



khogan@argonex.com

June 17, 1997

U.S. Nuclear Regulatory Commission, Region II
101 Marietta Street, N.W., Suite 2900
Atlanta, GA 30323-0199
Attention: Nuclear Material Licensing

To Whom It May Concern:

Enclosed please find an Application For Material License (NRC Form 313) and a check in the amount of \$1,500.00 to cover the cost of said application under Fee Category 3.M. of 10 CFR 170.31. This is a new license application for Argonex Holdings, Inc. of Charlottesville, VA, a biotechnology company focused on the discovery and development of drugs to modulate the immune system to a variety of diseases.

If you have any questions regarding this application, please do not hesitate to contact me.

Sincerely,

A handwritten signature in black ink that reads "Kevin T. Hogan". The signature is written in a cursive style with a large initial "K".

Kevin T. Hogan, Ph.D.
RSO & Senior Immunologist

257535

NRC FORM 313

APPLICATION FOR MATERIAL LICENSE

- 1. APPLICATION FOR: *New license application*
- 2. NAME AND MAILING ADDRESS: *Argonex Holdings, Inc.
706 Forrest Street, Suite 1
Charlottesville, Virginia 22903*
- 3. ADDRESS WHERE LICENSED MATERIAL WILL BE USED: *SAME AS IN ITEM 2.*
- 4. NAME OF PERSON TO BE CONTACTED ABOUT THIS APPLICATION: *Kevin Hogan, Ph.D.*
TELEPHONE NUMBER: *804-984-2040*
FAX NUMBER: *804-984-1737*

5. RADIOACTIVE MATERIAL:

A. ELEMENT AND MASS NUMBERS LIMIT	B. CHEMICAL AND/OR PHYSICAL FORM	C. MAXIMUM POSSESSION LIMIT
<i>Chromium 51</i>	<i>Sodium Chromate</i>	<i>150 mCi</i>
<i>Hydrogen 3</i>	<i>Thymidine</i>	<i>150 mCi</i>
<i>Iodine 125</i>	<i>Sodium Iodide</i>	<i>100 mCi</i>
<i>Phosphorous 32</i>	<i>P-32 dATP</i>	<i>50 mCi</i>
<i>Sulfur 35</i>	<i>Alpha S-35 dATP, L-methionine</i>	<i>50 mCi</i>

NOTE: The chemical forms listed are those presently required. However, Argonex would like authorization to possess these radionuclides in any chemical and/or physical form required to meet future research needs.

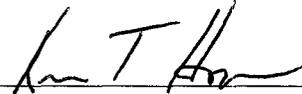
- 6. PURPOSES FOR WHICH RADIOACTIVE MATERIAL WILL BE USED: *Research and development as defined by 10 CFR 30.4*
- 7. INDIVIDUALS RESPONSIBLE FOR RADIATION SAFETY: *Kevin Hogan Ph.D., Radiation Safety Officer
Mark M. Ross, Director, Argonex
Dean Schlemmer, Consulting Radiation Safety Officer
(See attached resumes)*
- 8. FACILITIES AND EQUIPMENT: *See attachment*
- 9. TRAINING FOR INDIVIDUALS WORKING IN OR FREQUENTING RESTRICTED AREAS:
As a minimum, individuals will attend either the University of Virginia Radiation Safety Training Course or another course which is equivalent in scope and content. Individuals will also be required to read the Argonex Radiation Safety Guide and to attend a radiation safety orientation given by the Argonex Radiation Safety Officer and Facility Director. Supervised, on-the-job training will be required until a proficiency for working safely with radioactive material has been demonstrated. Annual radiation safety retraining will also be required of all employees working with radioactive material.
- 10. RADIATION SAFETY PROGRAM: *See attachment*

11. WASTE MANAGEMENT: *See attachment*

12. LICENSE FEES: FEE CATEGORY 3.M. AMOUNT ENCLOSED \$1,500.00

13. CERTIFICATION: The Applicant understands that all statements and presentations 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, 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



NAME:

KEVIN HOGAN, Ph.D.

TITLE:

RADIATION SAFETY OFFICER, ARGONEX HOLDINGS, INC.

DATE:

6/12/97

Attachments:

7. INDIVIDUALS RESPONSIBLE FOR RADIATION SAFETY:

Resumes of Kevin Hogan, Mark Ross, Dean Schlemmer

8. FACILITIES AND EQUIPMENT:

Copies of maps and building sketches.

10. RADIATION SAFETY PROGRAM

Description

11. WASTE MANAGEMENT

Description

Enclosures:

Argonex Radiation Safety Guide

CURRICULUM VITAE

Kevin T. Hogan, Ph.D.
Radiation Safety Officer & Senior Immunologist
Argonex, Inc.

Home Address:

Social Security Number:

Date and Place of Birth:

Marital Status:



Education:

1979	B.A., Biology, University of Missouri-St. Louis
1980 - 1982	Immunology, Wake Forest University, Laboratory of Donald L. Evans, Ph.D.
1982 - 1984	Ph.D., Immunology, University of Georgia, Laboratory of Donald L. Evans, Ph.D.

Postgraduate Training:

8/84 - 2/89	Postdoctoral, University of Virginia, Laboratory of Victor H. Engelhard, Ph.D.
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Professional Appointments:

3/89 - 6/94	Assistant Professor, Department of Microbiology, Medical College of Wisconsin
7/94 - 7/96	Associate Professor, Department of Microbiology, Medical College of Wisconsin
3/89 - 7/96	Full member, Medical College of Wisconsin Cancer Center
8/96 - 12/96	Senior Staff Scientist, Cytel Corporation, Charlottesville, VA
1/97 - Present	Senior Immunologist, Argonex Pharmaceuticals, Charlottesville, VA

Awards and Fellowships:

8/82 - 8/84	Research Assistantship, University of Georgia
9/85 - 8/88	N.I.H. Postdoctoral Fellowship, University of Virginia

Memberships in Professional Societies:

Amer. Assoc. of Immunologists (1989)
Amer. Assoc. for the Advancement of Science (1990)
Amer. Soc. Histocompatibility & Immunogenetics (1991)

Professional Activities:

Ad hoc review, Veterans Administration Immunology Section, National Science Foundation, and the Medical Research Council

Ad hoc review, Journal of Immunology
Autumn Immunology Conference (1991) "Cellular
"Regulation of the Immune Response" Workshop
Chairperson

Research Grants:

Cancer Center of the Medical College of Wisconsin, "Molecular Analysis of Epitopes on HLA-A2.1", \$7,850, 7/1/89 - 6/30/90, Principal Investigator.

Medical College of Wisconsin Biomedical Research Support Grant, "Cytotoxic T Lymphocyte Response to Reovirus", \$7,000, 6/1/89 - 5/31/90, Principal Investigator.

Cancer Center of the Medical College of Wisconsin, "Cellular and Molecular Analysis of T Cell Repertoire Development", \$10,000, 1/1/94 - 12/31/94, Principal Investigator.

NIH FIRST AI29574, "Molecular Analysis of B and T Cell Epitopes on HLA-A2" \$339,456, . 4/1/90 - 3/31/96; 50% effort; Principal Investigator.

Falk Foundation Award from the Cancer Center of the Medical College of Wisconsin, "Cellular and Molecular Analysis of T Cell Repertoire Development", \$20,000, 1/1/95 - 12/31/96, Principal Investigator.

Invited Presentations:

Transgenic Mice and Mutants in MHC Research Conference, The Jackson Laboratory, Bar Harbor Maine. June 24-28, 1989. Presentation entitled: The role of amino acid position and side chain structure in serological and CTL-defined epitopes on the HLA-A2.1 molecule.

Molecular Bases of Allorecognition Conference, Milwaukee, WI. September 12-14, 1989. Presentation entitled: Allogeneic and influenza-specific CTL differ in their fine-specificity patterns of recognition of HLA-A2 mutant molecules.

Department of Pathology, Medical College of Wisconsin. February 14, 1991. Presentation entitled: A molecular biological approach to understanding the structure-function relationships of class I major histocompatibility molecules.

Department of Microbiology and Immunology, University of Missouri School of Medicine, Columbia, MO. March 18, 1992. Presentation entitled: Definition of residues contributing to serologic and CTL-defined epitopes on HLA-A2.

Immunology Seminar Series, University of Wisconsin, Madison, WI. April 17, 1995. Presentation entitled: Regulation of cellular adhesion through class I MHC molecules.

