20503

NRC FORM 313
(1-84)
10 CFR 30, 32, 33, 34, 35 and 40

U.S. NUCLEAR REGULATORY COMMISSION
APPROVED BY OMB
3150-0120
Expires: 5-31-87

APPLICATION FOR MATERIAL LICENSE

030-

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.

FEDERAL AGENCIES FILE APPLICATIONS WITH:

U.S. NUCLEAR REGULATORY COMMISSION
DIVISION OF FUEL CYCLE AND MATERIAL SAFETY, NMSS
WASHINGTON, DC 20555

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

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

U.S. NUCLEAR REGULATORY COMMISSION, REGION I
NUCLEAR MATERIAL SECTION B
631 PARK AVENUE
KING OF PRUSSIA, PA 19406

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

U.S. NUCLEAR REGULATORY COMMISSION, REGION II
MATERIAL RADIATION PROTECTION SECTION
101 MARIETTA STREET, SUITE 2900
ATLANTA, GA 30323

IF YOU ARE LOCATED IN:

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

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

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

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

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

U.S. NUCLEAR REGULATORY COMMISSION, REGION V
MATERIAL RADIATION PROTECTION SECTION
1450 MARIA LANE, SUITE 210
WALNUT CREEK, CA 94596

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

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

- [X] A. NEW LICENSE
- [ ] B. AMENDMENT TO LICENSE NUMBER _____
- [ ] C. RENEWAL OF LICENSE NUMBER _____

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

Repligen Corporation
One Kendall Square
Cambridge, MA 02140

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

Same as 2.

4. NAME OF PERSON TO BE CONTACTED ABOUT THIS APPLICATION

Dr. Charles Scott

TELEPHONE NUMBER

(617) 225-6000

SUBMIT ITEMS 5 THROUGH 11 ON 8½ x 11" PAPER. THE TYPE AND SCOPE OF INFORMATION TO BE PROVIDED IS DESCRIBED IN THE LICENSE APPLICATION GUIDE.

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

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

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

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

9. FACILITIES AND EQUIPMENT.

10. RADIATION SAFETY PROGRAM.

11. WASTE MANAGEMENT.

12. LICENSEE FEES *(See 10 CFR 170 and Section 170.31)*

FEE CATEGORY 3E

AMOUNT ENCLOSED $ $230.

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

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

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

SIGNATURE/CERTIFYING OFFICER	TYPED/PRINTED NAME	TITLE	DATE

14. VOLUNTARY ECONOMIC DATA

a. ANNUAL RECEIPTS

- [ ] <$250K
- [ ] $250K–500K
- [ ] $500K–750K
- [ ] $750K–1M
- [ ] $1M–3.5M
- [ ] $3.5M–7M
- [ ] $7M–10M
- [ ] >$10M

b. NUMBER OF EMPLOYEES *(Total for entire facility excluding outside contractors)*

c. NUMBER OF BEDS

d. WOULD YOU BE WILLING TO FURNISH COST INFORMATION *(Dollar and/or staff hours)* ON THE ECONOMIC IMPACT OF CURRENT NRC REGULATIONS OR ANY FUTURE PROPOSED NRC REGULATIONS THAT MAY AFFECT YOU? *(NRC regulations permit it to protect confidential commercial or financial–proprietary–information furnished to the agency in confidence)*

- [ ] YES
- [ ] NO

FOR NRC USE ONLY

TYPE OF FEE	FEE LOG	FEE CATEGORY	COMMENTS	APPROVED BY
APP	Mar. 15	3E	9001250437 890327 REG1 LIC30 20-20503-02 PDR	S. Kimberly
AMOUNT RECEIVED	CHECK NUMBER			DATE
$230	030747			3/23/89

110401

PRIVACY ACT STATEMENT ON THE REVERSE

OFFICIAL RECORD COPY ML 10

MAR 08 1989

Form 313 Continued:

5a. Element and Mass Number: Cesium-137

5b. Physical Form: Sealed Source

5c. Possession Limit: 600 Curies

The Gammacell 1000, Model A Irradiator, is manufactured by AECL of Cannada and is listed in the Approved Sources and Devices of the USNRC.

6. Purpose For Which Licensed Material Will Be Used:

The irradiator will be used to irradiate cells and other biological material needed in biochemical and molecular biological experiments.

7. Individual Responsible For Radiation Safety Program:

Dr. Charles Scott will be the Repligen Radiation Safety Officer for the irradiation facility. Dr. Scott has 10 years experience in the use of radioactive material and used the Gammacell-40 and the Gammacell 1000 over the past six years. Please see Dr. Scott's attached curriculum vitae for applicable training and experience.

Dr. Bernadette Alford, the Repligen Radiation Safety Officer for NRC license # 20-20503-01, will serve as Dr. Scott's backup. Dr. Alford's radiation training and experience are on file with the NRC. A copy of this information is attached.

All use of the Gammacell-1000 will be under the direct supervision of Dr. Scott.

8. Training For Individuals Working In or Frequenting Resticted Areas:

All individuals who will use the irradiator will be trained in the safe use of radioactivity and radiation sources. This will include the principals and fundamentals of radiation safety, the use of radiation detection instruments, the design and operation of the irradiator, and specific operating and emergency procedures. In addition, all users of the irradiator will be required to pass an examination covering the above subjects. Please see the attached outline of the subject material to be covered during training sessions. Also attached is a copy of the Repligen Irradiator Examination with answers. A passing grade will be 17 correct out of 25 questions. Individuals not meeting this requirement will be given a one on one tutorial by the RSO in areas of deficiencies.

