NRC FORM 374
(10-86)

U.S. NUCLEAR REGULATORY COMMISSION

MATERIALS LICENSE

Amendment No. 07

Pursuant to the Atomic Energy Act of 1954, as amended, the Energy Reorganization Act of 1974 (Public Law 93-438), and Title 10, Code of Federal Regulations, Chapter I, Parts 30, 31, 32, 33, 34, 35, 39, 40 and 70, and in reliance on statements and representations heretofore made by the licensee, a license is hereby issued authorizing the licensee to receive, acquire, possess, and transfer byproduct, source, and special nuclear material designated below; to use such material for the purpose(s) and at the place(s) designated below; to deliver or transfer such material to persons authorized to receive it in accordance with the regulations of the applicable Part(s). This license shall be deemed to contain the conditions specified in Section 183 of the Atomic Energy Act of 1954, as amended, and is subject to all applicable rules, regulations and orders of the Nuclear Regulatory Commission now or hereafter in effect and to any conditions specified below.

Licensee	
1. T Cell Sciences, Inc. 2. 38 Sidney Street Cambridge, Massachusetts 02139	In accordance with letter dated November 24, 1992, 3. License number 20-20783-01 is amended in its entirety to read as follows: 4. Expiration date June 30, 1995 5. Docket or Reference No 030-22069

6. Byproduct, source, and/or special nuclear material	7. Chemical and/or physical form	8. Maximum amount that licensee may possess at any one time under this license
A. Hydrogen 3	A. Any	A. 175 millicuries
B. Carbon 14	B. Any	B. 60 millicuries
C. Phosphorus 32	C. Any	C. 75 millicuries
D. Sulfur 35	D. Any	D. 150 millicuries
E. Chromium 51	E. Any	E. 80 millicuries
F. Iodine 125	F. Any	F. 80 millicuries
G. Iodine 131	G. Any	G. 30 millicuries

9. Authorized use

A. through G. Research and development as defined in 10 CFR 30.4; including animal studies.

CONDITIONS

10. Licensed material may be used only at the licensee's facilities at 38 Sidney Street, Cambridge, Massachusetts.

11. A. Licensed material listed in Item 6 above is authorized for use by, or under the supervision of, the following individuals for the materials indicated:

Authorized Users	Material
120100	
Carol Toth, Ph.D.	All
James Levin, D.V.M.	All
Carolyn Pettey, Ph.D.	All
Amy Bolwerk	All
Savvas Makrides, Ph.D.	Hydrogen 3, Carbon 14, Phosphorus 32, Sulfur 35, Chromium 51
Ellen Essigmann, Ph.D.	Hydrogen 3, Carbon 14, Iodine 125, Iodine 131

MATERIALS LICENSE
SUPPLEMENTARY SHEET

License number 20-20783-01
Docket or Reference number 030-22069
Amendment No. 07

(11. Continued) CONDITIONS

B. The Radiation Safety Officer for this license is Ellen M. Essigmann, Ph.D.

12. The licensee shall not use licensed material in or on human beings or in field applications where activity is released except as provided otherwise by specific condition of this license.

13. Experimental animals administered licensed materials or there products shall not be used for human consumption.

14. The licensee may transport licensed material in accordance with the provisions of 10 CFR Part 71, "Packaging and Transportation of Radioactive Material".

15. The licensee is authorized to hold radioactive material with a physical half-life of less than 65 days for decay-in-storage before disposal in ordinary trash provided:

A. Radioactive waste to be disposed of in this manner shall be held for decay a minimum of 10 half-lives.

B. Before disposal as normal waste, radioactive waste shall be surveyed to determine that its radioactivity cannot be distinguished from background. All radiation labels shall be removed or obliterated.

16. Except as specifically provided otherwise in this license, the licensee shall conduct its program in accordance with the statements, representations, and procedures contained in the documents including any enclosures, listed below. The Nuclear Regulatory Commission's regulations shall govern unless the statements, representations and procedures in the licensee's application and correspondence are more restrictive than the regulations.