Medical College Committees:

Cancer Center Research Grant Review Committee (1990 - 1996)

Cell Culture Shared Facility Committee (1991 - 1996)

Library Committee (1991 - 1994)

Subcommittee on Library Journal Selection Process, Chair (1993- 1994)

Graduate Student Advisory Committees:

Major advisor: Ming Cao, Ph.D. (1990 - 1993)

Amy Tvinnereim (1993 - Present)

Committee member: Jeanette Bjerke, M.S. (1989 - 1992)
Mary J. Geiger, Ph.D. (1989 - 1990)
Lisa Hoffman, Ph.D. (1991 - 1994)
Jeri-Ann Lyons (1992 - 1996)
Jeanette Rutz, Ph.D. (1991 - 1994)
Ming Teng, M.D., Ph.D. (1990 - 1993)

Medical College Teaching:

Micro 201 Medical Microbiology

Fall 1989-1995

Four to five lectures were given annually covering the major histocompatibility complex, cellular immunity, and the regulation of the immune response. Was also responsible for one laboratory section, and one to two conference group sections when offered.

Micro 203 Introduction to Immunology

Fall 1990-1993

Course director. This course covered the immunology portion of Medical Microbiology and was intended for graduate students outside the Department of Microbiology.

Micro 232 Topics in Cellular and Molecular Immunology

Winter 1992, 1994,
1996

Participation included lectures and presentation of current papers in the literature.

Micro 234 Cellular and Molecular Immunology

Winter 1991, 1993,
1995

Course director beginning in 1995. Eight to ten lectures covering the major histocompatibility complex genes and proteins, antigen processing, cellular interactions and regulation, T-B cell collaboration, and tumor immunity.

Micro 242 Techniques in Molecular and Cell Biology

Winter 1991-1996

Annual lecture on site-directed mutagenesis.

Micro 270 Advanced Virology

Winter 1990

Lectured on the immune response to viral infections.

Micro 300 Seminar

Various

Worked with students on seminars to be presented to the department.

Biochem 216 Lipids, Carbohydrates, and Membranes

Winter 1991

Lectured on the membrane perturbations by porins and complement.

Path 200 Pathology

Fall and Winter, 1991

Lectured on the humoral and cellular mechanisms of autoimmunity.

Immunology Journal Club

Fall 1991-Summer
1996

Organized weekly meetings for presentation of the current immunological literature by graduate students, post-docs, and faculty.

Immunology Research in Progress Meetings

Fall 1992-1993

Organize meetings for the presentation of research results by graduate students, post-docs, and faculty.

BIBLIOGRAPHY

ARTICLES:

1. Evans, D.L., Hooper, C.J., Wiggins, T.B., Shehee, W.R., Hale, A.H., Hogan, K.T., and Johnson, K.D. (1982) Identification and partial purification of a receptor for tumor associated fetal antigens. *Oncodev. Biol. Med.* 3:365-378.
2. Evans, D.L., Carlson, R.L., Graves, S.S., and Hogan, K.T. (1984) Nonspecific cytotoxic cells in fish (*Ictalurus punctatus*). IV. Target cell binding and recycling capacity. *Dev. Comp. Immunol.* 8:823-833.
3. Evans, D.L., Hogan, K.T., Graves, S.S., Carlson, R.L., Floyd, E., and Dawe, D.L. (1984) Nonspecific cytotoxic cells in fish (*Ictalurus punctatus*). III. Biophysical and biochemical properties affecting cytolysis. *Dev. Comp. Immunol.* 8:599-610.
4. Hogan, K.T., and Evans, D.L. (1984) A software package for the calculation and statistical analysis of ^{51}Cr -release assays. *J. Immunol. Methods* 72:355-360.
5. Hogan, K.T., Hollingsworth, M.A., Seymour, R.E., Quinn, M.K., and Evans, D.L. (1984) Suppression of polyclonal, tumor cell and alloantigen-induced proliferation: Identification of cyclooxygenase pathway dependent and independent mechanisms. *Immunopharmacology.* 7:49-57.
6. Hogan, K.T., Harris, D.T., Plunkett, S.R., Raben, M., Hale, A.H., and Evans, D.L. (1985) Effects of tumor status on the regulation of natural killer cell activity by tumor-associated fetal antigens. *J. Biol. Response Mod.* 4:353-357.
7. Bernhard, E.J., Le, A.-X., Yannelli, J.R., Holterman, M.J., Hogan, K.T., Parham, P., and Engelhard, V.H. (1987) The ability of cytotoxic T cells to recognize HLA-A2.1 or HLA-B7 antigens expressed on murine cells correlates with their epitope specificity. *J. Immunol.* 139:3614-3621.
8. Hogan, K.T., Clayberger, C., Bernhard, E.J., Walk, S.F., Ridge, J.P., Parham, P., Krensky, A.M. and Engelhard, V.H. (1988) Identification by site-directed mutagenesis of amino acid residues contributing to serologic and CTL-defined epitope differences between HLA-A2.1 and HLA-A2.3. *J. Immunol.* 141:2519-2525.
9. Hogan, K.T., Clayberger, C., Le, A.T., Ridge, J.P., Walk, S.F., Parham, P., Krensky, A.M., and Engelhard, V.H. (1988) CTL-defined epitope differences between HLA-A2.1 and HLA-A2.2 map to two distinct regions of the molecule. *J. Immunol.* 141:4005-4011.
10. Hogan, K.T., Shimojo, N., Walk, S.F., Engelhard, V.H., Maloy, W.E., Coligan, J.E., and Biddison, W.E (1988) Mutations in the $\alpha 2$ helix of HLA-A2 affect presentation but do not inhibit binding of influenza virus matrix peptide. *J. Exp. Med.* 168:725-736.
11. Hogan, K.T., Clayberger, C., Bernhard, E.J., Walk, S.F., Ridge, J.P., Parham, P., Krensky, A.M. and Engelhard, V.H. (1989) A panel of unique HLA-A2 mutant molecules define epitopes recognized by HLA-A2 specific antibodies and CTL. *J. Immunol.* 142:2097-2104.
12. Hogan, K.T., Ridge, J.P., Walk, S.F., Parham, P., and Engelhard, V.H. (1989) Mapping of serologic and CTL-defined epitopes on HLA-A2 by site-directed mutagenesis. In: *Immunobiology of HLA, Vol. II. Immunogenetics and Histocompatibility*, Bo Dupont, ed., Springer-Verlag, New York, 101-103.
13. Hogan, K.T., Clayberger, C., Shimojo, N., Biddison, W.E., Krensky, A.M., and Engelhard, V.H. (1990) The role of amino acid position and side chain structure in serological and CTL-defined epitopes on the HLA-A2.1 molecule. In: *Transgenic Mice and Mutants in MHC Research*, Springer-Verlag, New York, 77-88.
14. Hogan, K.T., and Cashdollar, L.W. (1991) Clonal analysis of the cytotoxic T lymphocyte response to reovirus. *Viral Immunol.* 4:167-175.

15. Hogan, K.T., and Brown, S.L. (1992) Localization and characterization of serologic epitopes on HLA-A2. *Hum. Immunol.* 33:185-192.
16. DeVito, L.D., Mason, B.P., Gan-Jankowska, E., Hogan, K.T., Lutz, C.T., Sollinger, H.W., Burlingham, W.J. (1993) Epitope fine specificity of human anti-HLA-A2 antibodies. *Transplant. Proc.* 25:189-190.
17. DeVito, L.D., Mason, B.P., Gan-Jankowska, E., Hogan, K.T., Guo, J.W., Lutz, C.T., Sollinger, H.W., Burlingham, W.J. (1993) Epitope fine specificity of human anti-HLA-A2 antibodies: identification of four epitopes including a haptenlike epitope on HLA-A2 at lysine 127. *Hum. Immunol.* 37:165-177.
18. Teng, J.M.C., and Hogan, K.T. (1994) Residues outside of the HLA-A2 peptide-binding groove can abrogate or enhance recognition of influenza virus matrix peptide pulsed cells by cytotoxic T lymphocytes. *Mol. Immunol.* 31:445-457.
19. Teng, J.M.C., and Hogan, K.T. (1994) Both major and minor peptide-binding pockets in HLA-A2 influence the presentation of influenza virus matrix peptide to cytotoxic T lymphocytes. *Mol. Immunol.* 31:459-470.
20. Flomenberg, P., Gutierrez, E., and Hogan, K.T. (1994) Identification of class I MHC regions which bind to the adenovirus E3-19k protein. *Mol. Immunol.* 31:1277-1284.
21. Hoffman, L.M., Hogan, K.T., and Cashdollar, L.W. (1996) The reovirus nonstructural protein σ 1NS is recognized by murine cytotoxic T lymphocytes. *J. Virol.* In press.
22. Naumov, Y., Hogan, K.T. and Gorski, J. (1996) Sequence analysis of T cell receptor β -chains directed against HLA-A2 plus matrix peptide M1(58-66) reveals conservation of protein but not DNA sequence. *Eur. J. Immunol.* Submitted.
23. Hosenpud, J.D., Mauck, K.A., and Hogan, K.T. (1996) Cardiac allograft vasculopathy: IgM antibody responses to donor-specific vascular endothelium. *Transplantation.* In press.
24. Hogan, K.T. and Ferrone, S. (1996) Fine specificity of murine anti-HLA-A2 antibodies. In preparation.
25. Burlingham, W.J., DeVito-Haynes, L., Jankowska-Gan, E., Hogan, K.T., Claas, F.H.J., Mulder, A., Fechner, J.H., Wang, X.H., and Ferrone, S. (1996) Fine specificity, idiotypic profile and structural characteristics of three human anti-HLA-A2 monoclonal antibodies. Comparison with mouse anti-HLA-A2 monoclonal antibodies. Submitted.