Dr. Charles Scott will be reponsible for providing the above training. In addition, our consultants Bolton & Galanek provide radiation training seminars for all Repligen radiation workers. A record documenting the training of individuals who use the irradiator will be maintained by the RSO.

9. Facilities and Equipment:

The irradiator will be located in a locked laboratory in the Repligen facilities (see attached floor plan for location of irradiator). The only individuals with access to the facility will be those who have been properly trained as in #8 above. The irradiator facility will remained locked when not in use to prevent use by unauthorized persons.

The irradiator facility will be equipped with a portable radiation survey meter equipped with a GM detector. In addition, an area radiation monitor will be located in the laboratory to monitor ambient radiation levels. The area monitor will be equipped with an alarm feature that will be set to alarm if the ambient radiation levels exceed 2 milliroentgens per hour.

10. Radiation Safety Program:

The following is the Repligen Irradiator Radiation Safety Program which will compliment the existing radition safety program under NRC license # 20-20503-01:

10.1 Personnel Monitoring Equipment:

All irradiator users will be required to wear whole body film badge dosimeters when using the irradiator or working in the irradiator facility. The badges will have a monthly exchange frequency and will be supplied by R.S. Landauer. Records of personnel exposures will be maintained indefinitely.

10.2 Radiation Detection Instruments:

The facility will be equipped with a Ludlu Model 14C radiation survey instrument that is equipped with 2 Geiger Mueller detectors. The dose rate range in milliroentgens per hour is .02 to 2000. The instrument will be calibrated at six month intervals or after repairs. In addition, an area monitor will be located in the facility to measure ambient radiation levels.

Instruments will be calibrated by our consultants, Bolton & Galanek, Inc., NRC License #20-13302-01, using procedures accepted by the NRC.

10.3. Leak-Testing:

The Gammacell-1000 will be wipe tested for leakage at six month intervals. The leak tests will be performed by our consultants, Bolton & Galanek, Inc., NRC License #20-13302-01.

10.4 Operating and Emergency Procedures:

The following are the regulations and operating procedures for the Gammacell-1000 irradiation unit:

A. Operating Procedures:

1. Only persons trained and approved by Dr. Scott will be authorized to use the irradiator.

2. The Gammacell-1000 shall be operated and maintained in accordance with the AECL instruction manual. A copy of the manual shall be kept in the irradiator laboratory at all times.

3. No corrosive, explosive, pyrophoric, or highly flammable material shall be irradiated in the unit.

4. The irradiator laboratory will be kept locked when the room is unoccupied. Only persons authorized to operate the Gammacell-1000 will have access to the key.

5. A log of all use of the Gammacell-1000 shall be kept. Information recorded will include length of irradiation, anme of operator, and any unusual circumstances or occurances.

6. To minimize personnel exposures, operators should spend a minimum amount of time in close proximity to the unit.

B. Emergency procedures:

In case of an emergency, the use of the unit will be discontinued, the laboratory evacuated, and the Radiation Safety Officer notified immediately. In particular, the RSO will be notified if:

1. Higher than normal radiation levels are detected or suspected.

2. There is any reason to question the proper functioning of the area monitor.

3. The is any indication of maifunctioning of the Gammacell-1000 Unit involving radiation protection.

In the event that the RSO is notified of an emergency, the RSO will determine the nature of the emergency. If the emergency involves malfunctioning of the unit, AECL will be notified of the situation and the RSO's assessment. Operation of the unit will be discontinued until repair has been completed by AECL or its authorized representative and the machine has been determined to be ready for safe use by the RSO.

C. Radiation Monitoring Requirements:

Radiation monitoring requirements for the Gammacell-1000 laboratory will include the following three categories: Personnel; Gammacell-1000 laboratory; Gammacell-1000 unit.

1. Personnel: All persons authorized to operate the unit will be provided with film badges which will be worn whenever the person is in the irradiator laboratory.

2. Gammacell laboratory: The ambient radiation levels in the room will be monitored by an AC-operated area monitor that is set to alrm at radiation levels above 2 mr/hr.

Monthly inspections of the will be made by the RSO.

3. Gammacell unit: Wipe tests of the Gammacell-1000 unit will be performed at six month intervals.

All persons involved in the use of the Gammacell-1000 unit will comply with above regulations and procedures. A copy of these procedures will be posted in the irradiator laboratory.

11. Waste Management:

In the event that the irradiator is no longer of use to the Repligen Corporation, it will either be returned to the manufacturer, transferred to a licensee specifically authorized to possess the unit, or dispose of the radioactive sources through a licensed waste disposal contractor.

Radiation Training - Dr. Charles Scott

Dates	Location
1978	University of Connecticut School of Medicine- (4 hours)
1983	Harvard Medical School (4 hours)
1986	Danna Farber Cancer Institute (2 hours)
1988	Repligen Corporation (2 hours)

In all the above locations, the training consisted of radiation training seminars and classes which reviewed the priciples and practices of radiation protection, use of radiation survey instruments and other radiation detection equipment, radiation survey techniques including wipe testing and direct radiation measurements, emergency procedures, potential biological effects of exposure to ionizing radiation, maximum permissible exposures for radiation workers, waste disposal techniques, and other radiation safety related topics. In addition, I received training in the safe use of the gammacell irradiators at Harvard Medical School and at the Dana Farber Cancer Center. I have used the Gammacell-40 and Gammacell-1000 units extensively over the past 6 years at Harvard Medical School and the Dana Farber.

I have extensive experience working with millicurie quantities of the following radioisotopes during the past 10 years: H-3, C-14, P-32, S-35, Cr-51, and I-125.

CHARLES FREDERICK SCOTT, JR.