A. Application dated November 19, 1984
B. Letter dated February 7, 1985
C. Letter dated December 2, 1988
D. Application dated January 17, 1990
E. Letter dated May 4, 1990
F. Letter dated April 17 1992
G. Letter dated July 9, 1992
H. Letter dated August 14, 1992
I. Letter dated September 18, 1992
J. Letter dated September 24, 1992
K. Letter dated November 24, 1992

For the U.S. Nuclear Regulatory Commission

Date DEC 22 1992

By Original Signed By:
John D. Kinneman
Nuclear Materials Safety Branch
Region I
King of Prussia, Pennsylvania 19406

DEC 22 1992

License No. 20-20783-01
Docket No. 030-22069
Control No. 117470

T Cell Sciences, Incorporated
ATTN: Patrick C. Kung, Ph.D.
Executive Vice President
38 Sidney Street
Cambridge, Massachusetts 02139

Dear Dr. Kung:

Please find enclosed an amendment to your NRC Material License.

Please review the enclosed document carefully and be sure that you understand all conditions. If there are any errors or questions, please notify the Region I Material Licensing Section, (215) 337-5093, so that we can provide appropriate corrections and answers.

Please be advised that you must conduct your program involving licensed radioactive materials in accordance with the conditions of your NRC license, representations made in your license application, and NRC regulations. In particular, please note the items in the enclosed, "Requirements for Materials Licensees."

Since serious consequences to employees and the public can result from failure to comply with NRC requirements, the NRC expects licensees to pay meticulous attention to detail and to achie' the high standard of compliance which the NRC expects of its licensees.

You will be periodically inspected by NRC. A fee may be charged for inspections in accordance with 10 CFR Part 170. Failure to conduct your program safely and in accordance with NRC regulations, license conditions, and representations made in your license application and supplemental correspondence with NRC will result in prompt and vigorous enforcement action against you. This could include issuance of a notice of violation, or in case of serious violations, an imposition of a civil penalty or an order suspending, modifying or revoking your license as specified in the General Policy and Procedures for NRC Enforcement Actions, 10 CFR Part 2, Appendix C.

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ML 10

We wish you success in operating a safe and effective licensed program.

Sincerely,

Original Signed By:
John D. Kinneman

John K. Kinneman, Chief
Research Development &
Decommissioning Section
Division of Radiation Safety
and Safeguards

Enclosures:
1. Amendment No. 07
2. Requirements for Materials Licensees

DRSS:RI	DRSS:RI
Oberg/mlb	Kinneman
12/9/92	12/22/92

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T CELL SCIENCES

92 DEC 14 AM 10:57

November 24, 1992

030-22069

Tara Weidner
Mail Control No. 116503
United States Nuclear Regulatory Commission, Region 1
Nuclear Materials Safety Section B
475 Allendale Road
King of Prussia, Pennsylvania 19406

RE: Amendments to License No. 20-20783-01 and 20-20783-02

Dear Ms. Weidner:

As we discussed by telephone last week, Denise Aronson, our current RSO has resigned from T Cell Sciences, Inc. effective November 16. This letter constitutes a request for amendments to Materials License 20-20783-01 and Irradiator License 20-20783-02. The requested changes are that the Radiation Safety Officer named on our licenses be changed from Denise Aronson to Ellen M. Essigmann. I am also requesting that this amendment be evaluated on an expedited approval basis. A check for the amount of $940 is enclosed, the fee for the processing of these amendments.

A summary of my training and experience, as it relates to work with radioisotopes, is attached along with a copy of my curriculum vitae. Please note that I have held the positions of Assistant Radiation Safety Officer and Radiation Safety Officer at a previous place of employment. As Chairman of the Safety Committee at T Cell Sciences, Inc., I worked closely with the previous RSO, Jerry Carson, on matters relating to compliance with NRC requirements. In addition, I supervised Denise Aronson, the current Radiation Safety Officer, for a period of two years.

Please let me know if you require any additional information regarding my training and experience. Thank you for your assistance in this matter.

