



BioTechnica International, Inc.

55 Batten St. Cambridge, Massachusetts 02140 (617) 864-0040

Telex: 705219
Cable: BIOTEC

July 3, 1985

U.S. N.R.C.
LIC. FEE MGMT. BRANCH

85 JUL 15 AM 05

RECEIVED

U.S. Nuclear Regulatory Commission
631 Park Avenue
King of Prussia, PA 19406

RE: Materials License #20-20506-01

Dear Sir or Madam:

I am writing to request an amendment to materials license #20-20506-01, issued December 3, 1981. We are seeking authorization to hold and use radionuclides at another location approximately 1.2 miles from our current facility. The new location is the site of a subsidiary company being set-up by BioTechnica International (BTI) and will be named BioTechnica Diagnostics (BTD).

Except for the location of its physical plant, BTD will operate under the same guidelines and procedures as BTI. This includes the radiation protection program, radiation safety training, waste handling and disposal procedures, lab area surveys, etc. The three individuals named in Condition #12 of our 1985 amendment will continue to supervise the use of radioactivity at BTD.

The enclosed materials in duplicate, outline our plans for BTD in terms of radiation protection, training, and laboratory procedures. A description of the BTD laboratories is also included along with a floor plan of the facility.

No changes are being made in any of the BTI procedures or radiation safety program, which were previously described in the original application dated August 26, 1981 (updated November 5, 1981), the first amendment application dated July 20, 1983 (updated October 17, 1983), and in the second amendment application dated February 26, 1985 (updated April 9, 1985). All other statements found in the above documents that are not referred to in this amendment application, are still in effect both for BioTechnica International and BioTechnica Diagnostics.

8510280213 850815
REG. LIC. 30
20-20506-01

PDR

July-8-1
Applicant.....
Check No. 7812
Amount/Fee Category 3m \$120
Type of Pre. Cmd
Date Check Rec'd 7/15/85
Received By Jacques

"OFFICIAL RECORD COPY"

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ML10

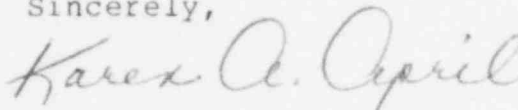
JUL 08 1985

U.S. Nuclear Regulatory Commission
RE: Materials License #20-20506-01
July 3, 1985
Page 2

All items are discussed in accordance with the pertinent section of the original application. References to the original 1981 application and 1983/1985 amendment applications have been made whenever possible.

Enclosed is a check for one hundred twenty dollars (\$120.00) to cover the current amendment fee. Please address all questions and comments regarding this request to me. Thank you for your time and consideration.

Sincerely,

A handwritten signature in cursive script that reads "Karen A. April".

Karen A. April
Deputy Director
Laboratory Services

Enclosures

KA/r1 0437A

Section 6. Individual(s) Who Will Use or Directly
Supervise the Use of Licensed Material.

Since we are amending our current materials license to incorporate only BTD's physical plant, the individuals named in the 1985 amendment, Condition #12, will continue to supervise the use of radionuclides at the BTD facility.

Karen A. April will regularly make weekly visits to the facility to inspect the laboratories, review the waste collection logs and to review and verify the incoming radioactive shipments log. She will also be available to the staff at BTD whenever necessary and especially in an emergency. BTD is located approximately 1.2 miles from BioTechnica which allows easy accessibility to the facility.

Karen K. Vaccaro has been named as the Director of Technical Operations for BTD. Dr. Vaccaro will be responsible for the following aspects of BTD's radiation protection program:

- monitoring of all incoming shipments of radioactivity, including package inspections and wipe tests
- maintaining an inventory of all radionuclides held on the premises of BTD
- daily collection of radioactive waste and maintenance of waste logs
- implementation of emergency procedures when necessary.

Dr. Vaccaro will be under the supervision and direction of Karen April and will be required to report any emergencies to Ms April.

A copy of Dr. Vaccaro's curriculum vitae has been included. All other responsibilities for the BTD radiation protection program will be handled by Ms April and will follow the same outline which was submitted as Appendix 1, in the 1985 amendment application, entitled "Duties of the Radiation Protection Officer".

