030-30706

INTERNATIONAL BIOTECHNOLOGY LABORATORIES, INC.

Log ..... Mar 13
Remitter .....
Check No. 807
Amount $120
Fee Category 3A
Type of Fee ADD
Date Check Rec'd. 4/26/89
Date Completed .....
By A. Krawiec

February 10, 1989

Mr. Francis M. Costello
Nuclear Materials Safety Section B
Division of Radiation Safety
and Safeguards
U.S. Regulatory Commission
475 Allendale Road
King of Prussia, PA 19406

RE: Appointment of IBL Radiation Safety Officer
NRC License Number 20-28253-01

Dear Mr. Costello:

As you know, Dr. Tubo has left our laboratory. Since Dr. Tubo's departure, Dr. Bernstine has been fulfilling the responsibilities of Radiation Safety Officer. Per our telephone conversation on March 8, 1989, I would like to request an amendment to the above-referenced license. In item 11.A., the name "Ross A. Tubo, Ph.D." should be removed. In item 11.B. as well, Dr. Tubo's name should be removed, and the name "Edward G. Bernstine, Ph.D." should be inserted. Since Dr. Bernstine is named on our license in item 11.A. as a supervisor and user of radioisotopes, it is logical and practical that he should become our Radiation Safety Officer.

Also, please find enclosed another curriculum vitae on Dr. Bernstine for your files. If you have any questions or concerns regarding this matter please do not hesitate to contact me.

Sincerely,

Ada L M Watson

Ada L. M. Watson
Manager of Administration

ALMW:mlh

enc.

110410

OFFICIAL RECORD COPY ML 10

MAR 13 1989

67 Rogers Street, Cambridge, MA 02142 (617) 868-0077
Telecopier: 617-661-6341 Telex: TWX 910-2500113 Easy Link: ESL 62013862

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INTERNATIONAL BIOTECHNOLOGY LABORATORIES, INC.

Edward G. Bernstine, Ph.D.
Vice President, Research and Development

Experience in Handling Radioactive Isotopes

Dr. Bernstine has 20 years of experience working with radioisotopes in both academic and industrial research environments. He received training in safety programs at Oak Ridge National Laboratory, where he was a member of the Senior Research Staff in the Biology Division, and at Integrated Genetics, where he was a Senior Research Scientist and Project Manager.

Princeton University (1966-1971)

Isotopes used: ^{3}H, ^{14}C, ^{32}P
Purposes: Protein and nucleic acid labeling by *in vivo* incorporation of amino acids and $^{32}P_i$. *In vitro* labeling of nascent protein chains with (^{3}H)- and (^{14}C)- amino acids.

Centre de Genetique Moleculaire (1971-1973)

Isotopes used: ^{3}H, ^{14}C
Purposes: *In vivo* labeling of protein and nucleic acids.

Oak Ridge National Laboratory (1974-1981)

Isotopes used: ^{3}H, ^{14}C, ^{35}S
Purposes: *In vivo* labeling of proteins.

Integrated Genetics, Inc. (1982-1986)

Isotopes used: ^{3}H, ^{125}I, ^{32}P, ^{14}C, ^{35}S
Purposes: *In vitro* labeling of nucleic acids, RIAs, *in vivo* protein labeling.

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INTERNATIONAL BIOTECHNOLOGY LABORATORIES, INC.

EDWARD G. BERNSTINE, PH.D.
Vice President, Research and Development

Education

Ph.D. Biology, 1972
Princeton Univeristy

A.B. Biology, 1966
Temple University

Professional Experience

1982-1986 Integrated Genetics, Framingham, Massachusetts, USA
Senior Research Scientist

Initiated and managed a program in human fertility hormones:

-Cloned the four cDNA's needed to express HCG, hLH and hFSH.
-Designed and constructed expression systems for bacterial, yeast and mammalian cells.
-Obtained first expression of dimeric, glycosylated recombinant products (mammalian cells).
-Demonstrated biological activity of all products.
-Scaled up production purification.
-Supplied material for clinical trials.

Responsible for a similar program for agricultural application:
-Cloned nine cDNA's or genes required to express bovine, porcine and equine gonadotropins.
-Expressed biologically active bovine LH and FSH.
-Supplied material for clinical trials.

By means of site-directed mutagenesis and the formation of fusion products constructed a series gonadotropin subunits for diagnostic and therapeutic use.

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1986-1987 President, Tritech International, Inc., Boston, Massachusetts, USA

1987-1988 Consultant for International Biotechnology Laboratories, Inc.

Other Experience

1971-1973 Post doctoral fellow at Centre de Genetique Moleculaire with the late Dr. Boris Ephrussi.

1973-1974 Post doctoral fellow at the Jackson Laboratory with Dr. Leroy C. Stevens. Purified marker of malignant stem cells, examined its expression in a series of somatic cell hybrids. Isolated a teratocarcinoma cell line that remains of great interest today.

1974-1982 Mammalian Genetics Section in the Biology Division of the Oak Ridge National Laboratory. Worked principally on the effects of gene dosage, on gene expression and the genetic regulation of gene expression.

Publications

Bernstine, E.G., Hooper M., Grandchamp, S. and Ephrussi, B. Alkaline Phosphatase Activity in Mouse Teratoma. Proc. Nat. Acad. Sci. USA, 1973; 70: 3899-3903.

Bernstine, E.G., Ephrussi, B. Alkaline Phosphatase Activity in Embryonal Carcinoma and Its Hybrids with Neuroblastoma In: Sherman, M.I. and Solter, D. eds. Teratomas and Differentiation, 1975; Academic Press, New York; 271-187.