Educational Background

1979 — M.D.,
University of Connecticut School of Medicine,
Farmington, CT

1973 — B.S. in Life Sciences,
Massachusetts Institute of Technology,
Cambridge, MA

Experience

1988 — Director of Immunology,
Repligen Corporation,
Cambridge, MA
Responsible for immunological aspects of all projects and production of monoclonal antibodies.

1987 — Instructor of Medicine,
Dana-Farber Cancer Institute,
Boston, MA

1985 to 1987 — Research Associate in Pathology,
Dana-Farber Cancer Institute,
Boston, MA

1981 to 1984 — Fellow in Pathology
Harvard Medical School,
Boston, MA

Clinical Experience

1984 to 1986 — Residency in Medicine,
Boston Veteran's Administration Hospital,
Boston, MA

1980 to 1981 — Fellow in Clinical Immunology,
University of California,
San Francisco, CA

1979 to 1980 — Internship in Medicine,
Children's Hospital of San Francisco,
San Francisco, CA

CHARLES FREDERICK SCOTT, JR.

Educational Background

1979	M.D., University of Connecticut School of Medicine, Farmington, CT
1973	B.S. in Life Sciences, Massachusetts Institute of Technology, Cambridge, MA

Experience

1988	Director of Immunology, Repligen Corporation, Cambridge, MA Responsible for immunological aspects of all projects and production of monoclonal antibodies.
1987	Instructor of Medicine, Dana-Farber Cancer Institute, Boston, MA
1985 to 1987	Research Associate in Pathology, Dana-Farber Cancer Institute, Boston, MA
1981 to 1984	Fellow in Pathology Harvard Medical School, Boston, MA

Clinical Experience

1984 to 1986	Residency in Medicine, Boston Veteran's Administration Hospital, Boston, MA
1980 to 1981	Fellow in Clinical Immunology, University of California, San Francisco, CA
1979 to 1980	Internship in Medicine, Children's Hospital of San Francisco, San Francisco, CA

Memberships

1986	Diplomate, American Board of Internal Medicine
1984	Member, American Association of Immunologists
1987	Member, Clinical Immunology Society
1983	Massachusetts Licensure No. 52292

Publications

Scott, Jr., C.F., Blattler, W.A., Lambert, J.M., Kalish, R.S., Morimoto, C., and Schlossman, S.F. (1988). Requirements for the Construction of Antibody Heterodimers for the Direction of Lysis of Tumors by Human T Cells. J. Clin. Invest. 81:1427-1433.

Scott, Jr., C.F., Lambert, J.M., Bolender, S., and Blattler, W.A. (1988). Resting Human Lymphocytes Can Be Activated to Cytolytic Function by Antibodies to CD3 in the Absence of Exogenous Interleukin-2. Cellular Immunology. 114:370-384.

Scott, Jr., C.F., Lambert, J.M., Kalish, R.S., Morimoto, C., and Schlossman, S.F. (1988). Human T Cells Can Be Directed to Lyse Tumor Targets Through the Alternative Activation/T11-E Rosette Receptor Pathway. J. Immunol. 140:8-14.

Scott, Jr., C.F., Goldmacher, V.S., Lambert, J.M., Chari, R.V.J., Bolender, S., Gauthier, M.N., and Blattler, W.A. (1987). The Anti-Leukemic Efficacy of an Immunotoxin Composed of a Monoclonal Anti-Thy-1 Antibody Disulfide Linked to the Ribosome Inactivating Protein, Gelonin. Canc. Immunol. Immunotherap. 25:31-40.

Scott, Jr., C.F., Goldmacher, V.S., Lambert, J.M., Jackson, J.V., and McIntyre, G.D. (1987). An Immunotoxin Composed of a Monocolonal Anti-Transferrin Receptor Antibody Linked by a Disulfide Bond to the Ribosome Inactivating Protein Gelonin; Potent in Vitro and in Vivo Effects Against Human Tumors. J. Natl. Canc. Inst. 79:1163-1171.

Publications

Scott, Jr., C.F., Lambert, J.M., Goldmacher, V.S., Blattler, W.A., Sobel, R., Schlossman, S.F., and Benacerraf, B. (1987). The Pharmacokinetics and Toxicity of Murine Monoclonal Antibodies and of Gelonin Conjugates of Those Antibodies. Int. J. Immunopharm. 9:211-25.

HayGlass, K.T., Naides, S.J., Scott, Jr., C.F., Benacerraf, B., and Sy, M-S. (1986). T Cell Development in B Cell Deficient Mice -- IV. The Role of B Cells as Antigens-Presenting Cells in Vivo. J. Immunol. 136:823.

Scott, Jr., C.F., Tsurufuji, M., Naides, S.J., and Sy, M-S. (1985) Regulation of Hapten-Specific T Cell Response -- II. Functional Analysis of Helper T Cells and Cytotoxic T Cells in Animals Suppressed by Azobenzenearsonate (ABA)-Specific Suppressor T Cells. Cell Immunol. 136:823.

Scott, Jr., C.F., Cashman, N., and Spitler, L.E. (1983). Experimental Allergic Encephalitis: Treatment with Drugs Which Alter CNS Serotinin Levels. J. Immunopharmacol. 4:153.

Scott, Jr., C.F. and Spitler, L.E. (1983). Lymphocytotoxic Antibody in Multiple Sclerosis: Activity Against T Cell Subsets and Correlation with Disease Activity. Clin. Exp. Immunol. 53:133.