AUTHORIZATION TO SUPERVISE THE USE OF LICENSED MATERIAL:

I, Karen A. April, hereby authorize Karen K. Vaccaro to oversee day-to-day responsibility for the BTD radiation protection program. Dr. Vaccaro is authorized to perform only the duties outlined above.

Karen A. April
Karen A. April

July 3, 1985
Date

Karen K. Vaccaro
Karen K. Vaccaro

July 2, 1985
Date

Section 8. Licensed Material

All quantities of radionuclides for BTB will be approved and ordered by Karen A. April at BioTechnica International.

Ms April will incorporate these quantities into the BioTechnica inventory of licensed material to insure that together, BTI and BTB are operating within the possession limits as specified in Item #8 of the 1985 amendment. All quantities will be shipped directly to BTB and received there only during the regular business hours of 8:30 am to 5:00 pm.

When necessary, any transfer of radioactive materials will comply with all NRC and DOT regulations.

General usage of radioactivity at BTB will be primarily Phosphorus-32 and Iodine-125. Routine experiments will involve approximately 1-2 milliCuries of these radionuclides. It is expected that no more than 10 milliCuries of either isotope will be at the facility at any one time.

Section 10. Radiation Detection Instruments

The following instrumentation is being purchased for use at BioTechnica Diagnostics:

-One Beckman LS 1800 Liquid Scintillation Counter

-One Beckman Gamma 5500 Radiation Counter

-Two Survey Meter/Geiger counter

Manufacturer: Ludlum Measurements, Inc.

Model #3

Radiation detected: beta/gamma

Radiation Detectors: 1) end window GM

2) NaI scintillation

Sensitivity range: 1) 0 - 200 mR/hr

or 500,000 cpm

2) 0 - 500,000 cpm

Service and repair contracts will be purchased for all of these instruments in order to insure proper maintenance. Each instrument will be calibrated every six months, as previously stated (Reference Section 11 of 1981 application).

Section 13. Facilities and Equipment

BioTechnica International, Inc. (BTI) is setting up a subsidiary company, BioTechnica Diagnostics, (BTD) to conduct research and development in the area of dental diagnostics. The company will be leasing existing laboratory facilities at 61 Moulton Street in Cambridge, approximately 1.2 miles from BTI. The building was previously occupied by BTC Diagnostics, an unrelated genetic R&D firm.

The facility consists of one large first floor and a smaller second floor mezzanine which together comprise approximately 6300 square feet.

An administrative area, lunchroom, conference room and a series of offices are located just inside the entrance to the building. This area will be maintained as such and absolutely no radioactivity will be permitted in this area. The access door (highlighted in green) to the laboratories from the office area will be kept closed at all times.

The main laboratories are composed of general work areas, a glassware/utilities kitchen, a cold room, an equipment room, one lab for high levels of radioactivity (hot lab), and numerous storage areas. The general working labs (G1 thru G4) are noted on the attached floor plan. Low levels of radioactivity will be permitted in these areas up to 1.0 mCi of activity, except for Iodine-125, which will be permitted only in the hot lab.

Work surfaces will consist of secured, standard laboratory benches (red slashes) and a number of stone-topped work tables. All surfaces will be covered with Kay-Dry absorbent paper whenever experiments are in progress.

Plumbed sinks are present in each general lab. Only one sink (highlighted in yellow) will be designated for the disposal of decayed Phosphorous-32 liquid waste. All other liquids will be shipped as radioactive waste.

Two fume hoods are located in laboratory G2. These are standard, six foot wide chemical hoods which will be tested and calibrated for proper air-flow every six months and will be maintained at no less than 100 linear feet of air per minute. Neither of these hoods will be equipped with charcoal filters. Therefore, experiments requiring Iodine-125 will be carried out in the hot lab only. One or two freezers in the general labs will be designated for the storage of low-level radioactivity. Lead pigs will be required when storing 1.0 mCi or more of radioactivity.

All of the standard items for handling and disposing of radioactive material will be supplied. These include lab coats, disposable gloves, plexiglass shields, disposal containers, zip-lock bags, survey meters, safety glasses, plastic waste bottles, and dry vermiculite. All other practices will be as previously described (Reference Section 13, pages 1-5, 1981 application).