ABSTRACTS:

1. Hogan, K.T., and Evans, D.L. (1982) Tumor associated fetal antigen induced suppression of rat natural killer cell activity. Southeastern Immunology Conference, Stone Mountain, GA.
2. Hogan, K.T., Harris, D.T., and Evans, D.L. (1982) Evidence for tumor-associated fetal antigen binding to human natural killer cells. *Fed. Proc.* 41:818.
3. Hollingsworth, M.A., Hogan, K.T., and Evans, D.L. (1982) Suppressor cells in tumor progressor and regressor rats. *Fed. Proc.* 41:413.
4. Plunkett, S.R., Harris, D.T., Hogan, K.T., Raben, M., and Evans, D.L. (1982) Regulation of natural killer cells by tumor-associated fetal antigens. *Fed. Proc.* 41:309.
5. Hogan, K.T., and Evans, D.L. (1983) Inhibition of rat natural killer cells by tumor-associated fetal antigens. *Fed. Proc.* 42:694.
6. Evans, D.L., Graves, S.S., Carlson, R.L., Hogan, K.T., and Dawe, D.L. (1984) Mechanisms of regulation of nonspecific cytotoxic cellular immunity in fish. *Animal Disease Workers in the Southern States*, Fayetteville, AR.

7. Hogan, K.T., and Evans, D.L. (1984) Possible role of tumor-associated fetal antigens in mediating suppression of tumor-bearing rats. *Animal Disease Workers in the Southern States*, Fayetteville, AR.
8. Hogan, K.T., and Evans, D.L. (1984) Suppression of NK cell activity in tumor bearing rats: Possible regulation by tumor associated fetal antigens. *Fed. Proc.* 43:1754.
9. Hogan, K.T., Holterman, M.J., Walk, S.F., and Engelhard, V.H. (1986) Determination of HLA-A2 structure-function relationships by site-directed mutagenesis. *Southeastern Immunology Conference*, Chapel Hill, NC.
10. Hogan, K.T., Holterman, M.J., Walk, S.F., Le, A.T., and Engelhard, V.H. (1987) Determination of HLA-A2 structure-function relationships by site-directed mutagenesis. *Fed. Proc.* 46:1496.
11. Hogan, K.T., Ridge, J.P., Walk, S.F., Parham, P., and Engelhard, V.H. (1987) Mapping of serologic and CTL defined epitopes on HLA-A2 by site-directed mutagenesis. *Tenth International Histocompatibility Conference*, New York, NY.
12. Hogan, K.T., St. John, A.L., Evans, D.L., and Damian, R.T. (1987) Natural killer cell activity in baboons infected with Schistosoma mansoni. *American Society of Parasitologists*, Oklahoma, NE.
13. Coligan, J.E., Hogan, K.T., Shimojo, N., Maloy, W.L., Engelhard, V.H., and Biddison, W.E. (1988) Mutations in the alpha 2 helix of HLA-A2 affect presentation but do not inhibit binding of influenza virus matrix peptide. *6th HLA/H2 Cloning Workshop*, Airlie, VA.
14. Hogan, K.T., Parham, P., and Engelhard, V.H. (1988) Site-directed mutagenesis of HLA-A2 identifies amino acid residues that are critical in the formation of serologic and CTL-defined epitopes. *FASEB Journal* 2:A1446.
15. Hogan, K.T., Clayberger, C., Parham, P., Krensky, A.M., and Engelhard, V.H. (1989) Definition of residues contributing to serologic and CTL-defined epitope differences among HLA-A2.1, -A2.2Y, and -A2.3. *UCLA Immunogenicity Symposium*, *J. Cell. Biochem.* 13A:228.
16. Shimojo, N., Mattson, D.H., Hogan, K.T., Engelhard, V.H., Maloy, W.L., Coligan, J.E., and Biddison, W.E. (1989) HLA-A2 structural requirements for presentation of influenza matrix peptide to HLA-A2.1-restricted peptide-specific CTL. *FASEB Journal* 3:A796.
17. Hogan, K.T., Clayberger, C., Shimojo, N., Maloy, W.L., Coligan, J.E., Biddison, W.E., Krensky, A.M., and Engelhard, V.H. (1989). Allogeneic and influenza-specific CTL differ in their fine-specificity patterns of recognition of HLA-A2 mutant molecules. *Molecular Bases of Allorecognition Conference*, Milwaukee, WI.
18. Cao, M., Brown, S.L., and Hogan, K.T. (1991) Definition of the HLA-A2 structural requirements for the presentation of influenza virus matrix peptide to CTL. *Autumn Immunology Conference*, Chicago, IL.
19. DeVito, L.D., Hogan, K.T., Sollinger, H.W., and Burlingham, W.J. (1991) Epitope specificity seen in purified anti-HLA-A2,9,28 CREG antisera. *Autumn Immunology Conference*, Chicago, IL.
20. Hogan, K.T., Cao, M., and Brown, S.L. (1992) Definition of residues in HLA-A2.1 that contribute to the epitopes recognized by MHC-restricted, influenza matrix peptide-specific cytotoxic T lymphocytes (CTL) and allogeneic CTL. *FASEB Journal* 6:A1126.
21. Hoffman, L.M., Cashdollar, L.W., and Hogan, K.T. (1992) Characterization of the reovirus cytotoxic T lymphocyte response. *American Society Virology*, Ithaca, NY.

22. Cao, M., Brown, S.L., and Hogan, K.T. (1993) Amino acid substitutions on the HLA-A2 molecule can abrogate or enhance recognition of influenza virus M1 peptide pulsed cells by cytotoxic T lymphocytes. Keystone Symposia on "Emerging principles for vaccine development: antigen processing and presentation. J. Cellular Bioch. 17C:54.
23. Tvinnereim, A.R., and Hogan, K.T. (1994) Induction of homotypic adhesion and apoptosis through class I MHC molecules. Autumn Immunology Conference, Chicago, IL.
24. Tvinnereim, A.R., Dineen, B.A., and Hogan, K.T. (1995) Induction of homotypic adhesion through class I MHC molecules. FASEB Journal, 9:A819.
25. Tvinnereim, A.R., and Hogan, K.T. (1995) Characterization of homotypic adhesion induced through class I MHC molecules. Autumn Immunology Conference, Chicago, IL.
26. Hogan, K.T., Gorski, J., and Naumov, Y. (1994) Sequence analysis of T cell receptor β -chains directed against HLA-A2 plus matrix peptide M1(58-66) reveals conservation of protein but not DNA sequence. FASEB Journal, 9:A817.
27. Tvinnereim, A.R., Naumov, Y., Gorski, J., and Hogan, K.T. (1996) T cell receptor BV-chain usage in the CTL response to HLA-B8 plus influenza nucleoprotein NP(380-388), FASEB Journal, 10:A1177.
28. Tvinnereim, A.R., Gorski, J., and Hogan, K.T. (1996) T cell receptor BV-chain usage in cytotoxic T lymphocytes which recognize HLA-A2 as an alloantigen. Autumn Immunology Conference, Chicago, IL.
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Training Received in Basic Radioisotope Theory and Handling:

Location	Course Title	Dates	Estimated Hours	Supervised Laboratory Experience
<i>Safe Handling of Radioactive Materials</i>				
WU	Self Study Manual	1979	1	80
BGSM	Self Study Manual	1980	1	80
UGA	Self Study Manual	1982	1	
UVA	Self Study Manual/Radiation Safety Course	1985, 1997	2	40
MCW	Self Study Manual	1989	1	
<i>Characteristics of Ionizing Radiation</i>				
UM	Chemistry, Biology, Physics, Genetics	1975-1979	8	
WU, BGSM, UGA, UVA, MCW	Self Study Manual/ Radiation Safety Course	1975-1997	5	
<i>Units of Radiation Dose and Quantities</i>				
UM	Chemistry, Biology, Physics, Genetics	1975-1979	8	
WU, BGSM, UGA, UVA, MCW	Self Study Manual/ Radiation Safety Course	1975-1997	5	
<i>Radiation Detection Instrumentation</i>				
UM	Chemistry, Biology, Physics, Genetics	1975-1979	8	
WU, BGSM, UGA, UVA, MCW	Self Study Manual/ Radiation Safety Course	1975-1997	5	

Previous Usage of Radioisotopes:

Radionuclide	Activity	Locations	Dates	Type of use
I125	5-10 mCi	WU, BGSM, UGA, UVA, MCW	1979-1996	Protein labeling
H3	5-10 mCi	BGSM, UGA, UVA, MCW	1980-1996	Cell proliferation
Cr51	10 mCi	BGSM, UGA, UVA, MCW	1980-1997	Cr-release assays
P32	5-10 mCi	UVA, MCW	1984-1996	DNA labeling
S35	5 mCi	UVA, MCW	1984-1996	DNA and protein labeling

Previous Experience in Directing a Laboratory Utilizing Radioisotopes:

Authorized user at MCW. This classification allowed the investigator to order radioisotopes for the laboratory and to train laboratory personnel in the safe handling of radioactive material. Responsible for all facets of radioisotope usage in the laboratory.

Abbreviation	Institution	Abbreviation	Institution
UM	University of Missouri (St. Louis and Columbia)	WU	Washington University
BGSM	Bowman Gray School of Medicine	UGA	University of Georgia
UVA	University of Virginia	MCW	Medical College of Wisconsin

DEAN M. SCHLEMMER

P.O. Box 5683
Charlottesville, VA 22905

University of Virginia
Office of Environmental Health & Safety
Charlottesville, VA 22903
(804) 982-4978

EDUCATION: B.S. Physics, University of Massachusetts, 1985

Standard coursework with concentration on radiation theory, instrumentation and detection, and astronomical applications. Also completed requirements for B.S. in Astronomy.

M.A. Astronomy, University of Virginia, 1989

Coursework in theoretical and observational astronomy with concentration in Astrometry. Thesis published as: "Membership in the Galactic Open Cluster NGC1039", *Astronomical Journal*, 105 (1), January 1993

EXPERIENCE: Radiation Safety Specialist, University of Virginia, Charlottesville, VA
(March 1992 - present)

Primary responsibilities include: radiation safety training of all prospective users of radioactive material, leak testing of all sealed sources of radioactive material, periodic surveys of approximately 139 active research laboratories, including Nuclear Medicine and several other patient treatment areas, commissioning and decommissioning of all radioactive material use areas, radioactive emergency response, review of monthly and quarterly personnel dosimetry reports.

Involvement and assistance in virtually all aspects of radiation safety at the University of Virginia, including: survey instrument calibration, shipment and receipt of radioactive material, radioactive waste pickups, processing, and disposal, review and implementation of state and federal regulations, assist with annual NRC inspections, preparation of the UVA Radiation Safety Guide and various policy and procedure writing for the radiation safety program. Assisted in fuel shipment from research reactor; participated in several emergency drills.

**Research Associate, National Radio Astronomy Observatory, Charlottesville, VA
(March 1990 - February 1992)**

Programming and database management for an astronomical image processing package for reduction of radio telescope data.

**Engineer, Boeing Advanced Systems, Seattle, WA
(January 1987 - December 1989)**

Research and development of infrared signature measurement and control of ground vehicles, airframes, and materials.

TRAINING: Radiation Health Physics Course, Department of Engineering, University of Virginia
(Spring semester 1993)
Transportation and Packaging of Radioactive Materials Course, Alfred Grella, C.H.P.
(September, 1993)

MEMBERSHIP: Virginia Chapter of the Health Physics Society

Mark M. Ross

Laboratory Director, Argonex, Inc.
706 Forrest St., Suite 1
Charlottesville, VA 22903
(804) 984-2040; -1737 (fax); email: mross@argonex.com

EDUCATION:

University of Virginia	B.A., Chemistry	1973-1977
Pennsylvania State University	Ph.D., Chemistry	1977-1981
National Research Council Associate, NRL	Postdoctoral	1981-1983
Biological Mass Spectrometry Laboratory, UVa	Sabbatical	1993-1994

EXPERIENCE:

Laboratory Director, Argonex, Inc. 1997-present
Responsible for all day-to-day administrative, budgetary, supervisory and scientific aspects of the laboratory, focused on discovery of peptide antigens.

Associate Director, Cytel Corporation 1995-1996
Developed and managed a new laboratory for Cytel (San Diego) in Charlottesville, VA ("Cytel East"): supervision of four employees, \$1M in capital equipment and oversight and performance of immunology/analytical chemistry research on the discovery of peptide antigens.

Head, Analytical Chemistry Section, Naval Research Laboratory 1990-1995
Responsibilities centered on supervision of staff research scientists, postdoctoral associates and technicians, financial control of the \$800K Section annual budget and scientific programmatic management. Section programs focused on basic and applied research in analytical chemistry, using mass spectrometry, with relevance to Navy and DoD problems.

Sabbatical Research, Biological Mass Spectrometry Lab, Univ. of Virginia 1993-1994
Learned the methods developed by Prof. D.F. Hunt and Dr. J. Shabanowitz for the sequencing of peptides and proteins at subpicomole levels.

MEMBERSHIP: American Chemical Society, American Society for Mass Spectrometry, American Association for the Advancement of Science

FORMAL RECOGNITION, AWARDS, COMMITTEES:

National Research Council/Naval Research Laboratory Research Associate - 1981 to 1983
NRL Invention Award - 1984
NRL Alan Berman Research Publication Award - 1986, 1990, 1993, 1994
Board of Directors of the ASMS - 1993 to 1995

RELEVANT TRAINING:

Radiation Safety Training	University of Virginia	April, 1996
Annual Safety Refresher Training	University of Virginia	February, 1997

REFERENCES, PUBLICATIONS, PRESENTATIONS: Available on request.

