded with solid radiation waste.

5. Record any signs of damage to the package or to the vial.

6. If there is contamination or an excessive radiation level, check the NRC regulations (10 CFR 20.205) to see if the NRC or the shipper must be notified.

7. The wipes shall be counted in the Liquid Scintillation Counter.

NemaPharm, Inc.

Radioisotope Receipt and Delivery

Radioisotope Ordered _____ Activity Ordered _____

Radioisotope Received _____ Activity Received _____

P.O. #_____ Date of Receipt_____

Location of Use_____

Contamination Survey
Counts per minute over 100 cm2 area: _____ cpm

Efficiency of counting instrument: _____ %

Contamination level (dpm) = cpm/effic. = _____ dpm

Contamination level (μCi) = ___ _____ dpm/2.22 x 106 d/μCi = _____ μCi

For S-35, P-32 and P-33 Packages of 10 mCi or greater :

Radiation Levels at Surface (mR/hr) : _____

Radiation Levels at 1 Meter (mR/hr) : _____

Acceptable levels:

'1 Red Bars' Package	0.5 mR/hr at surface	background @ 1m
'2 Red Bars' Package	50 mR/hr at surface	1 mR/hr @ 1mr
'3 Red Bars' Package	200 mR/hr at surface	10 mR/hr @ 1mr

Packages above acceptable limits are held for notification to vendor, shipper, and NRC. Contact the RSO immediately.

Date and Time of Delivery to User_____

Handling Procedures for Millicurie Quantities of Phosphorus-32

Phosphorus 32 emits a distribution of energetic beta particles, up to a maximum energy of 1.7 Mev, which can travel as far as 7 meters in air. The absorbed dose rate close to containers of Millicurie quantities of P-32 is on the order rads/min. A significant fraction of P-32 entering the body deposits in the bone structure. The annual limit of intake is 540 microcuries.

The following procedures should offer a guide to using sources of P-32 in excess of one Millicurie.

1. Prepare a written set of procedures and submit them to the RSO for approval prior to the run.

2. Avoid handling the vial directly. Use remote handling tools, such as tongs or special holders when handling the source containers.

3. Use low density shielding (e.g. a minimum of 0.3 in. of Plexiglas) to absorb the beta particles without generating significant amounts of X-rays by an interactive process called Bremsstrahlung. Heavy materials (high atomic number) must not be used close to the source because the Bremsstrahlung process is much more efficient for these materials. However, a small amount of lead on the outside of a plastic shield will absorb the Bremsstrahlung X-rays efficiently.

4. Always wear Safety glasses to protect eyes from splashes and unnecessary radiation when working with radioactive materials.

5. Wear two sets of gloves; strip the outer pair off and replace if they become contaminated. Keep the inner pair clean at all times.

6. Have immediately available a properly operating G-M survey meter for use in detecting contamination and radiation fields. Surveys must be done during the procedure to evaluate the dose to the experimenter and after to check for personal contamination and benchtop contamination.

7. Wear personal dosimeter and finger dosimeters. The finger dosimeters are important because they will monitor the dose given to the fingers which the body dosimeter will not see.

8. Carry out new procedures in a "dry run" with inactive materials before using radioactive materials.

9. Have your supervisor or the RSO observe during your first procedure.

10. After each procedure, survey the area to check for contamination.

Radioactive Waste Handling Procedures

Waste materials must be categorized. It is important that all waste be identified by isotope, quantity (mCi) and date. Please remember that different types of waste and different isotopes cannot be mixed. All waste must be segregated according to type and isotope.

SPECIFIC GUIDELINES FOR BAGGING DRY WASTE

Persons handling radioactive waste must wear a film badge, disposable gloves, and a lab coat. Persons must avoid working over the uncovered waste since an uncovered, direct path from a concentrated radioactive surface is not attenuated.

Make sure that dry waste is bagged in heavy duty polyethylene bags and that the bags are tightly sealed. Log the waste disposal amounts on the log sheet attached to the lid of the drum.

Procedure

1. Whenever possible, radioactive material will be stored for radioactive decay and subsequent disposal as non-radioactive waste. All such material must be held for a minimum of 10 half-lives and must be surveyed in a low background area with the appropriate survey instrument (Ludlum Model 44-9 pancake GM detector) completely prior to disposal. Survey results must be background before any material is disposed of as normal trash and all references to radioactive material will be removed or obliterated. A record of the radionuclide amount stored, date of storage, date surveyed, survey results and date disposed must be kept for all decay in storage (DIS) waste along with a record of the surveyor.

2. All solid material contaminated with radioactive material having a half-life of 120 days or less will be stored " in house" for radioactive decay and subsequent disposal as non-radioactive waste. Contaminated solids will be put in the waste containers provided in each laboratory. A record of the isotope and the amount being disposed will be maintained. When these containers are full, the waste will be transferred to 30 or 55 gallon steel drums and stored in the locked storage facility for decay. No liquids are to be put in the solid waste containers. The drums are to be labeled with the contents, the date the drum was full, and the date the waste has decayed through 10 half lives and is ready for survey.