Scott, Jr., C.F., Tsurufuji, M., Benacerraf, B., and Sy, M-S. (1983). Regulation of the Hapten-Specific T Cell Response -- I. Preferential Induction of Hyporesponsiveness to the D-End of the Major Histocompatibility Complex in the Hapten-Specific Cytotoxic T Cell Response. J. Immunol. 131:2184.

Scott, Jr., C.F., Tsurufuji, M., Lu, C., Finberg, R., and Sy, M-S. (1983). Comparison of Antigen-Specific T Cell Responses in Autoimmune MRL/Mp-lpr/lpr and MRL/Mp+/+mice. J. Immunol. 132, 2:633.

Scott, Jr., C.F. (1982). Length of Operation and Morbidity: Is There a Relationship? Plast. and Reconstr. Surg. 69:1017.

Spitler, L.E. and Scott, Jr., C.F. (1982). Immunotherapy of Melanoma in Melanoma Antigens and Antibodies. Plenum Press, New York, 355-3637.

Publications

Viola, M.V., Gann, K., Scott, Jr., C.F., and Rothfield, N. (1978). Absence of Measles Proviral DNA in Systemic Lupus Erythematosus. Nature 275:667.

Viola, M.V., Scott, Jr., C.F., and Duffy, P.D. (1978). Persistent Measles Virus Infection in Vitro and in Man. Arthritis and Rheum. 21(5):546.

Abstracts

Goldmacher, V.S., Scott, Jr., C.F., McIntyre, G.M., Lambert, J.M., Blattler, W.A., Collinson, A.R., Anderson, J., Chang, L.D., Cook, S., Slayter, H.S., Watlers, S., and Beaumont, E. (1987). Interaction of Immunotoxins with Cultured Cells. The Gordon Conference.

Scott, Jr., C.F., Goldmacher, V.S., Lambert, J.M., Chari, R.V.J., McIntyre, G.D., and Blattler, W.A. (1986). In Vitro and in Vivo Efficacy of Disulfide-Linked Conjugates of Murine Monoclonal Antibodies and the Ribosome-Inactivator, Gelonin. The Second International Congress of Immunoconjugates for Cancer.

Scott, Jr., C.F., Lambert, J., Goldmacher, V., Sobel, R., and Benacerraf, B. (1986). The Metabolism and Toxicity of Gelonin-Monoclonal Antibody Conjugates in Vivo. The First International Congress of Immunoconjugates for Cancer.

HayGlass, K.T., Naides, S.J., Scott, Jr., C.F., Benacerraf, B., and Sy, M-S. (1984). Studies of T Cell Function in B Cell Deficient Mice. Woods Hole, X, New England Immunology Conference.

Scott, Jr., C.F., Tsurufuji, M., Lu, C., and Sy, M-S. (1984). Hapten-Specific T Cell Responses in the MRL/MP-lpr/lpr Mouse. J. Cellular Biochem., suppl. 8A, p. 222.

Sy, M-S, Scott, Jr., C.F., Naides, S.J., Tsurufuji, M., Benacerraf, B. (1984). Regulation of the Hapten-Specific T Cell Response. J. Cellular Biochem., suppl. 8A, p. 121.

Scott, Jr., C.F., Tsurufuji, M., Benacerraf, B., and Sy, M-S. (1983). Preferential Induction of Immunological Hyporesponsiveness in H-2D End Restricted but Not H-2K End Restricted TNP-Specific Cytotoxic T Cells. Fed. Proc. 42:561.

GAMMACELL-1000 TRAINING PROGRAM

Time: Approx. 4 hours

I. Source Information:

1. Source
   a. Source radinuclide and activity
   b. Half life / energies
   c. Basic decay law

II. Machine Operation

1. Machine Design
   a. Machine Cut-aways
   b. Load Position / Irradiate Position
   c. Access Controls
   d. Control Panel Lights / Functions

2. Isodose Curves
   a. Ambient Radiation Levels: Load vs. Irradiate Positions
   b. Leakage radiation
   c. Doses to Samples

3. Pre-Operational Checks
   a. Survey Meter Readings
   b. Log of Experiments
   c. Area Ambient Radiation Monitor

III. Film Badge Program / Personnel Monitoring

IV. Facilities Monitoring

1. Radiation Survey Instrumentation
   a. Survey Instrument
   b. Area Monitor

V. Basic Health Physics Concepts

1. Time, Distance, Shielding
2. Inverse Square Law
3. Attenuation (e -ux); Half Value Layers
4. 10 CFR 19 and 20

VI. Emergency Procedures

1. Review Written Procedures
2. Discussion Of Previous Problems

VII. Gammacell-1000 Test

VIII. Hands On Training

RADIATION PROTECTION TRAINING PROGRAM

Outline of Subject Material

1. Concepts of Ionizing Radiation.

2. Units of Radioactivity and Radiation :

   A. Radioactivity
   B. Activity (Curie, Becquerel)
   C. Exposure (Roentgen)
   D. Absorbed Dose (Rad, Gray)
   E. Dose Equivalent (Rem, Seivert)
   F. Dose Rate
   G. Half Life
   H. Radioactive Decay Process

3. Biological Effects of Radiation:

   A. History of radiation exposure
   B. Acute vs. chronic exposure
   C. Threshold vs. linear relation between dose and effect
   D. Balancing risk vs. benefit
   E. Regulatory Guide 8.29

4. Maximum Permissible Exposures:

   A. Current MPE values
   B. Concept of ALARA
   C. Natural background radiation exposures.
   D. Occupational exposures
   E. Regulatory Guide 8.13

5. Measurement and Control of Radiation Exposures:

   A. External exposures (time, distance shielding)
   B. Internal exposures (ventillation, blocking agents)
   C. Dosimeters (film badges)
   D. In Vivo measurements

6. Radiation Survey Techniques:

   A. Wipe tests
   B. Radiation survey instruments
   C. Radioactivity analysis
   D. Environmental monitoring

7. Handling Radiation Emergencies:

   A. Emergency procedures
   B. Decontamination techniques

8. Waste Disposal Techniques

9. Safe Handling Techniques

10. Compliance with Regulations:

   A. NRC license conditions of approval
   B. Title 10, Parts 19 & 20
   C. State regulations
   D. DOT regulations

Appropriate reference material will be distributed at the time of the training lectures to futher reinforce the above concepts. Slide shows, video tapes, and hands on demonstrations will also be used to reinforce above concepts.