Sincerely,

Ellen M Essigmann

Ellen M. Essigmann, Ph.D.
Associate Director, Regulatory Affairs

Enclosures (2)

Log A22-2
Remitter
Check No. 22331 $940
Amount
Fee Category 3M
Type of Fee Amdt
Date Check Rec'd 12/1/92
Date Completed 12/1/92
By: BAB

92 DEC -1 P1:32

117470

OFFICIAL RECORD COPY ML 30

RECEIVED-REGION 1

DEC 01 1992

T Cell Sciences, Inc. 38 Sidney Street Cambridge, MA 02139-4135 USA 617-621-1400
Telex 9102401560 Telefax 1-617-621-1420

RELEVANT EXPERIENCE WITH RADIOISOTOPES:
Ellen M. Essigmann, Associate Director, Regulatory Affairs and Chairman, Safety Committee

Massachusetts Institute of Technology: 1976 - 1980

Training -

Received MIT general radiation safety orientation and on job training in use of radioisotopes, autoradiography and radiometric techniques. Course materials covered the following areas:

- principles and practices of radiation protection;
- biological effects of radiation;
- written procedures for routine and emergency operations; and
- NRC license requirements and relevant NRC regulations.

Work experience -

Worked with ^{3}H, ^{14}C from 1977 - 1980.

Possessed quantities of up to 150 mCi.

H.G. Pars Pharmaceutical Laboratories, Inc.: 1980 - 1986

Training -

Received general radiation safety orientation and on job training in use of radioisotopes. Course materials covered the following areas:

- principles and practices of radiation protection;
- biological effects of radiation;
- written procedures for routine and emergency operations; and
- NRC license requirements and relevant NRC regulations.

Work experience -

Worked with ^{14}C, ^{3}H and ^{123}I from 1980 to 1986. Possessed quantities of up to 200 mCi.

Study Director for weekly evaluations of ^{123}I-labeled fibrinogen which included rabbit blood clearance assays, rabbit pyrogen tests and general safety tests conducted in mice and guinea pig.

Wrote a comprehensive set of in-house standard operating procedures for the safe handling of radioisotopes and for work involving animal injections with radioisotopes.

Assistant Radiation Safety Officer, from 1982 to 1983, with responsibility for wipe testing, radiation waste management and manifesting.

Radiation Safety Officer from 1983 to 1986.

T Cell Sciences, Inc.: 1987 - present

Work Experience -

Chairman of Safety Committee from 1987 to present.

Supervised Assistant Radiation Safety Officer and Safety Officer from 1990 to present.

Assisted Radiation Safety Officers in matters of NRC compliance and employee safety, from 1987 to present.

CURRICULUM VITAE

ELLEN M. ESSIGMANN
15 Thatcher Street
Brookline, Massachusetts 02146
617 566-3886

EDUCATION:

PhD	1980	Massachusetts Institute of Technology, Department of Applied Biological Sciences Major field: Biochemistry and Metabolism Minor field: Experimental Animal Pathology
MS	1974	Northeastern University, Department of Biology
BS	1970	Northeastern University, Department of Biology Major field: Biology Minor field: Chemistry

PROFESSIONAL EXPERIENCE:

1987 to Present: Associate Director/Director of Regulatory Affairs and Chairman, Safety Committee; T Cell Sciences, Inc., Cambridge, Massachusetts

Established and directed a regulatory affairs department. Department responsibilities included company regulatory compliance, FDA documentation and submissions, clinical research, and employee health and safety.

1985 to 1986: Vice President of Clinical and Regulatory Affairs, H. G. Pars Pharmaceutical Laboratories, Inc., Cambridge, Massachusetts

Established and directed a new Regulatory and Clinical Affairs Department consisting of seven full time employees. Department's responsibilities included regulatory compliance, FDA documentation and submissions, and clinical research.

Routinely prepared long range development programs (preclinical and clinical research, regulatory affairs) for company drugs, including financial projections.