The hot lab (highlighted in yellow) is accessed through the general equipment room by one door which will be kept closed at all times. As indicated, on the floor plan, this lab is removed from the main work and traffic areas. It will be equipped with a six foot wide chemical fume hood, consisting of charcoal filtered exhaust and an impermeable, polymer surface with spill-containing lips. A small bench with a stainless steel top will run along one wall of the hot lab. All work surfaces in this room will be covered with absorbent paper. A small foot operated sink, is located just inside the door, to the left. Hot and cold water will be provided, but this will be a wash-up/utility sink, only. No liquid radioactive waste will be poured down this sink. All of the safety/protective items mentioned above will also be located in this lab. All personnel will be required to monitor their hands, feet, clothing, and work areas after using radioactivity in this lab and before leaving. This lab will have an under bench freezer for storing millicurie quantities of radioactivity.

The floor of this lab will consist of an impermeable molded covering and will be sealed. The walls will be painted with impermeable paint. All manipulations involving ^{125}I will be carried out in this room. Only samples already prepared for counting will be removed to the general equipment room.

The general equipment room will house the LS 1800 scintillation counter and the Gamma 5500 counter in order to be centrally located and accessible to all scientific personnel.

The storage areas (highlighted in blue) will house consumable laboratory items, dry chemicals and weighing balances. The kitchen will serve as a glass washing and media prep area. The two rooms located behind the kitchen were used by BTC Diagnostics as animal rooms. BTB will not be doing any experimentation on animals and therefore has no immediate plans for using these areas at all. Over the long-term, this space may be converted into office space, although no experimental work is ever planned for these rooms.

The mezzanine is approximately 500 square feet in area. It is lined with shelves on both walls and will be used exclusively for bulk storage. No radioactivity will be permitted to be used or stored in this area.

Section 14. Waste Disposal

Whenever possible radioactive compounds with a physical half-life of less than 65 days will be held on-site for decay at BTB, as stated in BioTechnica's 1985 amendment, Condition #15A and #15B. All other radionuclides will be shipped from BTB as previously described.

All radioactive waste will be kept in a storage room located adjacent to the receiving area (see Fig. BTB #1, highlighted in pink). Doors to this storage area will be kept closed and secured whenever possible.