ATTACHMENT TO NRC FORM 313

ITEM 8. FACILITIES AND EQUIPMENT

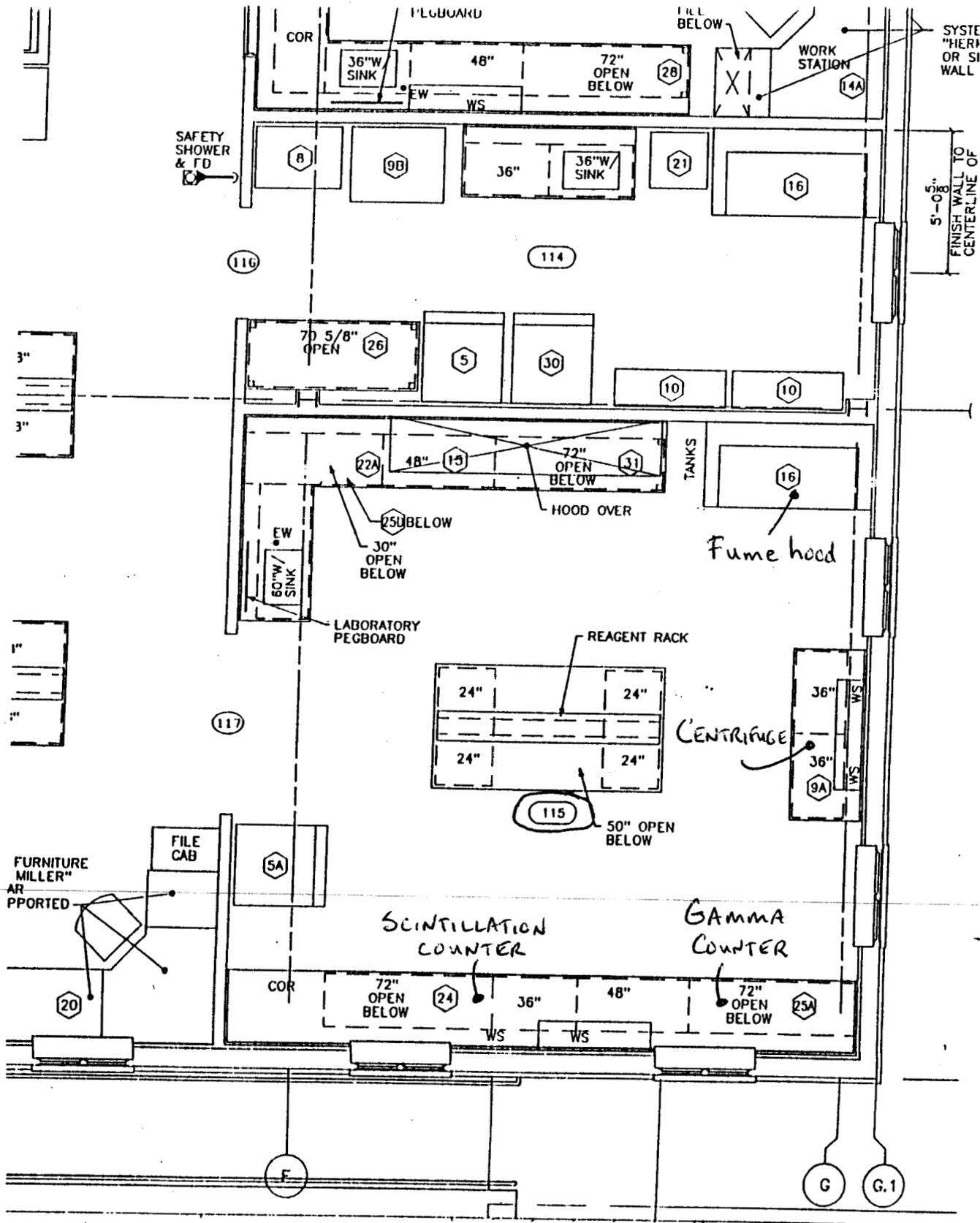
Description of Facilities and Equipment - Argonex Laboratory

<u>Room #</u>	<u>Room Name</u>	<u>Description and Equipment located therein</u>
101	Reception	Entrance for employees and visitors
102	Loading/unloading	Access through a service door for large deliveries
103	Bathroom	Women's bathroom
104	Bathroom	Men's bathroom
105	Utility room	Water heater, water backflow prevent valve, primary water purification, mop sink, telephone wire routing box
✓ 109	Washroom	Steam sterilizer, oven, dishwasher, double sink
✓ 110	Storage	Unrenovated, open storage space
✓ 111	Tissue culture	Cell growing: 2 laminar flow hoods, 3 incubators, 2 microscopes, centrifuge, freezer, refrigerator
113	Mass spectrometry	Analysis: 2 mass spectrometers, HPLC, fluorescence spectrometer, column building, microcentrifuge
114	General equipment	2 centrifuges, concentrator, freezer, refrigerator, fume hood, ice maker
✓ 115	Synthetic&isotopes	One half of the room: peptide synthesizer, HPLC, fume hood; second half: gamma counter, scintillation counter, centrifuge, freezer
116	General lab	General chemistry: 2 HPLCs, pH meter, balance, microbalance, spectrophotometer, 2 cold boxes, flow cytometer, microcentrifuge, computer work spaces across the front
118	Office	2 desks, meeting table

Radioactive materials will be used in Rooms 111 and 115 only, and stored for decay in Room 110.

Detail Map #5

ROOM 115





MICROSOFT AUTOMATED
Streets Plus

Argonex Laboratory
 (804) 984-2040; -1737 (fax)

ATTACHMENT TO NRC FORM 313

ITEM 10. RADIATION SAFETY PROGRAM

A. INTRODUCTION

Argonex Holdings, Inc. is a biotechnology company that is focused on the discovery and development of drugs to modulate the immune system response to a variety of diseases. The CEO of Argonex is Sheridan Snyder, the Chief Operating Officer is Ian Ratcliffe, and the administrative offices are located at 2044 India Road, Suite 202, Charlottesville, VA 22901. In January of 1997, Argonex acquired the rights to technology developed at the University of Virginia, in the laboratories of Professors Donald Hunt and Victor Engelhard. This acquisition has resulted in a new laboratory in Charlottesville, Virginia, where basic research in immunology and analytical chemistry will be performed and aimed at the identification of new peptide antigens that can be developed as drugs to stimulate the immune system against certain types of cancer.

The new laboratory, known in the company as ArgoLab, is located at 706 Forrest Street, Suite 1, Charlottesville, Virginia 22903. It is proposed that this facility be licensed by the Nuclear Regulatory Commission for possession of byproduct material for research and development (as defined by 10 CFR 30.4). No commercial distribution will be involved.

B. MANAGEMENT

Dr. Mark Ross is the director of the Argonex. Dr. Ross will supervise Dr. Kevin Hogan, Senior Immunologist, and Sam Cupp, Research Associate (chemist). Dr. Hogan will supervise Kristen Lekstrom, Research Associate (biologist). Dr. Jeffrey Shabanowitz (chemist) will work half-time at Argonex, while continuing his duties managing Professor Hunt's laboratory at the University of Virginia. University of Virginia Professors Hunt and Engelhard serve as consultants.

✓ A Radiation Safety Committee has been formed. This committee will meet at least four times each year to review licensed activities. The membership of the committee consists of Drs. Ross, Hogan, and Engelhard, and Mr. Dean M. Schlemmer (Office of Environmental Health and Safety, University of Virginia).

The primary users of radioactive material at Argonex will be Dr. Hogan and Kristen Lekstrom. Dr. Ross will be an infrequent user. Dr. Engelhard is an Authorized User of radioactive material at the University of Virginia.

The radiation safety program at Argonex is directed by the Argonex Radiation Safety Officer (RSO), Kevin T. Hogan, Ph.D., and the consulting Radiation Safety Officer (CRSO), Dean M. Schlemmer. The CRSO is a paid consultant who operates outside of the lines of authority of Argonex and reports to the Argonex Radiation Safety Committee and Argonex management. The CRSO will make reports on the status of the radiation protection program at least quarterly to the management of Argonex and the RSO. The CRSO will stay abreast of license conditions and applicable State and Federal regulations and will make written recommendations to management concerning any observed deficiencies or proposed changes in the radiation protection program. The management of Argonex will respond in writing to any recommendations by the CRSO concerning the radiation protection program. It is the responsibility of Argonex management to ensure that all activities at the Argonex laboratory facility meet the requirements of the NRC license.

C. SURVEY PROGRAM

Routine, systematic surveys shall be performed by Argonex employees and/or independent consultants in all areas where radioactive materials (RAM) are used or stored. Surveys will consist of radiation level measurements made with a suitably sensitive instrument and wipe tests measured with a liquid scintillation counter or gamma counter.

D. RECORDS MANAGEMENT SYSTEM

It will be the policy of Argonex to maintain all records pertaining to radioactive material use for an indefinite period of time. Records may be disposed of or destroyed only when authorized by the appropriate licensing authorities.

1. Personnel Dosimetry

Records of individual external dosimetry will be maintained in compliance with the provisions of 10 CFR; such records will be available to employees. A bioassay program will be established to monitor for intake of I-125 by personnel. This program will follow the guidance outlined in NRC Regulatory Guide 8.20.

2. Radioactive Material Inventory

Records will be maintained on all radioactive materials purchased or received by Argonex. These shall include at least the following:

- a. Identification of radionuclide
- b. Activity of radionuclide on a reference date
- c. Date of receipt of radionuclide

d. Ultimate disposition of radionuclide

Records of all radioactive waste disposed of by Argonex shall be maintained.

Inventory and waste records shall be coordinated in such a way as to continually account for the whereabouts of all radioactive materials received at Argonex, and to insure that the possession limits specified in the license are never exceeded.

3. Survey Records

All survey records shall be permanently maintained in a central location by Argonex personnel.

4. NRC Licensing Records

All NRC licenses, amendments and correspondence, and records of inspections, investigations, and follow ups shall be maintained in a central location by Argonex personnel.

E. SEALED SOURCE LEAK TEST PROCEDURES

No individual sealed source will be held in the possession of the licensee in a quantity requiring leak testing. Therefore, no leak test procedures are required at the time of this application.