Repligen Corporation Gammacell Users Quiz

1. The annual maximum permissible whole body dose to a radiation worker is:

   a. 1000 mrem
   b. 500 mrem
   c. 1250 mrem
   d. 5000 mrem

2. If the alarm in the irradiator facility is sounding, you should:

   a. continue your work as planned, the alarm was falsely sounded by an electrical surge.
   b. immediately evacuate the building.
   c. turn of the irradiator, leave and secure the room, notify the RPO.
   d. run through all the preoperative checks to determine the cause.

3. From the choices listed below, select the material that should not be irradiatied in the gammacell.

   a. biological material.
   b. pyrophoric, highly flammable material
   c. corrosive and explosive material
   d. a, b, and c.
   e. b and c only.

4. The annaual whole body dose to the general population is what fraction that allowed for a radiation worker.

   a. 1/5
   b. 1/4
   c. 1
   d. 1/10

5. The area monitor in the irradiator facility is set to alarm if the dose rate exceeds:

   a. 5 mrem/hr
   b. 10 mrem/hr
   c. 2 mrem/hr
   d. 50 mrem/hr

6. The half life of a radionuclide is:

   a. the time required for the radioactive substance to become non-radioactive.
   b. the time required for the radioactive substance to lose 10% of its activity by radioactive decay.
   c. the time it must be irradiated to become 50% radioactive.
   d. the time required for the radioactive substance to lose 50% Of its activity by radioactive decay.

7. Title 10 of the Code of Federal Regulations Part 19 describes:

   a. the limit of radiation exposure that a pregnant radiation worker can receive.
   b. the limit of radiation exposure that a radiation worker can receive.
   c. instructions workers must be provided concerning associated risks from radiation exposures, areas where exposures are likely to be received, and exposures that workers have received.
   d. radioactive waste disposal limits.

8. The quality factor, a linear-energy-dependent (LET) factor, allows us to describe absorbed dose on a common scale for all ionizing radiations. Match the following radiations and their quality factors.

a. alpha	10
b. gamma	20
c. beta	1
d. x-ray	5

9. The acronym ALARA means:

   a. As low as resonably achievable.
   b. As little as radaition allows.
   c. As low as radiation allows.
   d. As low as regulations allow.

10. Which of the following terms is used to describe the amount of radioactive material in the irradiator sources:

   a. roentgens
   b. grams
   c. curies
   d. rads

11. What type of survey instrument should be used to measure radiation levels around the irradiator.

a. Gas flow proportional counter.
b. Geiger Mueller (GM) detector.
c. NaI scintillation detector.
d. Long counter

12. The contents of Regulatory Guide 8.13 describe:

a. limit of exposure to minors from irradiators.
b. limit of exposure to pregnant radiation workers.
c. wipe test requiements for sealed sources.
d. bioassay requirements for tritum workers.

13. The sealed source in the Gammacell irradiator shall be tested for leakage at intervals not to exceed _____. The test shall be taken from appropriate accessible surfaces of the machine and the limit for removable contamination is 0.005 uCi.

a. 5 years
b. 2 years
c. 6 months
d. 1 year

14. The Gammacell Cs-137 source has a half-life of _____, and emits gamma rays with an energy of _____ .

a. 100 days, 2.00 MeV
b. 30 years, .67 MeV
c. 300 days, .67 MeV
d. 5.6 years, 1.17 MeV

15. Match the following acute whole body doses to the correct probable effect:

a. 0 25 rads	1. blood changes, some injury, no disability
b. 50 100 rads	2. no observable physical injury.
c. 450 rads	3. fatal within 60 days to 50% of the exposed.
d. >600 rads	4. 100% fatal.

16. Which of the following is used to describe absorbed dose to radiation:

a. rems
b. curies
c. kerma
d. rads

17. The green light on the front panel of the Gammacell-1000 is an indicator for:

a. the radiation level around the irradiator is safe.
b. the sample chamber is exposed to the radiation field.
c. the sample chamber is out of the radiation field and can be loaded.
d. the irradiation cycle has started.

18. The following radiaiton measuring device will be used to monitor exposures to irradiator users:

a. geiger mueller (GM) detectors
b. pocket dosimeters
c. film badges.
d. NaI scintillation detectors.

19. When using the irradiator, the RPO should be notified when:

a. there is any indication of malfunction of the Gammacell-1000.
b. higher than normal radiation levels are detected during operation.
c. the survey instrument in not functioning.
d. all of the above.

20. Which of the following access control procedures are in effect for use of the irradiator:

a. obtain key to irradiator facility from the RPO.
b. obtain key to irradiator control panel from RPO.
c. receive proper instruction and training from the RPO in the safe operation of the Gammacell 1000.
d. all of the above.

21. The Gammacell-1000 is a self contained irradiator designed for the sterilization of small biological samples. The unit consists of a radioactive source and a biological shield. The following best describes the way samples are irradiated in the unit:

a. the radioactive source is rotated 180° which places the source near the sample.
b. the sample is taken via elevator to a position near the radioactive source.
c. the sample chamber is rotated 180° which places the sample near the radioactive source.
d. the radioactive source is removed from the biological shield with tongs and placed near the sample.