Identified qualified Principal Investigators and performed pre-investigation visits. Established a team of clinical research scientists for monitoring of planned studies.

Prepared and initiated a large Phase I and II U.S. clinical program for the development of oral and parenteral forms of a mixed agonist/antagonist analgesic.

Project Director for preparation of New Drug Application for Delta-9-THC for use as an antiemetic for nausea and vomiting secondary to treatment with cancer chemotherapeutic agents.
Direct responsibility for preparation of preclinical overview and for individual summaries of animal pharmacology and toxicology studies.

Supervised a Data Management Specialist in developing and providing support services for the department and the company.

1983 (November) to 1985 (January): **Director of Clinical Pharmacology, H. G. Pars Pharmaceutical Laboratories, Inc.**

Supervised clinical research program for in-house drug candidates. Responsibilities included maintenance of INDs for all Pars drugs: preparation and filing of INDs, IND supplements, safety reports and annual reports to the FDA.

Overall responsibility for sponsoring new clinical investigations (protocol and case report form design, selection and evaluation of prospective investigators and investigation sites) and monitoring and reporting of trials. Drafting and revision of Investigator Brochures.

Wrote a comprehensive set of standard operating procedures for the sponsoring and monitoring of clinical investigations, reporting of adverse events and documentation of manufacture and disposition of clinical supplies according to Good Clinical Practice guidelines and regulations.

1983 (November) to 1985 (January): **Acting Director of Preclinical Pharmacology, H. G. Pars Pharmaceutical Laboratories, Inc.**

Supervised the completion and reporting of a $50,000 Phase I Small Business Innovation Research (SBIR) program designed to select a candidate analgesic for further development. Research included performance of primary dependence assays and screens for antinociceptive and CNS activity. Responsible for preparation of a two year Phase II SBIR proposal for the development of the selected analgesic. The proposal was awarded $500,000 over two years by the National Institute for General Medical Sciences. Acted as overall project director for this development program. Directly supervised design and reporting of preclinical research aspects of this program.

Project director for a $50,000 SBIR project designed to select a leading candidate for development as an antihypertensive agent. Supervised six-month evaluation of four compounds for antihypertensive and CNS activity.

Principal Investigator for a $50,000 Phase I SBIR project designed to evaluate the choline-deficient rat model for use as a bioassay for identifying potential chemical carcinogens.

Supervised preclinical research conducted on a cannabinoid antiglaucoma drug candidate, including: use of ocular normotensive and ocular hypertensive rabbits for determining the mechanism of action of the compound; use of ocular

normotensive rabbits in the conduct of bioequivelence assays and ocular irritation assessments for various formulations of the comPound.

1983 to 1985 (January): Director of Toxicology, H. G. Pars Pharmaceutical Laboratories, Inc.

Supervised the Manager of Toxicology in the operation of the Toxicology Department. Interacted with sponsors during preinvestigational stage of studies. Held overall responsibility for the scientific integrity of protocols and reports. Interacted with Quality Assurance Officer to ensure adequate compliance of department with relevant state and federal regulations.

1983 to 1986: **Additional Experience, H. G. Pars Pharmaceutical Laboratories, Inc.**

Drug Enforcement Administration (DEA) Officer. Overall responsibility for assuring that research quantities of Schedule I to V substances were handled in compliance with federal regulations.

Radiation Safety Officer. Responsible for assuring that radioisotopes utilized in research and safety assays were handled and disposed of in compliance with state and federal regulations. Wrote a comprehensive set of in-house standard operating procedures for the safe handling of radioisotopes.

Chairman of Animal Welfare Committee. Responsible for assuring that animals were handled and cared for in compliance with the Animal Welfare Act and relevant NIH USDA, and Massachusetts Department of Public Health regulations. Directed the Supervisor of Animal Husbandry. Obtained and maintained AAALAC accreditation during this period.