F. ARGONEX RADIATION SAFETY DOCUMENTS

Included with this application is the Argonex Radiation Safety Guide. This describes the radiation safety program in more detail. This document will be issued to all personnel working with radioactive material or frequenting restricted areas at Argonex.

ATTACHMENT TO NRC FORM 313

ITEM 11. WASTE MANAGEMENT

INTRODUCTION

The disposal of all radioactive waste will be coordinated by the Radiation Safety Officer. No radioactive waste shall be disposed of in the ordinary trash. Radioactive waste may be disposed of by shipment to a licensed radioactive waste disposal company, by release to the sanitary sewer system or by decaying the waste in storage and disposing of it as normal trash.

Radioactive waste will be put in appropriately labeled containers. A running record of the contents of containers shall be maintained. When containers are full they will be packaged, labeled, and placed in storage for ultimate disposal. Filled waste containers will not be allowed to accumulate. The waste will be disposed of or packaged and labeled for ultimate disposal.

1. RADIOACTIVE WASTE CATEGORIES:

- a. Solid Waste
- b. Stock Vials
- c. Liquid Waste
- d. Scintillation Vials and Fluid
- e. Mixed Waste (hazardous and radioactive)

2. RADIOACTIVE WASTE DISPOSAL OPTIONS

a. Off-Site Shipment

Waste may be packaged and transferred to a licensed radioactive waste disposal broker for disposal by burial or other licensed disposal method.

b. Release into the Sanitary Sewerage

Radioactive liquid waste may be disposed of by release to the sanitary sewerage if the material is readily soluble and if the concentration of the release, when diluted with other releases from the Argonex facility, are below allowable levels. This concentration is determined by dividing the radioactivity released to the sewer in 1 month by the average

monthly volume of water release into the sewer. The concentration limits are specified in parts 20.2003 and Table 3 of Appendix B to Part 20 of 10CFR. The "sum of the fractions" calculation will be used when more than one radionuclide is released to the sewer. The total quantity of radioactive material that is released to the sanitary sewerage system in a year may not exceed 5 curies of H-3 and 1 curie of all other radioactive materials combined.

c. Decay in Storage

Radioactive waste may be held for decay in storage and disposed of as non-radioactive waste. Such waste must contain radionuclides with half-lives of less than 90 days and be held a minimum of 10 half-lives. Following the decay period, the waste will be monitored with an appropriately sensitive radiation detection system to verify that it is indistinguishable from background radiation levels. Any radioactive warning labels on the waste will be removed or defaced prior to disposal.

d. Scintillation Counting Media

Liquid scintillation counting medium may be disposed of without regard for its radioactivity if it contains only H-3 and the activity per gram of medium does not exceed 0.05 μCi .

3. RADIOACTIVE WASTE DISPOSAL RECORDS

Records of all radioactive material disposals will be maintained. Records will include the date of disposal, radionuclides disposed of, activities, volumes, physical form, disposal method, disposal broker (if used), dilution calculations and other associated documents such as shipping manifests.

ENCLOSURE

ARGONEX LABORATORY

"ARGOLAB"

RADIATION SAFETY GUIDE

Charlottesville, Virginia

June 17, 1997

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I. INTRODUCTION

The ARGONEX radiation safety program has been established to protect radioactive material (RAM) users, other individuals working at the ARGONEX facility, and the general public from unwarranted exposure to radiation. Uses of RAM are governed by and in accordance with Federal regulations and conditions specified in the ARGONEX RAM license issued by the Nuclear Regulatory Commission. Copies of ARGONEX's radioactive materials license and pertinent Federal regulations are available at the ARGONEX facility for review.

All persons working with RAM or frequenting RAM use areas at ARGONEX are required to read and be familiar with the contents of this Guide. The primary focus of the Guide is on regulatory requirements, personnel responsibilities, and general radiation safety rules and procedures. The contents of this Guide may be modified only with permission from the Radiation Safety Committee and only if such changes are in accordance with Federal regulations and ARGONEX RAM license conditions.

A. Organization

1. Radiation Safety Committee (RSC)

The RSC consists of the Radiation Safety Officer (RSO), the Consulting Radiation Safety Officer (CSRO), and RAM users selected by ARGONEX management. The RSC is responsible for developing radiation safety policy and insuring its implementation. The RSC reports to ARGONEX's Chief Operating Officer (Ian Ratcliffe).

2. Radiation Safety Officer (RSO)

The RSO is a full time employ of ARGONEX who is responsible for day-to-day oversight of radioactive material use. His responsibilities include:

- insuring compliance with Federal regulations and NRC license requirements
- issuing radiation dosimetry and maintaining dosimetry records
- managing radioactive waste disposal including shipments and releases to the sewer system
- managing routine laboratory radiation survey program
- managing the cleanup of spills of radioactive materials and other incidents involving radioactive materials
- managing radioactive material procurement and the inventory records system
- insuring that employees receive appropriate formal and on-the-job training
- insuring that employees receive appropriate annual retraining
- arranging annual radiation detection instrument calibration with the Consulting RSO or other licensed facility
- maintaining all required records including an up-to-date radioactive material facility inventory.

3. Consulting Radiation Safety Officer (CRSO)

The CRSO is a paid consultant who operates outside of ARGONEX's normal reporting chain. He is responsible to the RSC and ARGONEX's management. His responsibilities include:

- performing quarterly facility inspections
- reviewing radiation dosimetry records to insure that exposures are as low as reasonably achievable (ALARA)
- performing the NRC required annual radiation safety program review.
- consulting with the ARGONEX RSO, RSC and employees
- maintaining awareness of regulatory changes and assisting with compliance
- acting as liaison between ARGONEX and the NRC.

4. RAM Users

The responsibilities of users of radioactive material include:

- being familiar with and following radiation safety rules and regulations applicable to ARGONEX
- working with radioactive material in a safe manner
- maintaining radioactive material security
- wearing appropriate dosimetry when warranted
- performing radiation surveys during and after RAM uses
- cleanup of radioactive material spills or contamination and reporting them to the RSO
- appropriately packaging and labeling RAM waste for disposal

B. Radiation Dose Limits

Radioactive material use will be conducted in such a way as to insure occupational doses and doses to members of the general public are as low as is reasonably achievable (ALARA). Notwithstanding this philosophy, the following limits specified in the Code of Federal Regulations, Title 10, part 20, subpart B apply.

1. Adult annual limits.

The occupational dose limits for adults (individuals 18 years of age or older) are:

- An annual limit, which is the more limiting of:
 - a) 5 rem (0.05 sievert) total effective dose equivalent (TEDE)
 - b) 50 rem (0.5 sievert) total of deep dose equivalent and the committed dose equivalent to any organ or tissue other than the lens of the eye
- An annual limit to the lens of the eye of 15 rems (0.015 sievert).
- An annual limit to the skin or to any extremity of 50 rems (0.50 sievert)

These dose limits are in addition to background and medical radiation received by the worker.

2. Occupational Dose Limits for Minors

The annual dose limits for minors (individuals under 18 years of age) are 10% of those specified for adult workers.

3. Dose to an Embryo/Fetus

The dose to the embryo/fetus of a declared pregnant woman is limited to 0.5 rem during the entire pregnancy. A declared pregnant woman is defined by the NRC as a "woman who has voluntarily informed her employer, in writing, of her pregnancy" and the estimated date of conception. The dose to an embryo/fetus is the sum of the deep-dose equivalent to the declared pregnant woman and the dose from radionuclides in the embryo/fetus and in the declared pregnant woman.

All employees must read NRC Regulatory Guide 8.13, Instruction Concerning Prenatal Radiation Exposure (see Appendix B). Questions regarding the content of the guide may be addressed to the RSO and/or CRSO.

II. RADIOACTIVE MATERIAL USE

A. General

All radioactive material uses shall be conducted in accordance with the ARGONEX NRC license. This license specifically authorizes the use of the following radionuclides for the uses described. Specific descriptions for uses other than those listed below must be submitted to, and approved by, the Radiation Safety Committee prior to the start of such work.