3. Special Handling Procedures for S-35 Waste. When 3/4 full, each plastic bag will be fastened closed such that there is enough empty space to safely "flatten" it (to increase surface area and decrease density) as it is placed into storage barrel. (Given that 35-S is a weak beta emitter, this procedure should facilitate detection of radioactivity above background at the end of 10 half-life storage.) Each bag will be labeled with a "caution-radioactive materials" tag specifically noting the nuclide, the date, the activity, and the identity of the employee who completed the tag.

Note that individual plastic bags must contain no more than a maximum activity of 100 uCi.

When the labeled bags are moved to the Radiation Waste Storage Room, the tags will be affixed to the barrels in which the waste is placed for storage and tags will be co-signed by the RSO (or his designee) as the bags are placed into the barrels. Duplicate copies will be maintained by the RSO or assistant. Log sheets taped to each barrel will maintain a running

record of the contents as bags of waste are added to each barrel, including date(s) of placement, and accumulating activity.

As each barrel becomes full, it will be sealed closed and based upon the information on the Log Sheet for that barrel, the "OUT" date will be calculated as the earliest future date by which a minimum of 10 half-lives will have elapsed based upon the most recent (i.e. the last) bag of waste added to the barrel just prior to its being closed. At the time the barrel is closed, a duplicate copy of the log sheet will be made and placed in the RSO files.

At the end of the ten half-life storage period, the barrel will be surveyed using pancake GM probe. If a dose rate is detected, the barrel will be returned to storage. If there is no radioactivity above background, the barrel will be removed to an area in the facility where background radiation is low. Each plastic bag will be carefully surveyed on the two "flattened" sides using a pancake GM probe. With a background count of approximately 40 cpm it is impossible to detect 1.5 x background or 20 net cpm. Thus if we find a hot spot and count for a minute at an efficiency of about 15%, we will be able to detect 6E-5 uCi/cpm. By counting for a full minute we are able to minimize the standard deviation at the 95% confidence level to 1.2 E-4 uCi.

35-S generated radioactive waste, and all other licensed wastes, will be stored in DOT-approved 17H fifty-five or thirty gallon metal drums. In compliance with NRC Regulatory Guide 90-09, please see Attachment V1 of this document for a description of the storage facility for the radiation waste generated by 35-S and all other wastes to be licensed under this application.

4. Liquid radioactive waste will be disposed of via the sanitary sewage system in accordance with the new 10 CFR 20.2002 and the applicable concentrations in Table I. Any liquids which cannot meet these requirements will be absorbed and disposed of as low level radioactive waste. We have based our calculations on 50,000 cubic feet/year (3.87 X 10+6 cc/day) sewer discharge volume for this facility. We have calculated our proposed monthly limits based upon principles of ALARA, upon our expected monthly rates of usage, and upon the requirements of Part 20.2003. In no case shall the annual totals exceed 1Ci of 3-H, 1 Ci of 14-C, (at this time NemaPharm does not have authority to order, use or store 3-H or 14-C) and 1 Ci of all isotopes combined and in no case shall the monthly sum of the fractions of each nuclide disposed of in this way exceed unity. Records will be maintained and used to monitor monthly outflow volumes via the sanitary sewer system and will be amended upon determination of water flow after receipt of water usage bill. The RSO will periodically reaffirm and may modify (increase or decrease) the maximum allowable monthly limits to maintain compliance with 10 CFR Part 20.2003.

The NemaPharm maximum proposed monthly limits listed below are well within the NRC maximum calculated limits which are based upon total sanitary outflow and the allowable concentrations listed in Appendix B of 10 CFR 20.

Table I

Isotope	Allowable [uCi/cc]	Monthly Limit (mCi)
Potassium - 32	9 E-5	10.47
Potassium - 33	3 E-4	23.27
Sulfur-35	3 E-4	28.54

If the aqueous waste is significantly higher than the daily limits, they can be disposed in concentrations that will not exceed 10% of monthly levels.

5. Liquid scintillation vials containing isotopes should be put into a plastic-lined cardboard radiowaste container labeled "Liquid Scintillation Vials only".

6. Pipettes, syringes, needles and broken glass should be placed in a labelled sharps container and held in the radioactive waste room for the decay period prior to disposal.

If you have additional questions regarding the disposal of radioactive waste, please contact the Radiation Safety Officer.

Storage Plan for Long Lived Radioactive Waste

The company will follow the guidelines as established by the Nuclear Regulatory Commission in Information Notice 90.09.

The format below follows the outline found in NRC Information Notice 90-09 and is on file with the RSO.

1. Identification of waste to be stored.

a. It will not be necessary to increase the possession limits for extended interim storage of Low Level Waste. The possession limits have been determined to compensate for this problem with the submission of the application.

b. Not to exceed 7.5 cubic feet per year.

c.1. All waste is Class A
2. All stored waste is solid including contaminated bench pads, gloves, glassware and paper.
3. It is company policy to employ volume reduction through the use of a compactor and planned waste avoidance.
4. The material stored will have no additional non-radiological properties.

d. N/A

e. The storage will not necessitate any additional permits.