22. Which of the following methods can be used alone or in combination to minimize or control external radiation exposures:

a. time
b. distance
c. shielding
d. a and b only
e. b and c only
f. a, b, and c.

23. The red light on the front panel of the Gammacell-1000 is an indicator for:

a. the radiation level around the irradiator is safe.
b. the sample chamber is exposed to the radiation field.
c. the sample chamber is out of the radiation field and can be loaded.
d. the irradiation cycle has started.

24. What is the maximum dose rate deviation within the irradiation chamber of a properly operating system:

a. + 5%
b. + 10%
c. + 20%
d. + 50%

25. The recommended maximum permissible whole body exposure for pregnant radiation workers is:

a. 100 mrem
b. 200 mrem
c. 500 mrem
d. 1000 mrem
e. 5000 mrem

Answers:

1. d
2. c
3. e
4. d
5. c
6. d
7. c
8a. 20
8b. 1
8c. 1
8d. 1
9. a
10. c
11. b
12. b
13. c
14. b
15a. 2
15b. 1
15c. 3
15d. 4
16. d
17. c
18. c
19. d
20. d
21. c
22. f
23. b
24. c
25. c

CURRICULUM VITAE

Bernadette L. Alford

EDUCATION

1974 Ph.D., Molecular Biology, TWU, Denton, Texas.
Research: Estimation of Nucleohistones of Cerebral Tissue

1973 M.S., Biology, TWU, Denton, Texas.
Research: Histone Fractionation and Characterization

Graduate coursework in Radiation Biology and Radiation Protection through Radiation Biology Department

1971 B.S., Biology, Marywood College, Scranton, Pennsylvania

EXPERIENCE

Radioisotope Experience: ^{125}I, ^{14}C, ^{35}S, ^{3}H (quantities up to curie amounts)

1987-present **Repligen Corporation, Cambridge, Massachusetts**
Director of Quality Assurance and Regulatory Affairs

Annual radiation training session offered by MIT's Radiation Protection Office.

Responsible for establishing and maintaining regulatory affairs and quality assurance departments consistent with industry standards involving regulated drugs, devices and other related products.

Responsible for establishing and guiding a company Health and Safety Program, including organizing a committee, writing a company manual and scheduling training sessions on biosafety, chemical safety and radiation safety.

1978-1987 **Collaborative Research, Inc., Bedford Massachusetts**

Annual radiation training session offered by MIT's Radiation Protection Office

1985-1987 Director, Quality Assurance; Director, Patents & Licensing

Responsible for regulatory affairs from town to federal level, quality assurance/quality control processing and documentation activities for CGMP products. Responsible company-wide for the preparation of contract proposals, licensing, consulting and contract agreements and their administration; responsible for the preparation and prosecution of patent applications and maintenance of existing patents.

Organized company's Health & Safety Program including radiation, biosafety and chemical safety programs, manuals and training sessions.

1984-1985 Patents and Licensing Administrator

Responsible for monitoring licensing, consulting and contract agreements and assisting in their preparation; preparation of contract proposals. Operated as a liaison between the scientists and legal firm in the preparation of patent applications and maintenance of existing patents; assisted in all phases of regulatory affairs.

1982-1984 Patent Coordinator

Responsible for monitoring licensing, consulting and contract agreements. Assisted in the preparation of contract proposals, and operated as a liaison between the scientists and legal firm in the preparation of patent applications and maintenance of existing patents.

1980-1982 Senior Staff Scientist

Responsible for all phases of development and production of molecular biology products for the company's Biomedical Products business. Activities included product scheduling, inventory control, marketing/sales, and assay development for inspecting product by analytical methods employing biological materials and radiolabelling techniques.

1978-1980 Senior Research Scientist

Directed NIH-funded project involving research investigating integration of foreign genes into the genome of mammalian cells. Played an integral role in the expression of a mammalian rennin protein in E. coli and yeast with primary responsibility in protein purification and antibody production, as well as assay development and protein characterization using ^{125}I-immunoassay techniques.

1976-1978 **NIH Postdoctoral Fellow, Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts**

Radiation protection courses (2) and seminars; radiation training through the Institute's Radiation Protection Office

Research: Aminoacylation and Misaminoacylation of transfer RNAs (utilized ^{3}H- and ^{14}C-labelled amino acids)

Advisor: Dr. Sidney Hecht

1975-1976 **NIH Postdoctoral Fellow, Department of Biochemistry, Baylor College of Medicine, Houston, Texas**

Research: Purine Transport and Subsequent Regulation (utilized ^{3}H- and ^{14}C-labelled purines)

Advisor: Dr. Eugene M. Barnes, Jr.

1974-1975 **Research Associate, Department of Biochemistry, Baylor College of Medicine, Houston, Texas**

Research: Purine Transport and Subsequent Regulation (utilized ^{3}H- and ^{14}C-labelled purines)

Advisor: Dr. Eugene M. Barnes, Jr.