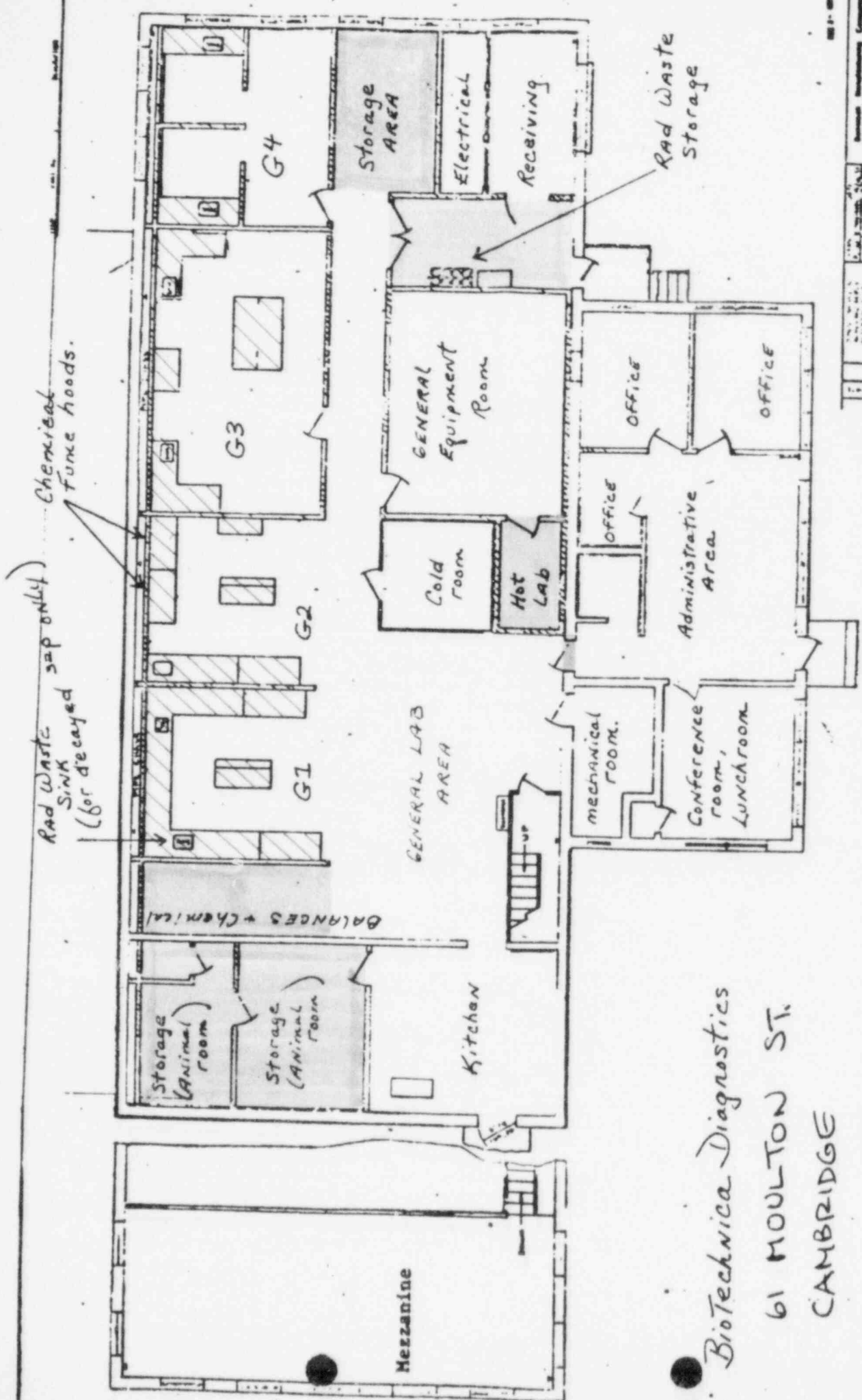
Disposal of radioactive waste will be done under the supervision of Karen A. April. This includes disposal of waste which has decayed on site and shipments of waste made by our commercial waste disposal service (Reference Section 14 of 1985 amendment application).

All other procedures for the handling of waste will be the same as those described in Section 13, pg. 5, part c of the 1981 application, Section B, pg.5, part 4 of the 1983 amendment application, and Section 14 of the 1985 amendment application.

Section 15. Radiation Protection Program.

Radiation safety at BioTechnica Diagnostics will be implemented and supervised by Karen A. April, the Radiation Protection Officer at BioTechnica International. Ms April will be responsible for training all BTI personnel, using the BTI Health and Safety manual. A copy of BioTechnica's radiation safety procedures was submitted to the NRC in the original license application (Reference 1981 application, Section 15 pages 6-13). Specific safety measures pertinent to the BTI facility, such as the location and procedures for radioactive waste will be reviewed with the employees during their Radiation Health and Safety training session.

As stated in Section 6 of this amendment application, Karen K. Vaccaro will be responsible for general, day-to-day safety procedures which, for BTI, will be identical to those already practiced at BTI and accepted by the NRC.



