

030-19343

June 17, 1988

U.S. Nuclear Regulatory Commission
Region One
475 Allendale Road
King of Prussia, PA 19406

RECEIVED

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Gentlemen:

Repligen Corporation, NRC license #20-20503-01, requests the amendment of our license to reflect a change in the Radiation Safety Officer position and to increase the possession limits for two of the radioisotopes currently being handled. We request the following two changes:

1. Dr. Bernadette L. Alford will replace Mr. Steven Nigro as the Repligen Radiation Safety Officer. Dr. Alford's curriculum vitae is enclosed. Mr. John McIsaac will function as Dr. Alford's Assistant Radiation Safety Officer. Mr. McIsaac was responsible for some of the day-to-day radiation protection activities under Steve Nigro (radiation surveys, waste disposal, environmental air monitoring, etc.). Mr. McIsaac attended the Harvard School of Public Health "Radiation Protection" course in March, 1988.
2. The possession limit for Fe-55 should be increased from two (2) millicuries to five (5) millicuries, and the limit for Cr-51 should increase from five (5) millicuries to twenty (20) millicuries. These increases are needed due to increased use by the laboratory personnel.

Enclosed please find a check for one hundred twenty dollars (\$120.00), the fee for an amendment to a Category 3M license. Thank you in advance for your cooperation with these requests. If additional information is needed, please do not hesitate to call me.

Sincerely,

Bernadette L. Alford
Bernadette L. Alford, Ph.D.
Director of Quality Assurance
and Regulatory Affairs

jac

Enclosures

cc: M. Galanek
J. McIsaac

9001190182 881112
REG1 LIC30
20-20503-01 PDR

Jul - 1 - I
27421 returned for sig.
1988 JUN 27 PM 1:40
RECEIVED-REGION
8/2/88
8/2/88
S. Kimberly
109104
6-2-88

"OFFICIAL RECORD COPY" ML10

28 JUN 1988

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

EXPERIENCE

Radioisotope Experience: ^{125}I , ^{14}C , ^{35}S , ^3H

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

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 & 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

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

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 ¹²⁵I-immunoassay techniques.
- 1976-1978 **NIH Postdoctoral Fellow, Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts**
- Research: Aminoacylation and Misaminoacylation of transfer RNAs (utilized ³H- and ¹⁴C-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 ³H- and ¹⁴C-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 ³H- and ¹⁴C-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)

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

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

PUBLICATIONS

Muir, 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.* 52, 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, 6973.

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.* 160, 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.

JUL 14 1988

Repligen Corporation
ATTN: Bernadette L. Alford, Ph.D.
Director of Quality Assurance
and Regulatory Affairs
One Kendall Square
Building 700
Cambridge, MA 02139

Gentlemen:

We are returning for signature Check No. 27421 (\$120) which accompanied your June 17, 1988 letter for an amendment to Materials License 20-20503-01. Upon receipt of the signed check, your application will be forwarded to the Region I Licensing staff located at 475 Allendale Road, King of Prussia, Pennsylvania 19406 for processing. When resubmitting the check, please refer to CONTROL NUMBER 109104.

Sincerely,

Signed by:
Glenda Jackson

Glenda Jackson
License Fee Management Branch
Division of Accounting and Finance
Office of Administration and
Resources Management

Enclosure:
Check No. 27421 (\$120)

cc: Region I

DISTRIBUTION:
Pending Fee File
ARM/DAF R/F
LFMB R/F (2)
DW/RI/RepliGen

(Contacted
Janet Casaubon
617-225-6000
that we received
check.)

OFFICE: ARM/LFMB *Sp*
SURNAME: MMessier:rej
DATE: 7/14/88

ARM/LFMB *G*
GJackson
7/14/88

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
EXP. DATE: 19920229
FEE COMMENTS:
:.....

LICENSE FEE TRANSMITTAL

A. REGION Y

1. APPLICATION ATTACHED
APPLICANT/LICENSEE: REPLIGEN CORP.
RECEIVED DATE: 880628
DOCKET NO: 3019343
CONTROL NO.: 109104
LICENSE NO.: 20-20503-01
ACTION TYPE: AMENDMENT

2. FEE ATTACHED
AMOUNT: 120.00
CHECK NO.: 27420

3. COMMENTS

SIGNED BP
DATE 6/29/88

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 8/2/88