HONORS

Postdoctoral Fellow of the National Cancer Institute, National Institutes of Health (1976-1978)
Postdoctoral Fellow of the National Cancer Institute, National Institutes of Health (1975-1976)
Texas State Doctoral Fellowship (1974)
TWU University Fellowship (1972-1974)
College Scholarship from Pennsylvania Junior Academy of Science (1967-1971)

COMPETITIVE GRANTS

NIH Grant Award on oligonucleotide synthesis (1981)

PATENTS

"Recombinant DNA Means and Method"
Alford, et al.
Patent Number 4,666,847

Pending U.S. and Foreign Patent Applications

TRAINING

Review course on pharmaceutical quality assurance and control (1985, 1986, 1987, 1988)

Review course on regulatory compliance and the FDA (1985, 1986, 1988)

HIMA Annual Seminar Courses (1984, 1985, 1986)

Patent Bar Review Course and Course in Litigation,
Practising Law Institute, New York

Collaborative Research, Inc., Management Training Program
(Conducted by Associated Industries of Massachusetts)

Various law courses

Radiation Training:

Graduate coursework in Radiation Biology and Radiation Protection through Radiation Biology Department, TWU (1972-1973)

Radiation Protection Courses and Seminars and radiation training through Radiation Protection Office at MIT (1976-1978)

Annual Radiation Protection sessions offered by MIT's Radiation Protection Office (1979-1988)

PUBLICATIONS

Moir, D., Mao, J.-I., Schumm, J., Vovis, G.F., Alford, B.L. and Taunton-Rigby, A. (1982). Molecular cloning and characterization of double-stranded cDNA coding for bovine chymosin. Gene 19, 127.

Alford, B., Taunton-Rigby, A., Gill, T., Aubin, C. and Georgette, Y. (1981). Optimizing the enzymatic reactions of oligonucleotides and molecular linkers. Fed. Proc. 40, 1849.

Alford, B.L., Chinault, A.C., Jolly, S.O. and Hecht, S.M. (1979). Preparation of tRNAs terminating in 2'- and 3'-deoxyadenosine. Methods Enzymol. 59, 121.

Alford, B.L., Pezzuto, J.M., Tan, K.H. and Hecht, S.M. (1979). Both positional isomers of aminoacyl-tRNAs are bound by elongation factor Tu. J. Biol. Chem. 254, 6894.

Alford, B.L. and Hecht, S.M. (1979). Transfer RNA control of the activation of isomeric tRNA Trp's. J. Biol. Chem. 254, 6873.

Alford, B.L. and Hecht, S.M. (1978). 2'- versus 3'-OH specificity in tRNA aminoacylation. Further support for the "secondary cognition" proposal. J. Biol. Chem. 253, 4844.

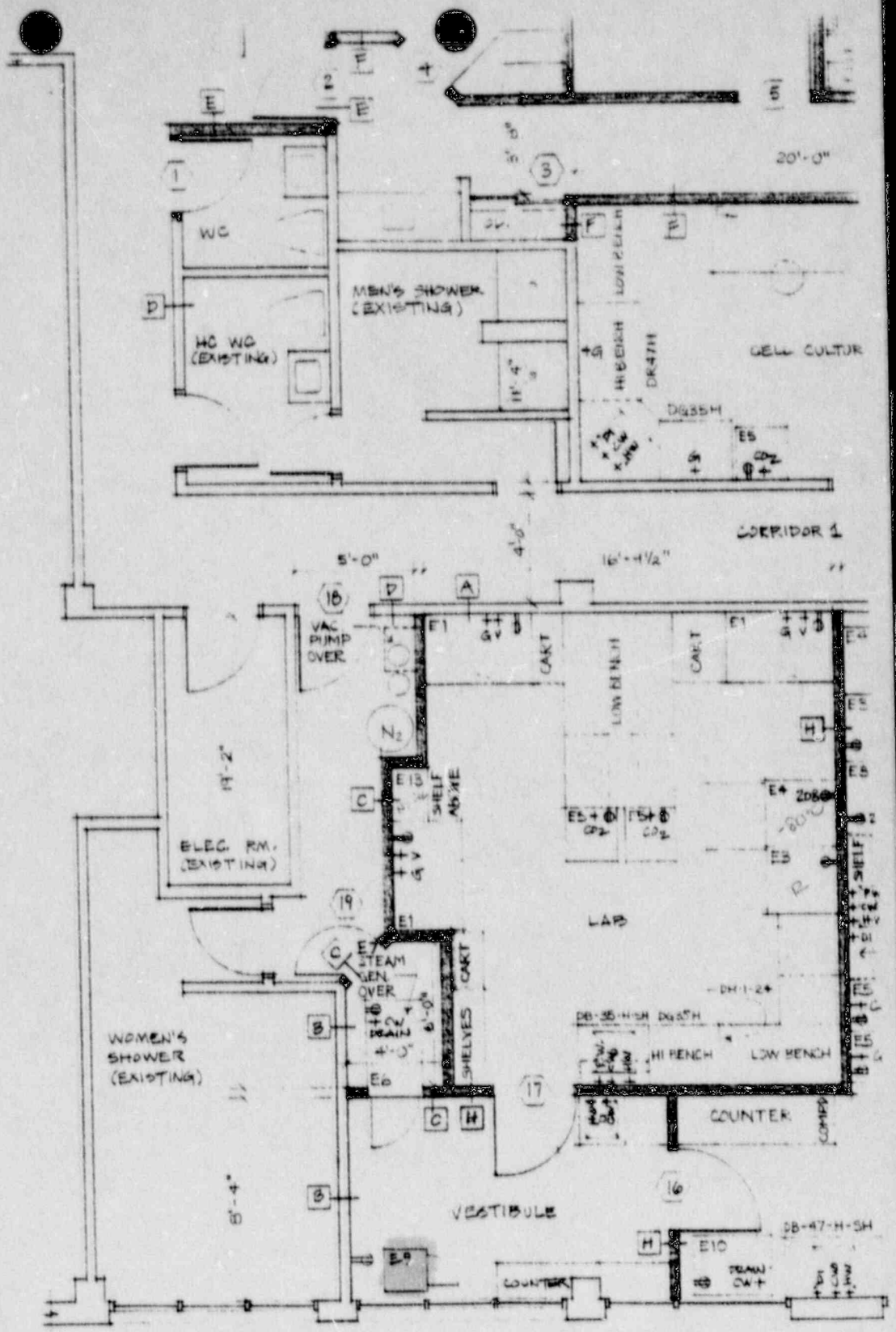
Hecht, S.M., Alford, B.L., Kurado, Y. and Kitano, S. (1978). "Chemical aminoacylation" of tRNA's. J. Biol. Chem. 253, 4517.