Biotechnica Diagnostics
 61 MOULTON ST.
 CAMBRIDGE

General Information		Company Name		Address	
Project Name		Project No.		Project Date	
Project Description		Project Status		Project Manager	
Project Budget		Project Cost		Project Completion	
Project Start Date		Project End Date		Project Duration	
Project Lead		Project Sponsor		Project Stakeholder	
Project Risk		Project Impact		Project Outcome	
Project Review		Project Feedback		Project Lessons Learned	
Project Status		Project Progress		Project Next Steps	
Project Contact		Project Phone		Project Email	
Project Website		Project Social Media		Project Other Info	
Project Notes		Project Comments		Project Attachments	
Project History		Project Changes		Project Version	
Project Approval		Project Sign-off		Project Final Review	
Project Archive		Project Backup		Project Restore	
Project Security		Project Access		Project Permissions	
Project Compliance		Project Audit		Project Reporting	
Project Documentation		Project Manuals		Project Templates	
Project Training		Project Courses		Project Certifications	
Project Support		Project Helpdesk		Project Tickets	
Project Feedback		Project Surveys		Project Interviews	
Project Evaluation		Project Metrics		Project KPIs	
Project Summary		Project Overview		Project Details	
Project Conclusion		Project Results		Project Impact	
Project Final Report		Project Final Review		Project Final Sign-off	
Project Archive		Project Backup		Project Restore	
Project Security		Project Access		Project Permissions	
Project Compliance		Project Audit		Project Reporting	
Project Documentation		Project Manuals		Project Templates	
Project Training		Project Courses		Project Certifications	
Project Support		Project Helpdesk		Project Tickets	
Project Feedback		Project Surveys		Project Interviews	
Project Evaluation		Project Metrics		Project KPIs	
Project Summary		Project Overview		Project Details	
Project Conclusion		Project Results		Project Impact	
Project Final Report		Project Final Review		Project Final Sign-off	

RESUME

KAREN K. VACCARO

18 Massasoit Road
Wellesley, MA 02181
(617) 235-2542

EDUCATION:

HARVARD MEDICAL SCHOOL
Boston, MA
Post-doctoral Fellow in Physiology 1977-1980

TUFTS UNIVERSITY
Medford, MA
Ph.D., Department of Biology 1977

BRANDEIS UNIVERSITY
Waltham, MA
A.B., Biology 1971

CURRENT

POSITION:

DIRECTOR OF TECHNICAL OPERATIONS May 1985-
BIOTECHNICA DIAGNOSTICS
85 Bolton Street
Cambridge, MA 02140

Responsible for establishment and development of a reference laboratory to perform DNA probe analysis of periodontal disease microorganisms from human samples. Major responsibilities will include development of company facility, hiring of technical staff, direction of scale-up activities, and participation in design and development of user-friendly diagnostic kits.

WORK

EXPERIENCE:

DIRECTOR OF PRODUCT ASSURANCE July 1984-
TRAVENOL-GENENTECH DIAGNOSTICS April 1985
600 Memorial Drive
Cambridge, MA 02139

Responsible for 70 people in three departments: quality control, quality assurance (QC/QA) and technical support and development (TSD). Major QC/QA objectives center around GMP compliance for all documentation and testing associated with the current RIA product line and development of QC procedures for class III level tests, infectious diseases tests and non-isotopic technologies. TSD activities are described below.

Supervised the handling of up to 40 milli-Curies of Iodine-125, and up to 1 milliCurie of Phosphorous-32.

KAREN K. VACCARO

DIRECTOR,
TECHNICAL SUPPORT AND DEVELOPMENT
TRAVENOL-GENENTECH DIAGNOSTICS

Jan. 1984-
July 1984

Department of 18 people (4 Ph.D.s). Responsible for resolving technical issues related to existing RIA product line, and all product improvements and development of new isotopic technologies and assays. Current organization includes an antisera group, with responsibility for animal farm program management. A β -hCG RIA kit using a monoclonal antibody generated in-house was developed and market released July 1984.

Supervised the handling of up to 40 milli-Curies of Iodine-125, and up to 1 millicurie of Phosphorous-32.

MANAGER, TECHNICAL SUPPORT
CLINICAL ASSAYS
600 Memorial Drive
Cambridge, MA 02139

Sept. 1982-
Dec. 1983

Department of nine people (3 Ph.D.s). Responsible for all technical issues related to manufacturing and quality control of 26 RIA products (diagnostic tests). Development, scale-up and transfer to the marketplace of an improved coated tube T3 RIA and a high sensitivity TSH RIA were the major accomplishments during this period.

GROUP LEADER, RESEARCH & DEVELOPMENT
CLINICAL ASSAYS

Jan. 1980-
Sept. 1982

Hired to analyse non-isotopic immunoassay technologies and instrumentation and to demonstrate feasibility of one technology in-house. Supervised technical staff of three people (2 w/Masters Degree). Major accomplishments during this time:

- (1) Demonstration of prototype coated tube enzyme immunoassays for therapeutic drugs and thyroid function testing.
- (2) Development, scale-up and transfer to the marketplace of a combined total and direct free thyroid hormone coated tube radioimmunoassay kit.