1. Tritium (H-3)

Tritium will be used to measure cellular proliferation of cells by 3H-thymidine and as a labeled probe for mycoplasma. The mycoplasma probe is purchased in kit form. It will also be used for cell proliferation. Cells in 96-well microtiter plates are pulsed with 3H-thymidine (1 μ Ci/well) 12-18 hours prior to harvesting on fiber strips. Scintillation cocktail is then added to individual samples which are then counted by scintillation counting. The mycoplasma detection kit is used in accordance with manufacturers instructions and is prepackaged in accordance with 10CFR 31.11. Most assays will utilize 100-500 μ Ci. Occasional assays may utilize as much as 2 mCi.

2. Phosphorus 32 (P-32)

P-32 will be used for kinasing oligonucleotides for use experiments as probes in DNA and RNA blotting procedures. Oligonucleotides are end labeled using T4 DNA kinase. In some cases, the probe is separated from unincorporated label on an NENsorb[®] column. Generally 1-6 probes are labeled simultaneously and 150-200 μ Ci is used per probe.

3. Sulfur 35 (S-35)

S-35 will be used for DNA sequencing and protein labeling experiments. DNA sequencing is done by the dideoxy method using alpha 35SdATP. Polyacrylamide gels are then run to determine the

sequence. Protein labeling is done by incubating cells in methionine free media plus L-methionine(S-35). Following labeling, cells are detergent lysed and immune precipitated. The recovered protein is then run on polyacrylamide gels to determine what molecular species are present. 25-100 μCi are used for sequencing experiments. 10 μCi will be used for each labeling.

4. Chromium 51 (Cr-51)

Chromium 51 (Cr-51) will be used to measure cell death in 51Cr-release assays. Cells will be incubated in the presence of 100-200 μCi of sodium chromate (51Cr) for 1-3 hours. The cells are washed three times and added to microtiter plates as targets for cytotoxic T lymphocytes and natural killer cells. The amount of killing is quantitated by measuring the release of 51Cr into the supernatant by counting samples on a gamma counter. Generally 4-6 cell lines (but as many as 20) are labeled simultaneously.

5. Iodine 125 (I-125)

Iodine will be used for labeling antibodies for RIA procedures, peptides for use in peptide binding studies, and cell surface proteins. Labeling of antibody and peptides is done by standard iodogen procedure using 200 μCi per antibody. Cell surface protein labeling is done by lactoperoxidase labeling and utilized 1-5 mCi per cell line labeled. A hood will be used for all labeling experiments. Generally, only 1 antibody or peptide will be labeled at a time. Labeling will generally be performed using 100-200 μCi at a time.

B. Training

All users of radioactive material at ARGONEX must have appropriate training in the safe use of radioactive material. This can be obtained by attending either the University of Virginia Radiation Safety Training Course or another course which is equivalent in scope and content. Individuals requiring retraining can either attend one of the University of Virginia Annual Retraining sessions or receive instruction which is equivalent in scope and content. Prior to being permitted to work independently with radioactive material, personnel must discuss their proposed uses with the RSO and CRSO, and satisfy them that their knowledge of the ARGONEX rules and procedures is adequate. Additionally, supervised, on-the-job training will be required until a proficiency for working safely with radioactive material has been demonstrated.

C. Procurement, Receipt and Shipment

All radioactive material procurement and shipping shall be coordinated through the RSO and/or the CRSO. Materials received at ARGONEX must be logged in, surveyed for leakage or damage and added to the RAM inventory to insure that license possession limits are not exceeded. In accordance with 10 CFR 20.1906 ARGONEX personnel will monitor for radiation levels and radioactive contamination the external surface of each labeled package received. "Labeled" refers to a package with a Radioactive White I, Yellow II or Yellow III label. Any package known to contain radioactive material (labeled or not), which upon receipt, shows signs of degradation, such as dampness or crushing shall be monitored for radiation levels and radioactive contamination.

All radioactive material shipments from ARGONEX shall be in accordance with NRC and DOT regulations. Shipments must be documented and approved by the RSO and/or CRSO. Prior to

shipment of any radioactive material to a licensed recipient, ARGONEX must obtain and file the recipients NRC or Agreement State License documenting authorization to receive the type and form of radioactive material transferred.

ARGONEX personnel shall keep appropriate inventory records. Records should reflect all receipts, disposals and transfers out of the facility. Tracking records will also be maintained to document the location of all radioactive material (including waste) at the facility. These records shall be presented to the RSC at the regular meetings.

D. Personnel Monitoring

In accordance with 10 CFR 20.1502, ARGONEX will monitor the exposures to radioactive material and radiation of all personnel working in or frequenting rooms where radioactive, gamma ray-emitting and high energy beta particle emitting (P-32) radionuclides are used to demonstrate compliance with occupational dose limits. Evaluations of the need for personnel monitoring in areas where radioactive materials are stored will be made by the RSO and/or CRSO. A bioassay program to detect internal radiation exposures from ingested radionuclides is established in accordance with NRC Regulatory Guide 8.20, Applications of Bioassay for I-125 and I-131 (see Appendix A). Analysis of worker urine samples and external monitoring of I-125 levels in worker thyroids will be performed as required.

1. External Dosimetry

ARGONEX will use the dosimetry services of a NAVLAP approved radiation dosimetry vendor. All persons using I-125, P-32 or Cr-51, or frequenting rooms where these radionuclides are used, shall be issued and will wear dosimeters if there is the potential that their exposures may exceed 10% of their occupational limits. The type of dosimeter used and the frequency of the dosimeter reading will be determined by the RSO and/or CRSO.

2. Bioassay Program

Persons using I-125 at activity levels and in manners described in the table are required to participate in the bioassay program. A baseline thyroid bioassay will be performed prior to beginning work. Users of I-125 must inform the RSO following such uses so that a thyroid uptake measurement can be arranged. Bioassays will also be performed in the event of an accident where the likelihood of radiouclide ingestion exists.

TYPE OF OPERATION	ACTIVITY HANDLED IN UNSEALED FORM MAKING BIOASSAY NECESSARY	
	Volatile or Dispersible Form	Bound to Nonvolatile Agent
Open use / Bench top	0.1mCi	1.0mCi
Use in certified fume hood	1.0mCi	10.0mCi

E. General Rules and Guidelines

1. Security of Radioactive Material

Radioactive material security is very important to protect from theft or misuse of radioactive material, and to limit unwarranted radiation exposure to the public. The NRC requires that ARGONEX “secure from unauthorized removal or access licensed materials that are stored in controlled or unrestricted areas”. Access to the ARGONEX facility shall be controlled by keeping all doors locked or posting a receptionist at any entrance which is not kept locked. Any suspected loss of radioactive material must be reported to the RSO immediately.

2. Posting and Labeling Requirements

Each area or room in which radioactive materials are used or stored must be conspicuously posted with a sign or signs bearing the radiation symbol and the words “CAUTION RADIOACTIVE MATERIAL(S)”. Additionally, postings are required for “Radiation Areas” (5 millirem per hour at 30 centimeters) and “High Radiation Areas” (100 millirem per hour at 30 centimeters). Individuals should consult with the RSO and/or CRSO should radiation levels above 5 millirem per hour at 30 centimeters exist.

Radioactive material containers (including waste containers) and storage units must also be posted with “Caution Radioactive Material” labels. Labels should provide sufficient information (such as the radionuclide(s) present, and an estimate of the quantity of radioactivity, the date for which the activity is estimated, radiation levels, and kinds of materials to permit individuals handling or using the containers, or working in the vicinity of the containers, to take precautions to avoid or minimize exposures. Equipment and items contaminated with radioactive material must be labeled.

3. Surveys of Work Areas

Radiation surveys of areas where radioactive materials are used should be performed after each use. It is good laboratory practice to survey work areas immediately following use or at the end of a day when radioactive material is used continually. Surveys must be performed immediately following a spill where the potential for radioactive material contamination exists. Complete documentation of radiation surveys by users is required at least weekly when radioactive materials are used. Additionally, the CRSO will perform a survey of the ARGONEX facility quarterly and present the findings of these surveys to the RSC.

Weekly, documented radiation surveys shall be performed using both a portable thin-window Geiger-Mueller (GM) type instrument (except for H-3, which cannot be detected by a GM) and wipe tests. Wipe tests of surfaces and floors will be performed and analyzed using either a liquid scintillation counter (LSC) or gamma counter. The GM instrument(s) shall be calibrated annually by the CRSO or other licensed instrument calibration company. Operation tests of the GM should be performed prior to each use. Documentation of proper GM operation (Op Check) will be performed and documented quarterly by the CRSO. Quality assurance checks should be performed on the LSC and gamma counter by counting background and standard samples routinely. The results should be recorded at least monthly.