Alford, B.L. and Barnes, E.M., Jr. (1978). Hypoxanthine transport by cultured Chinese hamster lung cells. Twenty-third Rheumatism Review.

Alford, B.L. and Barnes, E.M., Jr. (1977). Regulation of hypoxanthine transport by cyclic nucleotides in cultured Chinese hamster lung fibroblasts. Arch. Biochem. Biophys. 180, 214.

Alford, B.L. and Barnes (1976). Carrier-mediated hypoxanthine transport by cultured Chinese hamster fibroblasts. Fed. Proc. 35, 1758.

Alford, B.L. and Barnes, E.M., Jr. (1976). Hypoxanthine transport by cultured Chinese hamster lung fibroblasts. J. Biol. Chem. 251, 4823.



BUILDING 600 - FIFTH FLOOR

KEY TO SERVICES

- Electric
- Computer outlet
- G Gas
- V Vacuus
- CW Cold water
- HW Hot water
- DI - Deionized water
- PW Pure water

KEY TO SYMBOLS

- E.2 Equipment number
- (2) Door number
- A Partition type

N
W E
S

PA
Py
A
B
C
D

REPLIGEN CORPORATION
EQUIPMENT SCHEDULE

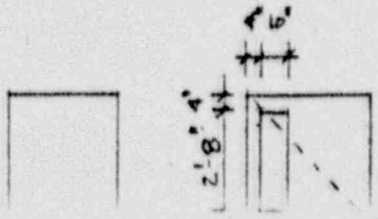
Item No.	Description Dimensions	Manufacturer Model No.	Services	Status*
E1	Laminar flow hood 53.5w 34d 88h	Baker SterilGard SG-400	E:110V 20A gas vacuum	FOIC
E2	Laminar flow hood 79w 34d 88h	Baker SterilGARD SG-600	E:110V 20A gas vacuum	FOIC
E3	Refrig/freezer 33w 35d		E:110V	FIBO
E4	-80°C freezer 33w 35d		E: 208V	FIBO
E5	Incubator 25w 26d	Queue	E:110V CO_2	FOIC
E6	Autoclave 28w 43d 72h	AMSCO	E:110V water drain steam	FOIC
E7	Steam generator	Reimers RH-18	E:208V 30A 3ph water	FOIC
E8	Ultracentrifuge 35w 33d	Beckman	E:208V 30A 1ph	FIBO
E9	Cell Irradiator	AECL Gammacell 1000	E:110V	FIBO
E10	Ice machine 38w 29d		E:110V water drain w/pump	FOIC
E11	Water bath 37w 32.5d 80		E:110V	FIBO
E12	-20°C freezer		E:110V	FIBO
E13	Nitrogen freezer 19w 24d 36h		N_2	FIBO

* FIBO - Furnished and installed by owner
FOIC - Furnished by owner, installed by contractor

DOOR SCHEDULE

No.	From	To	Size
1	Corr 1	WC	3-0x7/- (re-us
2	Corr 2	Corr 1	3-0x7-(
3	Closet	Corr 2	pair 2-0x7-(
4	Corr 2	Office 1	2-8x7-(
5	Corr 2	Office 2	3-0x7-(
6	"	Office 3	"
7	"	Office 4	"
8	"	Office 5	"
9	"	Office 6	"
10	"	Office 7	"
11	"	Office 8	pair 1-6x7-(
12	Corr 2	Corr 1	3-0x7-(
13	Corr 1	Cell Culture 2	3-4x7-(
14	Corr 1	Cell Culture 1	3-4x7-(
15	Cell Culture 1	Corr 1	3-4x7-(
16	Vestibule	Cell Culture 1	3-4x7-(
17	Lab	Vestibule	3-4x7-(
18	Corr 1	Corr 3	3-0x7-(
19	Autoclave	Corr 3	2-0x7-(

All frames are hollow metal, 5 7/ otherwise noted. Verify frame d (1, 2, 12, 13, 14, 15, 18.)



MS-10
87

(FOR LFMS USE)
INFORMATION FROM LTS

PROGRAM CODE: _____
STATUS CODE: 3
FEE CATEGORY: _____
EXP. DATE: 0
FEE COMMENTS: _____

BETWEEN:

LICENSE FEE MANAGEMENT BRANCH, ARM
AND
REGIONAL LICENSING SECTIONS

LICENSE FEE TRANSMITTAL

A. REGION 1

1. APPLICATION ATTACHED
APPLICANT/LICENSEE: REPLIGEN CORPORATION
RECEIVED DATE: 890308
DOCKET NO: 3031049
CONTROL NO.: 110401
LICENSE NO.:
ACTION TYPE: NEW LICENSE

2. FEE ATTACHED
AMOUNT: $230.00
CHECK NO.: 30749

3. COMMENTS

SIGNED R. J. Brown
DATE 89-03-13

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

1. FEE CATEGORY AND AMOUNT: 3E $230

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

3. OTHER _____

SIGNED _____
DATE 3/23/89