KAREN K. VACCARO

(3) Development of new tube coating technologies, which have been applied to other products at Clinical Assays.

(4) Development of a solid phase chemiluminescent Rubella immunoassay and analysis of prototype instrumentation in terms of application to clinical lab.

RESEARCH

EXPERIENCE:

Laboratory of DR. ROBERT PERLMAN 1977-1980
Department of Physiology,
Harvard Medical School
Boston, MA

Established a tissue culture facility. Conducted study of the control of synthesis and secretion of catecholamines in cultures of a rat tumor of the adrenal gland. Investigated effects of antibiotics known to increase heart rate and blood flow on the synthesis of catecholamines.

Laboratory of DR. ELI SIEGEL 1971-1977
Department of Biology, Tufts University
Medford, MA

Doctorate awarded for study of mutation frequencies in strains of bacteria defective in repair and replication of DNA. Developed expertise in classical genetic techniques of strain construction and selection methods using bacterial viruses as vectors.

- PUBLICATIONS: Vaccaro, K.K. and Siegel, E.C. "Increased levels of certain frameshift mutations in DNA polymerase I - deficient strains of *Escherichia coli*". Mol Gen. Genet. 141: 251-262 (1975).
- Vaccaro, K.K. and Siegel, E.C. "The frameshift mutability of polA1 derivatives of mutator strains of *Escherichia coli*". Mutat. Research 42: 443-446 (1977).
- Siegel, E.C. and Vaccaro, K.K. "The reversion of trp frameshift mutations in *mut*, *polA*, *lig* and *dnaE* mutant strains of *Escherichia coli*". Mutat. Research 50: 9-17 (1978).

KAREN K. VACCARO

Vaccaro, K.K., Liang, B.T., Perelle, B.A. and Perlman, R.L. "Tyrosine 3-monooxygenase regulates catecholamine synthesis in pheochromocytoma cells". J. Biol. Chem. 255: 6539-6541 (1980).

Liang, B.T., Vaccaro, K.K., Perelle, B.A. and Perlman, R.L. "Studies on dihydropteridine reductase activity in pheochromocytoma cells". J. Neurochem, 37: 1164-1169 (1981).

Vaccaro, K.K., Ferrazza, D., Sullivan, J. and Groman, E.V. "Enzyme Immunoassays of Total and Free T4 in a coated tube". Clin. Chem. 27: 1070 (1981).

Vaccaro, K.K., Liang, B.T., Sheard, B.E. and Perlman, R.L. "Monensin inhibits catecholamine synthesis in pheochromocytoma cells". J. Pharm., Expt. Ther. 221: 536-540 (1982).

Shapiro, R., Chan, J., Vaccaro, K., Pierson, A. and Quick, J. "The use of protein-enhanced fluoroscein chemiluminescence in an immunoassay for Rubella antibody". Clin. Chem. (in press, 1984).

GRANTS &
SOCIETIES:

Post doctoral Fellowship awarded from National Institute of Health	1977-1980
Am. Assoc. for Clin. Chem. (AACC)	1980-
Clinical Ligand Assay Society (CLAS)	1981-

BETWEEN: William O. Miller, Chief
License Fee Management Branch
Office of Administration

John E. Glenn, Chief
Nuclear Materials Section B
Division of Engineering and
Technical Programs

LICENSE FEE TRANSMITTAL

A. REGION 1

1. APPLICATION ATTACHED

Applicant/Licensee: BioTechnica International, Inc.

Application Dated: 7/3/85

Control No.: 04061

License No.: 20-20506-01

2. FEE ATTACHED

Amount: \$ 120.00

Check No.: 7812

3. COMMENTS

Signed Branda Platchek

Date 7/9/85

03620

B. LICENSE FEE MANAGEMENT BRANCH

1. Fee Category and Amount: 3M - \$120 11/86

2. Correct Fee Paid. Application may be processed for:

Amendment ✓

Renewal

License

Signed J. Jackson

Date 7/16/85