4. General Laboratory Safety Practices

- Wear laboratory coats and gloves when working with or around radioactive materials.
- Wear appropriate dosimetry when required. Store dosimetry devices in a low background area when not in use.
- Never pipette by mouth.
- Do not smoke, eat, drink, or store food in radioactive material use areas.
- Work with radioactive material on a washable tray or other protected surface.
- Use volatile I-125 only in a fume hood.
- Arrange, in advance, to have thyroid bioassays performed following iodination procedures.
- Wash hands after using radioactive material.
- Report all spills to the RSO as soon as possible; begin decontamination procedures immediately.
- Put all potentially contaminated items into an appropriate radioactive waste container.
- Deface all radioactive symbols from clean items to be disposed of in ordinary trash.
- Clean, survey, verify free of contamination, and remove all labels from items to be released as non-radioactive.

5. Minimization of Radiation Exposure

Users of radioactive material should keep exposures to radiation and radioactive material at a minimum. Methods to employ to accomplish this goal are:

- Store radioactive material and waste in appropriately shielded containers or locations.
- limit time of exposure to radioactive material
- maintain safe distances from radioactive material. Use handling tools to manipulate vials containing large amounts of P-32, Cr-51 and I-125.
- use appropriate shielding when working with radioactive material. Use lead or other dense materials to shield Cr-51 and I-125. Use lucite or other low density material to shield P-32. If P-32 beta particles generate x-rays (bremsstrahlung) which require further shielding, add a layer of lead to the outer surface of the lucite. (Consult with the RSO or CRSO prior to using lead as a shielding material for P-32.) No shielding is necessary for low energy beta particle emitters such as C-14, S-35 and H-3.

F. Radioactive Waste

The disposal of radioactive waste will be coordinated by the RSO. No radioactive waste shall be disposed of in the ordinary trash. Radioactive waste may be disposed of either by shipment to a licensed radioactive waste disposal company, by release to the sanitary sewer system, or by decaying the waste in storage and disposing of it as normal trash.

Radioactive waste must be put into appropriately labeled containers. Do not mix different radionuclides or physical forms in the same container without the approval of the RSO. A running record of the contents of each container shall be maintained. When containers are full they should be sealed and then placed in storage for ultimate disposal. Filled waste containers should not be allowed to accumulate.

1. Radioactive Waste Categories:

a. Solid Waste

- Solid waste consists of dry paper, glass, plastic, metal, etc.
- Contaminated sharps, such as needles, razor blades, and sharp pipettes, should be placed in specially designed puncture-resistant containers.

b. Stock Vials

- Waste stock vials containing high activities should be collected in separate containers from all other waste types.
- Radiation exposure from waste stock vial containers should be monitored and shielded if necessary.

c. Liquid Waste

- Pour liquid waste into appropriate containers using a funnel.
- Do not fill containers completely.
- Keep the cap on the container when not adding waste.
- Store the funnel on a protected or washable surface.
- Keep iodination waste in a separate container and store in a fume hood.

d. Scintillation Vials and Fluid

- Use environmentally safe (aqueous-based) scintillation fluid.
- Waste scintillation vials may be collected in trays or in appropriate containers.
- Containers used for the collection of vials should be suitable to collect leaking fluid.

e. Mixed Waste (hazardous and radioactive)

- Radioactive waste containing hazardous chemicals cannot be mixed with other wastes.
- Prior to generating mixed waste, the users should consult with the RSO so that disposal methods can be planned.
- Minimize the volume of mixed waste created since disposal options may not currently exist or may be very expensive.

2. Radioactive Waste Disposal Options

a. Off Site Shipment

Waste may be packaged and transferred to a licensed radioactive waste disposal broker for disposal by burial or other licensed disposal method.

b. Release to the Sanitary Sewerage

Radioactive liquid waste may be disposed of by release to the sanitary sewerage if the material is readily soluble and if the concentration of the release when diluted with other releases from the ARGONEX facility are below allowable levels. This concentration is arrived at by dividing the

radioactivity released to the sewer in 1 month by the average monthly volume of water release into the sewer. The concentration limits are specified in parts 20.2001-20.2402 of 10 CFR, appendix B, table 3. The "sum of the fractions" calculation will be used when more than one radionuclide is released to the sewer. The total quantity of radioactive material that is released to the sanitary sewer system in a year may not exceed 5 curies of H-3 and 1 curie of all other radioactive materials combined.

Releases to the sewer system of collected liquid wastes must be approved by the RSO prior to release. Calculations to verify compliance with release limits must be performed prior to release.

c. Decay in Storage

Radioactive waste may be held for decay in storage and disposed of as non-radioactive waste. Such waste must contain radionuclides with half-lives of less than 90 days and be held a minimum of 10 half-lives. Following the decay time the waste must be monitored with an appropriately sensitive radiation detection system and found to be indistinguishable from background radiation levels. Any radioactive warning labels on the waste must be removed or defaced prior to disposal.

d. Scintillation Counting Media

Liquid scintillation counting medium may be disposed of without regard for its radioactivity if it contains only H-3 and the activity per gram of medium does not exceed 0.05 μCi .

3. Waste Disposal Records

Records of all radioactive material disposals must be maintained. Records should include the date of disposal, radionuclides disposed of, activities, volumes, disposal method, disposal broker (if used), dilution calculations and other associated documents such as shipping manifests. Waste disposal should be documented in inventory records.

III. EMERGENCY PROCEDURES

A. General

In cases of emergencies involving radioactive material, attention to the medical needs of injured persons takes precedence over radiological concerns. All individuals involved in administering first aid and emergency medicine must be notified of the potential for contamination. Precautions to prevent the spread of contamination may be taken provided that the medical needs of injured persons are not compromised.

In the absence of injury, or after injured persons have been attended to, the goals of radiological emergency response actions are to:

- Limit exposures to radiation and radioactive material.
- Limit the spread of contamination.

To accomplish these goals, emergency actions should be to:

- Control access to all potentially contaminated areas.

- Notify other building occupants of the emergency
- Turn off building ventilation when there is the possibility of airborne contamination.
- Use absorbent materials to contain a spill.
- Seek assistance from the RSO in evaluating the extent of the emergency and in planning cleanup.

B. Radiological Accidents Involving Injury

1. Call 911 and inform the operator if radioactive materials are involved.
2. Notify the RSO as soon as possible.
3. Inform rescue squad of potential for contamination.
4. Make a record of the radionuclides and activities involved in the accident.
5. Refer to section C. below for further actions to take.

C. Radioactive Material Spills

If a radioactive material spill occurs, common sense should dictate which of the following steps should be taken and in which order they should be followed. Decisions should be based on the radionuclide involved, volatility, activity, chemical form, volume, and the potential for personnel contamination. If in doubt, seek assistance from the RSO, the laboratory supervisor, or a co-worker.

1. Alert others in the vicinity of the spill.
2. Seek the assistance of the RSO if he is available.
3. Provided there is no potential for their contamination, ask individuals not involved with the spill or its cleanup to leave the area.
4. Prevent non-essential personnel from entering the area.
5. Check individuals near the spill for contamination.
6. Contaminated persons should take precautions not to spread contamination (especially if it is found on shoes).
7. Remove, bag, and label any contaminated clothing.
8. Confine the spill using paper towels or other absorbent materials.
9. Take care not to use a containment or cleaning material which will react with the spilled material.
10. Disperse charcoal onto volatile iodine spills.
11. Carefully dampen spills of powders.
12. Turn off building ventilation when there is the possibility of airborne contamination.
13. Notify the RSO and seek assistance or guidance in spill cleanup.
14. Perform and document surveys to ensure successful cleanup.
15. Document the details of the spill, persons involved, decontamination activities, and measures to prevent future incidents.
16. Seek guidance from the RSO and/or CRSO in determining the need to perform bioassays.

1. Personnel Contamination

If an individual becomes contaminated on the surface of the skin, decontamination should be performed as soon as possible. Removal of skin contamination should begin with the least abrasive method, as vigorous attempts to decontaminate increases the chances of absorption. Surveys of the

surface of the affected area should be performed after successive washes. Repeated cleaning using mild techniques, such as with a soft brush, soap, and warm water, is better than one intensive effort. Consult with the RSO if contamination is not readily removable with mild techniques.

IV. APPENDICES

- A. NRC Regulatory Guide 8.20, Applications of Bioassay for I-125 and I-131
- B. NRC Regulatory Guide 8.13, Instruction Concerning Prenatal Radiation Exposure