1980 to 1983: **Senior Toxicologist, Sisa Toxicological Laboratories, Inc. (A wholly owned subsidiary of H.G.Pars Pharmaceutical Laboratories, Inc.)**

Project Coordinator and Study Director on acute, sub-chronic, and reproductive toxicity studies. Responsibilities included involvement at virtually every stage of the toxicity assessment of chemicals, pharmaceuticals and clinical diagnostic agents. This involved direct interaction with clients and, when necessary, regulatory officials. During the course of toxicity evaluations, responsibilities included supervision of technical personnel, direct implementation of some facets of experimental procedures, assurance of compliance with protocol requirements and GLP/CMP regulations, evaluation of interim results, and liaison with both client and in-house departments (i.e. Quality Assurance, Clinical Pathology, Histopathology and Analytical Chemistry). After study completion, duties included compilation and statistical analysis of data, interpretation of results and preparation of final reports.

Other major responsibilities included: staff training; preparation of project cost analyses; preparation of Drug Master Files for FDA submission; preparation of preclinical toxicology sections of IND applications; and preparation of in-house standard operating procedures for Animal Welfare, handling of hazardous substances and performance of sub-acute and sub-chronic safety studies.

1982: Institute of Applied Pharmaceutical Sciences

Attended a three-day course offered by the Center for Professional Advancement, entitled "Preparing Investigative New Drug and New Drug Applications and The Mechanics of FDA Regulations".

1980: Internship in Industrial Toxicology, Toxicol Laboratories, Ltd.

Two month internship in quality assurance and performance of acute, sub-acute and sub-chronic toxicity studies at site of sister company in Ledbury, England.

1974 to 1976: Research Assistant, Howe Laboratory of Ophthalmology, Harvard Medical School, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts

Participated in the conduct of ocular-perfusion studies designed to investigate the causative factors of several types of human glaucoma, particularly open-angle glaucoma and glaucoma associated with vitreous hemorrhage. Characterized the ultrastructure (transmission and scanning electron microscopy) of pathological specimens from the human anterior segment.

1972 to 1974: Biology Instructor, Bridgewater State College, Bridgewater, Massachusetts

ACADEMIC EXPERIENCE:

1976 to 1980: Doctoral Candidate in Experimental Animal Pathology, Massachusetts Institute of Technology

Thesis Title: Mouse Hepatic Neoplasia.

This research consisted of an investigation of the morphology, biochemistry and biological behavior of spontaneous and induced mouse hepatic nodules for the purpose of (1) determining the malignant potential of the nodules, (2) determining new diagnostic criteria for nodule classification, and (3) evaluating the mouse as a carcinogen bioassay system.

The following research techniques were utilized in the conduct of the thesis research: light and transmission electron microscopy, development and use of a double-perfusion apparatus for the in vivo perfusion/fixation of the liver, autoradiography, enzyme histochemistry, isoenzyme analysis (cellulose acetate and polyacrylamide gel electrophoresis, and spectrofluorometric, radiometric and histochemical methodologies), tumor transplantation studies, tumor angiogenesis factor analysis and computer analysis of data using BMDP biomedical statistical programs.

Additional Research Experience:

Assisted in the design and supervision of a 1200 animal chronic feeding study designed to determine the carcinogenic potential of an organochlorine pesticide. Assured performance of study in accordance with proposed EPA guidelines for Good Laboratory Practice.

Assisted in the design and supervision of a pilot study designed for the purpose of developing an animal model for arsenic-induced lung tumors. Utilized neutron activation analysis for detection of low levels of arsenic in the tissues of treated rats.

Assisted in the design and conduct of a histopathology study for assessing the acute effects of inhaled ozone on guinea pig bronchial epithelium and the rate of pinocytosis in intestinal epithelium overlying lymphoid tissue in the large intestine.

Additional Experience:

Instructor for an EPA sponsored course in toxicology held at MIT (July, 1979).

Authored a manual for MIT use, entitled "Manual for the Safe Handling of Carcinogens in the Research Laboratory."

1970 to 1974: Northeastern University, Graduate Student in Biology

Thesis Research: A light and electron microscope study of the morphology and light adaptation mechanisms of the eye of a marine mollusc.