2. Final Disposal Policy and Plan

a. Current projection for the necessity of on site storage is upon receipt and use of isotopes.

b. Unknown at this time. The ultimate storage plan will be determined by the Commonwealth of Massachusetts. The Low Level Waste Management Board will have to make the decision in a timely fashion.

c. It is the Company's policy to ship as soon as a disposal facility is available. The volume of stored waste will be relatively small and waste will be transferred immediately.

3. Physical Description of Storage Area

a. A plan identifying the location and size of the Storage Area is part of Attachment II of this application. Visual inspection and access to the drums by authorized personnel will be non problematic. Air sampling will be conducted by portable air sampler in the room, if at all necessary. No volatiles will be in the room.

b. Maximum storage capacity is 3 - 55 gallon steel drums, which is ten years of storage based on current projections and usage patterns. i.e. one half (1) drum per year.

c. Waste storage is internal to the leased space and protected from the weather at all times.

d. The waste storage facility will be locked at all times with keys, keypad code or card access controlled by the RSO.

e. General room air ventilation will be designed to operate properly and will be adequate for this type of waste.

f. The storage of the company waste will be in a room equipped with and protected by the base building sprinkler system.

g. N/A.

h. N/A.

4. Package and Container Integrity

a. Company policy will be to package radioactive waste in 30 or 55 gallon steel drums which are currently the accepted packaging for transportation and final disposal. The waste shall be such to pose no hazard to the integrity of the container and the container should last indefinitely.

b. Routine radiation monitoring shall be done in the storage area along with visual inspection of the stored containers.

c. The low level use of beta and weak gamma emitters will not require any remote handling equipment nor will the metal barrels require any repackaging. Any possibility of damage to the barrels or leakage is very remote but action would be supervised by the RSO. Any leakage would be absorbed and decontamination procedures instituted and repackaged in other barrels.

5. Radiation Protection

a. The plan does not call for the storage of tritium and carbon-14. There will be no radiation dose rates from the storage containers. Monthly calibrated surveys of the storage area will be done. The door to the area will be posted with the appropriate "Caution Radioactive Material" sign in accord with 10-CFR-20.1902.

b. The radionuclide and the activities to be used will not generate any dose rates and thus special shielding will not be required. Special personnel monitoring will not be necessary.

c. The name and home telephone number of the RSO will be posted on the door. The emergency procedure adopted are part of our OSHA required Chemical Hygiene Plan and will be coordinated with local fire, police and medical personnel.

d. All drums will be appropriately labeled with the required information about the drums contents. Each bag of waste placed in storage will have a radioactive materials tag with the radionuclide, amount, date of packaging, and the person responsible for generating the waste. A running record will be kept on each barrel with an outdate when the ten half lives have transpired. A log will also be maintained of the inventory of the activity at any time.

6. Training

Company policy requires all workers handling radioisotopes including waste to attend our radiation worker training seminars which include instruction on waste minimization, packaging, handling, radiation survey techniques, and emergency procedures.

7. Financial Assurance

a. The proposed possession limits in the application do not require posting of financial assurance.

8. Emergency Plan

a. Our proposed possession limits requested at this time in this application do not require an emergency plan per 30.32 (i)(1).

NemaPharm, Inc.

Radioactive Waste Inventory

Disposed of empty container: _____ User: _____

Date	Radioisotope	Activity	User

TOTALS: (To be completed when the radioactive waste is shipped.)

Radioisotope _____ Total Activity (mCi) _____

APPENDIX 5

NUCLEAR REGULATORY COMMISSION REGULATIONS AND GUIDES

10 CFR 20.1001 - 10 CFR 20.2402: "Standards for protection against radiation"

10 CFR 19: "Notice, Instructions and reports to workers"

Regulatory Guide 8.10:

Regulatory Guide 8.13: "Instructions covering prenatal exposure"

Regulatory Guide 8.21: " Health Physics Survey"

BETWEEN:

LICENSE FEE MANAGEMENT BRANCH, ARM
AND
REGIONAL LICENSING SECTIONS

(FOR LFMS USE)
INFORMATION FROM LTS

PROGRAM CODE: 03620
STATUS CODE: 3
FEE CATEGORY: ---
EXP. DATE: 0
FEE COMMENTS: ---
DECOM FIN ASSUR REQD: _

LICENSE FEE TRANSMITTAL

A. REGION I

1. APPLICATION ATTACHED
APPLICANT/LICENSEE: NEMAPHARM, INC.
RECEIVED DATE: 970128
DOCKET NO: 3034350
CONTROL NO.: 124166
LICENSE NO.:
ACTION TYPE: NEW LICENSEE

Rec'd 2/4/97 BB

2. FEE ATTACHED
AMOUNT: $1500.00
CHECK NO.: 003147

3. COMMENTS

SIGNED M. A. Perkins
DATE 1/28/97

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

1. FEE CATEGORY AND AMOUNT: 3M $1,500

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

3. OTHER ---

SIGNED ---
DATE ---

I (97)

Log Feb 7
Reviewer
Check No. 03147
Amount $1,500
Fee Category 3L
Type of Fee Apl
Date Check Rec'd 2/3/97
Date Completed 2/7/97
By: BB