Bernstine, E.G., Koyama, H. and Ephrussi, B. Enhanced Expression of Alkaline Phosphatase in Hybrids Between Neuroblastoma and Embryonal Carcinoma. Somat. Cell. Genet, 1977; 3: 217-225.

Bernstine, E.G. Genetic Control of Mitochondiral Malic Enzyme in the Mouse. Genetics 88 (4 part 2), 1978; S9-S10.

Bernstine, E.G. et. al. Effects of Gene Dosage on Expression of Mitochondrial Enzyme in the Mouse Musculus. Nature (London), 1978; 271: 748-750.

Bernstine, E.G. Genetic Control of Mitochondrial Malic Enzyme in the Mouse. Genetics 88 (4 part 2), 1978; S9-S10.

Bernstine, E.G. Satellite DNA Content of Chromatin Fractions Isolated from Eco R1-digested Mouse Liver Nuclei. Exp. Cell Res., 1978; 113: 205-208.

Bernstine, E.G. Genetic Control of Mitochondrial Malic Enzyme in Mouse Brain. J. Biol. Chem, 1979; 254: 83-87.

Bernstine, E.G. Regulation of Mitochondrial Malic Enzyme Synthesis in the Mouse Brain. Proc. Nat. Acad. Sci. USA, 1979; 76: 6539-6541.

Bernstine, E.G. and Koh, C. A Cis-active Regulatory Gene in the Mouse : Direct Demonstration of Cis-active Control of the Rate of Enzyme Subunit Synthesis. Proc. Nat. Acad. Sci. USA, 1980; 77: 4193-4195.

Beck, A, et. al. Cloning and Expressions of cDNAs Coding for Human Choriogonadotropin and Luteinizing Hormone. 7th International Congress of Endocrinology, Abstracts, 1984, p.308.

Birken, S., et. al. An Immunochemical Method to Assess the Structure of the Carbohydrate and Peptide Components of the Beta COOH-terminus of hCG and Application to Studies of Expressed hCG. Ibid, 1984, p.310.

Lustbader, J., et. al. Characterization of hCG Expressed from Cloned cDNA. Ibid, 1984, p.863.

Beck, A., et. al. Cloning and Expression of DNA's for Follicle-Stimulating Hormone. DNA, 1985; 4: 76.

Reddy, V.B., et. al. Expression of Human Choriogonadotropin in Monkey Cells Using a Single SV40 Vector. Proc. Nat. Acad. Sci., USA, 1985; 82:3644-3548.

Gharib, S.D., et. al. Hormonal Regulation of FSH Subunit Gene Expression in the Rat. Clin. Res., 1986, 34: 644A.

Maurer, R.A. and Beck, A, et. al. Isolation and Nucleotide Sequencing of a Cloned cDNA Encoding the Beta-subunit of Bovine Follicle-stimulating Hormone. DNA, 1986; 5: 363-369.

Lustbader, J. et. al. Characterization of the Expression Products of Recombinant Human Choriogonadotropin and Subunits. J. Biol. Chem, 1987; 262: 14204-14212.

Watkins, P.C. et. al. DNA Sequence and Regional Assignment of the Human Follicle-stimulating Hormone Beta-subunit Gene to the Short Arm of Human Chromosome 11. DNA, 1987; 6:205-212.

MAR 27 19

International Biotechnology
Laboratories, Inc.
ATTN: Ms. Ada L. M. Watson
Manager of Administration
67 Rogers Street
Cambridge, MA 02142

Gentlemen:

This refers to your letter dated February 10, 1989, for an amendment to Materials License 20-28253-01.

An amendment fee of $120 is required as specified in §170.31 (3M) of 10 CFR 170, copy enclosed. Payment should be made to the U.S. Nuclear Regulatory Commission and mailed to my attention at our Washington, D.C. address.

Your application will be processed by the Region I Licensing staff located at 475 Allendale Road, King of Prussia, Pennsylvania 19406. The fee, however, is required prior to issuance of the amendment. When submitting the fee, please refer to CONTROL NUMBER 110410.

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 and will void this action.

Sincerely,

Signed by:
Glenda Jackson

Glenda Jackson
License Fee Management Branch
Division of Accounting and Finance
Office of the Controller

Enclosure:
10 CFR 170

cc: Region I

DISTRIBUTION:
Pending Fee File
OC/DAF R/F
LFMB R/F (2)
DW/REGI/BIOTECH

OFFICE:	OC/LFMB	OC/LFMB
SURNAME:	SKimberley:kb	GJackson
DATE:	03/27/89	03/27/89

BETWEEN:

LICENSE FEE MANAGEMENT BRANCH, ARM
AND
REGIONAL LICENSING SECTIONS

(FOR LFMS USE)
INFORMATION FROM LTS

PROGRAM CODE: 03620
STATUS CODE: 0
FEE CATEGORY: 3M (Exempt 2/89)
EXP. DATE: 19931031
FEE COMMENTS: ----------

LICENSE FEE TRANSMITTAL

A. REGION 1

1. APPLICATION ATTACHED
APPLICANT/LICENSEE: INTERNATIONAL BIOTECHNOLOGY LABS
RECEIVED DATE: 890313
DOCKET NO: 3030706
CONTROL NO.: 110410
LICENSE NO.: 20-28253-01
ACTION TYPE: AMENDMENT

2. FEE ATTACHED
AMOUNT: $0
CHECK NO.: ----

3. COMMENTS

SIGNED R. F. Bores
DATE 89-03-15

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

1. FEE CATEGORY AND AMOUNT: 3M $ 120

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

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

SIGNED S. Kimberly
DATE 4/26/89