PROFESSIONAL SOCIETIES, ACADEMIC HONORS

Phi Sigma Society (Biology honor society)
1970 - 1971 President
1969-1970 Vice-President
Sigma Xi
Electron Microscopy Society
The Academy of Northeastern University
Drug Information Association
Regulatory Affairs Professionals Society

PUBLICATIONS AND PRESENTATIONS

Howes, J. F., Villarreal, J. E., Harris, L.S., Essigmann, E.M. and Cowan, A. Xorphanol. In: Drug and Alcohol Dependence, 14, Elsevier Scientific Publishers, Ireland, 1985, 373-380, Elsevier Scientific Publishers Ireland Ltd.

Pars, H. G., Razdan, R. K., Harris, L. S., Dewey, W. L., Essigmann, E. M., Meltzer P. C. and Cowan, A. Analgesic and Narcotic Antagonist Activity of Synthetic Cannabinoids. Presented at American Society of Pharmacology and Experimental Therapeutics Boston (August, 1985).

Cowan, A., Pars, H. G., Razdan, R. K., Harris, L. S., Dewey, W. L. and Essigmann, E.M. Antinociceptive activity of Menabitan. In: Marihuana '84. Proceedings of the Oxford Symposium on Cannabis. Edited by D.J. Harvey, W. Paton and G.G. Nahas, IRL Press Ltd, Oxford England pp 693-699. 1985.

Fox, J. C., Ackerman, J. I., Maxwell, K. and Essigmann, E.M. Campylobacter jejuni associated diarrhea in juvenile beagle dogs. Presented at the 24th Annual Session of the American Association for Laboratory Animal Science in San Antonio, Texas. (November 1983).

Essigmann, E. M., McConnell, R. G. and Newberne, P. M. Transplantation studies on induced and spontaneous nodules from B6C3F1 mouse liver. Toxicologic Pathology 12: 211-220, 1984.

Essigmann, E. M. The evaluation of a synthetic polymer "Wipe On" burn covering in the miniature pig. In: Burn Wound Coverings, Vol. II, CRC Press, Boca Raton, Fla., 1984.

Essigmann, E.M. and Newberne, P.M. Transplantation studies with mouse hepatic nodules. Presented at the Annual Meeting of the Society of Toxicology Boston (February 1982).

Essigmann, E.M. and Newberne, P.M. Enzymatic alterations in mouse hepatic nodules induced by a chlorinated hydrocarbon pesticide. Cancer Research 41: 2823-2831 1981.

Essigmann, E. M., McConnell, R.G. and Newberne, P.M. A comparison of aryl hydrocarbon hydroxylase activity in spontaneous and chemically induced mouse hepatic nodules. Presented at the Annual Meeting of the Society of Toxicology, New Orleans (March, 1979).

Campbell, D. C. and Essigmann, E. M., Hemolytic Ghost cell glaucoma, further studies. Archives of Ophthalmology 97: 241-246, 1979.

Essigmann, E.M. and Campbell, D. C., Ghost cell glaucoma, further studies. Presented at the Annual Meeting of the Association for Research in Vision and Ophthalmology, Sarasota, Fla. (April, 1974).

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: 19950630
FEE COMMENTS: ----------
DECOM FIN ASSUR REQD: N

LICENSE FEE TRANSMITTAL

A. REGION

1. APPLICATION ATTACHED
APPLICANT/LICENSEE: T CELL SCIENCES, INC.
RECEIVED DATE: 921201
DOCKET NO: 3022069
CONTROL NO.: 117470
LICENSE NO.: 20-20783-01
ACTION TYPE: AMENDMENT

2. FEE ATTACHED
AMOUNT: $ 940.00
CHECK NO.: 8444/008991

3. COMMENTS
Reference 117471
03+07 approved
for 12/3/92

SIGNED R. J. Brown
DATE 12/4/92

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

1. FEE CATEGORY AND AMOUNT: 3M 870

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

3. OTHER ---

SIGNED L Barrett
DATE 12/16/92